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In this issue of the Journal, a patient describes her experiences in an Omani hospital and her encounter with the health care teams, after a road traffic accident. Every road traffic crash like hers or so many others should raise the question of whether we are doing enough for our community to prevent road traffic crashes, reduce the injuries and death that result from these accidents, and reduce the long term negative impact on the victims and their families. Have you ever answered the mobile phone while driving? Have you ever neglected to fasten your seatbelt? Have you read your email in your phone or sent an SMS while driving or waiting at a traffic light? Have you ever accelerated to go through a yellow light? Have you exceeded 120 km an hour on the highway? If you have answered “yes” to any of these questions, you are a part of the problem!

According to the Royal Oman Police (ROP) website, there were 119 road traffic accidents in just the first week of this year resulting in 13 deaths and 141 injured, and those statistics are not unusual. In the first 11 months of 2009, there were 369 traffic accidents simply as a result of dangerous overtaking alone, resulting in 156 deaths and 881 injuries. In the first 10 months of 2009, a total of 810 people died and 8,325 were injured on the road. The Oman Tribune newspaper, in quoting these figures from the ROP, pointed out that this “means more than 20 people were killed and injured on the roads everyday” in Oman.

To further highlight the current interest in this problem, there was recently a two-day workshop on Road Safety Research, organised jointly by The Research Council (TRC) and the ROP in Muscat. The TRC plans to invite research proposals on road safety and give scholarships to postgraduate students willing to participate in this research effort. At the workshop, TRC invited experts from various parts of the world to discuss the optimal research topics that can be suggested to researchers in Oman. His Majesty Sultan Qaboos Bin Said’s words were received with all seriousness by TRC. During his Royal Tour last year, His Majesty said: “What is happening on our roads should be of everybody’s concern. Misuse of vehicles of different categories by different people causing many deaths is an irritating and worrisome phenomenon.” When a breadwinner loses his life or ability to earn, the burden on the family is beyond the easy understanding of those who are either comfortably well off or have never been affected by the road traffic crash disease. The orphans and the widows are the real victims of this burden. Oman ranks 5th in the list of countries with the highest road accident rates in the world according to WHO statistics as quoted by Oman Tribune on 24th February 2010. It is disturbing that the number of road traffic casualties in Oman is rising, while it is falling in many developed countries such as Great Britain. In Britain, total casualties fell by 3% between 2004 and 2005, and they have been declining ever since, while pedestrian deaths are at a 40-year low. Norway, Sweden and Australia have all halved or better than halved their road deaths between 1970 and 2000, and seen further...
Life Loss and Disability from Traffic Accidents
It is imperative we all act now.

In comparison, Oman had 681 road deaths in 2006, 798 in 2007, 951 in 2008 and estimated between 1000 and 1100 in 2009 with approximately 50,000 injured in 2009. Most of the developed countries with these declining death rates have been using the Haddon’s Matrix since William Haddon developed it in 1970. Haddon’s Matrix analyses injury by looking at certain factors which when simplified are “Host or Road User Factors, Vector or Vehicle Factors, Physical or Road Factors, and Socio-economic Environmental Factors” in the horizontal axis of the matrix and “Pre-Event (Crash), during Event and Post-event” in the vertical axis. It should be appreciated that currently the ROP is taking a lot of steps to reduce traffic fatalities, but we still need much more. The fatality rate in Oman has now reached 30 per 100,000 people and 127 per 100,000 vehicles and 111 per 100,000 licensed drivers, compared to 14 and 17 and 21 respectively for the USA. We definitely need more initiatives from the ROP, from non-governmental organizations (NGOs) and from all of us individual drivers who can play a dramatic role in reducing the death rate if we make more individual and concerted efforts. To do this we need more road safety education for the public. We need more road safety education in the media both on TV and radio programmes than currently. We need them in both Arabic and English because many of the accidents that occur in Oman are caused by people who do not speak Arabic. Better road safety education in Oman is not only needed for adults but also for pre-license age groups, and this should be a priority in conjunction with speed management. We need to work harder at changing driver behaviour and attitudes towards the risks associated with high speed.

The world’s first road traffic death involving a motor vehicle is alleged to have occurred on 31st of August 1896. The coroner at that time is reported to have said, “This must never happen again.” We need to ensure that Oman goes on record as working towards seeing that that coroner’s words come true here.

It is very disheartening to drive on the roads of Oman and see children, unsecured by seat belts, freely moving about in cars and even jumping up and down. We see mothers driving with their baby sitting on their lap. The baby is a good shield for the mother in case of an accident, but is that what the mother really wants? We need more vigorous education of such parents. We need to work at eliminating such practices mainly through education, but when necessary, appropriate penalties.

Another major problem we are having in Oman is talking on the telephone while driving. This is a cause of numerous accidents. Worse than talking on the phone is sending text messages (SMS & MMS) while driving. A study carried at Monash University Accident Research Center in Melbourne, Australia, has shown that text messaging results in more than double the risk of crashing than talking.
on the cell phone. They recommend more effective road safety measures to prevent and mitigate the adverse effects of the cell phone.

Road safety is currently one of the top priority subjects that are discussed in different countries and by various world organisations, and so should it be also in Oman. On 10 March 2010, the UN General Assembly is scheduled to discuss a new resolution on road safety. This Resolution is sponsored by the government of the Russian Federation, and it is based on the “Moscow Declaration” which was declared at the First Global Ministerial Conference on Road Safety held in Russia on 19–20 November 2009. At that Conference, there were as many as 1,500 participants, including senior ministers of several countries and representatives of UN Agencies. The participants declared 2011 to 2020 as a “A Decade of Action for Road Safety”. It became clear at that Global Conference that the statistics for road traffic crashes are much worse than initially thought. And indeed, it further confirmed the much higher incidence of deaths and injuries from road traffic accidents in developing and poor countries. The key components of the initiative for the Decade would include governmental technical assistance; road traffic education; road safety curriculum development; helmets for kids; safe routes to school; research and evaluation and setting up non-profit helmet assembly plants that employ the physically disabled.

The Moscow Declaration that resulted from that meeting in November 2009 acknowledged the roles played by the WHO, the World Bank, and the United Nations Road Safety Collaboration. They also acknowledged that road traffic injuries are major public health problem leading to more than 1.2 million deaths a year and as many as 50 million injuries or disabilities a year, and confirmed road traffic crashes as the leading cause of death among children and young adult between age 5 and 29. The Moscow Declaration also showed concern that more than 90% of road traffic accidents occur in low-income and middle-income countries. The annual cost of these deaths and injuries run to over US $65 billion. The Declaration was convinced that by year 2020, without appropriate action, road traffic deaths will become one of the leading causes of death in low-income and middle-income countries.

The Conference invited the UN General Assembly also to declare the decade 2011-2020 as “Decade of Action for Road Safety” with a goal to stabilise and then reduce the forecast of global road deaths by 2020. They declared an 11-point resolution that covered all the necessary points related to road traffic accidents from encouragement of collaboration, to improving national data collection, and strengthening of the provision of free hospitals and hospital trauma care. The Declaration also suggested adopting a standard definition of “road death” as, “a person killed immediately or dying within 30 days as a result of road traffic crash”, to facilitate data collection and international cooperation.

The Moscow Declaration stimulated the formation of several NGOs as well as inspiring many individuals and organisations to act to reduce road crash deaths and injuries. They asked the international donor community to provide additional funding in support of global, regional, and country road safety particularly in low and middle-income countries. Michael Bloomberg committed US $125 Million to reduce deaths and injuries on world roads. In conjunction with this First Global Ministerial Conference on Road Safety, the Asia Injury Prevention Foundation (AIPF) also launched a global helmet vaccine initiative in Moscow. Seven multilateral development banks (MDBs) issued a statement in November 2009 outlining a broad package of measures that each would implement in order to reduce the alarming rise in number of fatalities and casualties in developing countries. The participating MDBs included the African Development Bank, the Asia Development Bank, the European Bank for Reconstruction and Development, the Islamic Development Bank and the World Bank. They are committed to taking leading role in addressing this problem. They stressed the need for a systematic and multi-sectorial response to improving road infrastructure, vehicles and positively influencing road-users as well as enhancing post-crash services. In other words, they are determined to address all the elements of road safety [Figure 1] with their shared approach. If nothing is done, road traffic accidents will become the third highest cause of death worldwide by the end of this decade.

All nations need to be more active in road safety, particularly the low-income and the middle-income nations. All nations need to implement the basic
Life Loss and Disability from Traffic Accidents

It is imperative we all act now

Three Pillars of Road Safety, namely Infrastructure, Safe Vehicles, and Road User Behaviour [Figure 2].

In addition, as the framework for the decade of action declared, there are two additional pillars, namely Road Safety Management and the Post-Crash Care. Thus there are Five Pillars that need to be given much more attention to save lives.

In Oman, by far the commonest cause of road deaths is excessive speed which caused 57% of all deaths in 2007; overtaking comes next followed by drivers’ neglect and then improper acts by drivers and vehicle condition. Thus 4 out of top 5 causes of death in Oman are road user error, and they constituted 89% of the causes of road deaths in 2007. This does not include other road user related factors such as tiredness and alcohol, which constitute a total of only 2% of causes of road deaths in Oman.

We need to do much more in Oman. TRC and ROP have already started doing something for Oman and kudos to them. At the recent workshop, they discussed to varying degrees all the Five Pillars of Road Safety. The main objectives of that workshop were to create public and media awareness regarding the objectives of TRC research programmes on road safety. The international experts who attended exchanged knowledge, views, ideas, and research experience on road safety. The workshop discussed the documentation of social and economic cost; legislation and social policy and programmes; social and human behavioural causes of RTA; the social impact of traffic incidents and the role of the family; the effectiveness of awareness programmes; legal and compliance issues; analysis of crashes and trauma care. At the workshop, it was preferred to replace the word “accident” with the current terms in vogue: “collision” and “crash”. The Workshop dissected the post-crash services in Oman and pointed out major discrepancies in the care that exist in the different regions of Oman. This naturally has a major impact on the health outcomes of Omani victims of road crashes. The pathways of care and the disparities of emergency care in different regions of Oman need to be urgently standardised. We all need to take His Majesty’s words on road traffic accidents and injuries more seriously.

Globally, more than half of the total accidents involve drivers aged 15–44 years, and 73% of them are males, according to the World’s Worst Drivers.

The WHO reports that currently the number of deaths is approximately 1.4 million, which means that more than 3,000 people die on the world’s road everyday. In addition, 400,000 young people under the age of 25 are killed on road traffic crash every year, namely 1,049 youngsters everyday. Most of these traffic deaths occur in low and middle income countries, particularly among pedestrian cyclists, motorcyclists and those using public transportation according to WHO archives.

Hazen, from the School of Public Health in Alabama, USA, has written that road traffic injuries are leading cause of morbidity, disability and mortality in less developed countries, quoting the figure of >85% of the 1.2 million deaths in 2006 (new figures now show up to 1.4 million deaths per annum) with 10 times that figure in injuries. He points out that road traffic injuries will rank third of all major causes of morbidity and mortality globally by 2020. He also indicates that often many of these are preventable, and the technology and the knowledge to achieve success do exist. In this review article, he highlights the problem and the contributing factors as well as the possible actions to be taken, especially the interventions that have proven effective in industrialised nations, many of which have not yet been adopted in less developed countries.

Basically, what we need to do in Oman is what the ROP and TRC have started to do, but we all have to participate and we have to be much more vigorous. We have to address all the Five Pillars mentioned above and follow the activities of the UN Road Safety Collaboration, which are a part of the Decade of Action for Road Safety. Oman has to join the Decade of Action for Road Safety! We have to be advocates for road safety at the highest governmental levels, increase awareness of risk factors and run activities such as the Road Safety Week and Annual Remembrance Day of Prayers for victims of road traffic and support the NGO initiatives. We need to adopt the Safe System Approach [Figure 1] and the Road Safety Strategy “Towards Zero”. We also need to provide guidance to the public for good practice such as seatbelts for front and back passengers; mandatory car seats and secure booster seats for children, and other vital actions. We have to be more vigorous in the provision of general road safety education through bilingual audio and visual media as discussed above. Relevant research, cost-effective intervention and knowledge management must be combined with
the will and determination to develop the Science and Art of better Road Safety. We should all see the necessity and urgency of participating passionately and zealously in this effort.

References

IN THE PAST SEVERAL DECADES, THERE HAS been an incredible increase in the privatisation of medical education with rapid expansion in the number of private medical schools. This trend has had widespread implications globally and influenced medical educational policies all over the world.

Privatisation is the act of reducing the role of government or increasing the role of the private institutions of society in satisfying people’s needs; it means relying more on the private sector and less on government.1 Hence the privatisation of medical education can be defined as “Medical Education being imparted by an organization which is not a part of the government bureaucracy.” Private medical schools can be totally autonomous or partially autonomous (controlled at various levels and in various degrees by government). They can be profit-generating institutions (revenues which enrich one individual or a consortium) or non-profit institutions which are more society centered. This article is essentially based on print and electronic data available from the World Directory of Medical Schools published by WHO,2 the International Medical Education directory maintained by Foundation for Advancement of International Medical Education and Research and medical literature.3

GLOBAL NATURE OF THE TREND: EXAMPLES

There has been a worldwide boom in private medical education. India tops the list with the largest numbers of medical schools within one country (271). Out of these about 137 are privately owned institutions.4,5,6 Next comes the United States with 62 private institutions out of a total of 131 medical schools.7 American private universities are heavily supported by government research grants and usually are non-profit institutions.8 In Asia, there are 79 medical schools in Japan, with 50 governmental and 29 private colleges.9 Other countries like Malaysia (11 private institutions),10 Thailand,3 and the Philippines 3 have also ventured heavily into private medical education. In Europe, the United Kingdom, with a total of 44 medical schools, private medical education is a relatively new entrant with only one private school, the University of Buckingham Medical School.3,11,12 Similarly, Germany also has only one private school out of a total of 36.13 Medical education in Greece14 (seven medical schools ) and the Netherlands (eight medical schools)15 is fully government funded, while Spain has only two private institutions out of a total of 28.16 In the Oceania region, Australia has 19 medical colleges with only two being private medical universities.3,16 New Zealand has two schools, both of which are government funded.18 The Pacific islands have 6 schools, most of which are private.3,16 Recently there has been a spurt of private medical colleges in the Caribbean region.
Many of these 56 schools are private institutions which have become alternate destinations for aspiring American and Canadian students. In South America, Chile has a total of 60 schools, 35 of them private, while in Africa, Nigeria has only 2 private medical colleges out of a total of 34 schools whereas Sudan has eight. In the Gulf Cooperative Council countries (GCC countries), there are a total of 32 medical colleges. Yemen has four private medical colleges, the United Arab Emirates (UAE) has three and Bahrain has two. Saudi Arabia, Qatar and Oman have one private medical college each. Kuwait has no private medical college. However, in countries like China, France, South Africa and Canada medical training is under the full control of the state.

**Forces bringing about the Trend**

The reasons for the sudden increase in private medical schools are manifold. On the one hand, in many developing countries, due to the population explosion, the demand for places at medical schools is greater than the available supply. In addition, governments are unable to meet the medical needs of society due to both economic constraints and limited infrastructure. On the other hand, the booming private sector economy means more aspirants from the expanding middle class are entering the medical field. This increase of wealth amongst a subset of society has led to a differential growth of private medical schools in the richer and healthier states/countries. In the developed countries, the emergence of new private schools has been driven by workforce shortages. The demands of the population for increased use of recent technological advances in medicine as well as higher average life spans has increased the requirement for medical services in these countries.

Globalisation has resulted in an increased demand for medical professionals from foreign countries (outsourcing). This lure of increased income has led to more entrants into health professions. This enhanced need for medical schools is fulfilled by private medical schools. Indian physicians form the bulk of foreign trained physician in all the major five developed countries (UK, US, Canada, Australia and New Zealand) and this correlates with the fact that India has the greatest number of private medical institutions in the world.

India has also become the leading country promoting ‘medical tourism’. A similar situation can also be found in countries like Malaysia and Thailand which advertise cheaper medical care to foreign patients. This lucrative demand for exported medical services may be instrumental in the mushrooming of private medical colleges in India and Malaysia.

Changes in government policies in many countries have resulted in the climate being more conducive to privatisation. In India, relaxed regulations resulted in a growth spurt in private medical colleges in the mid-1980s. Political leaders and businessmen found new avenues to make large earnings from private medical schools in the form of high tuition fees. Many regional governments want to appease their electorate from different caste and ethnic groups. Hence they also support the opening of private medical schools by specific minority and ethnic groups.

Total or partial lack of medical education facilities in some countries (Eritrea, Somalia, Namibia, Botswana) or stringent admission criteria (USA, Canada) may have resulted in the residents of these countries going to other countries for their medical education.

**Advantages of Privatisation**

More medical schools, whether private or public, can meet the need of an ever expanding population and have the potential of enhancing access to health care for all sections of society. There is a strong relationship between the number of medical schools and physician density; hence, more medical schools in low density areas will certainly increase the physician density. The dependency of the local population on expatriate doctors can also be reduced and the health care needs of the local population can be adequately catered for.

More medical schools (public or private) will also create more job opportunities for everyone. There will be a healthy competition between the private and public medical institutions benefiting the prospective job candidate. Chances of improvements in the government-run colleges will be greater so as to ‘keep up’ with the private sector. The monopoly in medical education by government-
run institutions will be substantially reduced, as alternatives become available for students, faculty and the community.

A further advantage is that, with privatisation, medical education will not be dependent on policies driven by political scenarios and could eventually become the sole responsibility of various private medical institutions. In some private medical colleges, with sound financial backing, up to date facilities and technology can reach the students faster than in government colleges. There will be no “red tape” involved as far as infrastructure and facilities are concerned.

Disadvantages of Privatisation

Usually, the primary intention of the trusts/agencies running the profit generating medical colleges is to earn money through a business venture. This is typically the yardstick against which all decisions regarding the institution are made. The common factor in all the private medical colleges around the globe is that they are more expensive than the public medical schools. Medical education has become costlier over time and the burden of debt on medical school graduates increases due to the high tuition fees in private medical schools.5,33,34

The quality of students entering programmes in private institutions is more often dependent on their paying capacity rather than their merit. Some institutions do insist on minimum standards of admissions, but these standards are definitely below those required by state-owned schools. Hence the quality of the doctors coming out of these institutions is likely to be compromised.35

The quality of training provided in private medical colleges is also questionable.35,36 Major problems facing the private medical colleges are poor staffing, poor quality of training and high student /teacher ratios. The staff frequently lack proper training in medical education.36 Many of the faculty work in these colleges on a part-time basis, or are appointed only for the purpose of accreditation (short term appointments). In some countries, the increased demand for teaching faculty is met by faculty with dual appointments.36,37 Deficiencies in physical infrastructure with a shortage of equipment, laboratories, cadavers or prospected specimens and chemicals are also rampant.34

There is also a reduced availability of patients for clinical teaching in private medical schools. This is because the number of in-patients in the private hospitals of richer countries tends to be less due to their reduced length of stay, sicker patients avoid examinations by students, and an admission of increasing number of elderly patients who are in no condition to give a history due to cognitive impairment.38 Scarcity of “clinical material” in private medical colleges in the poorer developing countries is due to the lack of patient paying capacity as the private hospitals are much costlier than the government-run hospitals.6

It has been observed that government support has always helped to improve the quality of education, in particular by covering the increases in costs as laboratory science has evolved. This means that “When government support declines, so too do intellectual standards.”39

Many newly formed private colleges are not accredited by the national accreditation body. Accreditation is a quality control measure for maintaining high standards of medical education and of health care for the nation. It also instills public confidence in medical schools and ensures that graduates’ competencies comply with national standards.40 The absence of accreditation for some of these private medical colleges will result in a questionable future for their graduates as their qualifications may not be nationally and internationally recognised.

A further disadvantage of privatisation is that there is a lack of social and racial diversity in private institutions. Their medical students usually come from privileged backgrounds.34,29,41 Also with an increase in tuition fees there will be a further rise in the socioeconomic status of these students.42,43 As a result of the high tuition fees, under-represented minority groups will have restricted access to medical education. Racial diversity among health professionals results in better communication and improved health care delivery for ethnic minority patients; formation of a culturally competent health care workforce; maintenance of high quality of medical education and increased medical and public health research.44,45 This lack of racial and socioeconomic diversity in private medical colleges will, in the long run, affect patient care.

Most of the private institutions are set up in richer and healthier states or regions with a higher
ratio of medical school admissions to population.\textsuperscript{5,6,27} Medical students from rural areas are more likely to practice in rural areas than those from urban upbringings.\textsuperscript{4,6,7} Hence these factors will result in a misdistribution of doctors and resources and favour urban over rural areas.

More medical colleges will result in an anticipated oversupply and misdistribution with too many new doctors entering the medical profession. This will result in a future lack of job opportunities for fresh graduates. Already in Malaysia, there has been a ban on opening any more private medical colleges due to the projected excess of doctors.\textsuperscript{10}

Some private medical schools isolate medical education from the health care system, as they are exclusively an educational industry. All the immigrant medical students in these schools are obligated to go to their home country after education. In fact, the whole purpose of many of the newly opened medical schools (in the Caribbean Islands, for example) is to produce doctors for the USA or Canada.\textsuperscript{4,10,31}

### Guidelines for Privatisation of Medical Education

The deficiencies found in private medical colleges can be removed if there is stringent monitoring and enforcing of international standards by government and health agencies. Fees should be standardised and more stringent entry criteria should be imposed for candidates so that the quality of the graduates does not suffer.

To ensure availability of patients for clinical teaching, medical schools with no training hospitals or inadequate clinical materials should be required to sign memoranda of understanding with teaching hospitals, general practice clinics, and private hospitals. Private universities can become community-based medical schools, with the majority of students’ exposure to patients in the community rather than in hospitals.\textsuperscript{17} Multidisciplinary clinical skills laboratories can help the students learn basic clinical skills in simulated environments using models and simulators, simulated patients, and standardised patients.\textsuperscript{38}

Mandatory accreditation should be introduced and non-compliant institutions should be placed on probation with their student enrollment suspended or accreditation withdrawn. In fact, with the mobility of the health professional workforce, international accreditation seems to be the way of the future. Regulating accreditation boards should ensure that the curricula in all private medical schools are clearly defined and tailored to meet the needs of the society. The curriculum should be scrutinised carefully and the colleges kept up to date with the recent advances in science, medical education and health. Continuous curriculum evaluations done by the medical colleges themselves should become a norm. Current teaching and learning methods promoting student-centered, competency-based learning and problem-solving abilities should be emphasised. The ‘ideal’ overall teacher-student ratio should be maintained. Faculty development programmes should be made mandatory.

The number of private medical schools should be limited and a reduction in student intake enforced. Quality, rather than quantity, should be the priority. A regulatory cap should be imposed on regions with very large numbers of medical colleges and measures should be taken to ensure more medical colleges are set up in rural areas. The access to medical education for students from ethnic and social minorities should be increased. This can be done by affirmative action, as in US schools, or by a reservation system as in India.

### Conclusion

In light of the limitations of the available information, concrete conclusions on the merits and demerits of privatisation cannot be formulated. Nevertheless, privatisation is definitely a useful tool for addressing some of the problems faced today in the field of medical education and it also serves to enlarge the health manpower resources. However, as with any other powerful tool, if used indiscriminately, it can cause more harm than good.

The way forward is more stringent monitoring of private institutions by governments and other authorities. Private institutions should be goal directed and outcome focused. They should assume responsibility for their products, be they medical graduates, research results, or models of health service delivery. They should accept the kudos as well as the brickbats for the outcomes. Privatising medical education should not mean that governments lose the ability to direct medical
education. The unplanned growth of substandard medical colleges should be curtailed and quality should be emphasised over quantity. As advocated so long ago by Flexner, the numbers of sub-standard medical schools should be drastically reduced by closing those not meeting the stipulated standards, while encouraging the growth of those, public or private, which have the potential to contribute to the health of the nation.

ACKNOWLEDGMENT
The author is grateful to Professor RC Bandaranayake for his guidance and encouragement.

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The contemporary history of health care in Oman dates back to 1970 when the reign of His Majesty Sultan Qaboos commenced. In just about 40 years, the Omani Renaissance has brought prosperity, social and economic progress to all the people of Oman with health being a primary concern.1

Health care up to 1970 was scarce and limited. Before 1958, Oman had two hospitals; one was opened in 1935 by the American Arabian Mission and was named the Knox Memorial Hospital while the other was established in 1948. The latter received partial financing from the Sultan at the time and was staffed and administered by the British Consulate.2 People had to travel up to four days just to reach a hospital, where hundreds of patients would already be waiting in line to see one of the few (expatriate) doctors.3 At that time, only 13 physicians served the entire nation, implying a physician-population ratio of 1 per 50,000. Morbidity and mortality rates were very high. One out of every eight infants born alive died before reaching their first birthday, and one out of every five died before reaching the age of 5 years. Out of every three people in the population, one had an episode of malaria, and out of every thousand persons, thirty were reported to be infected with trachoma, eight with pulmonary tuberculosis and six with hepatitis. The average life expectancy was only 49.3 years in 1970.4

In the early 1970s, there were no laws or regulatory systems to define how institutions should function, their principles and goals, or the rights and duties of employees. Actually, the codification of government began only in the mid-1970.5 A royal decree was issued on 22nd of August 1970 to establish the Ministry of Health (MOH) in Oman.6
The ministry was responsible for the organisation and development of the national health service, and spent 534,282 Omani Rials (USD 1,387,620) on health service development projects. In July 1975, the Royal Decree #26/75 introduced laws to regulate the administration. It set out the Council of Ministers and other government bodies with powers and responsibilities, in tandem with the first Civil Service Law in the Royal Decree #27/75, which outlined civil servants’ rights and duties. Since then, the MOH has been able to build from scratch a modern national system that offers all Omani citizens universally accessible health services free of charge. Such developments were only possible through proper health planning.

Health Planning in Oman

Since its establishment in 1971, the MOH faced great challenges to build the national health system and improve the health of the people of Oman. Therefore, the MOH developed Five-Year Health Development Plans to achieve its goals, the first of which started in 1976. Since then, seven Five-Year Health Development Plans have been implemented.

Health planning in Oman has passed through three phases. The first phase stretched from 1976 to 1990. During this period, three five-year plans were implemented. They were mainly investment plans that aimed at building health infrastructure. The second phase covered 1991 until the end of 2005. During this period, the Fourth, Fifth and Sixth Five-Year Plans for Health Development were implemented. At the beginning of this period, a planning agency was established and health services were decentralised by establishing 10 health regions. Local health administrations were set up at the wilayat (district) level. That period of development showed an increase in the numbers of health centres and hospitals. It also witnessed the start of a number of preventive programmes, each one of them addressing a priority health or health-related problem(s). With the beginning of the Seventh 5-Year Plan that started in 2006, the new phase of strategic planning started in the country.

In the Seventh Five-Year Health Development Plan, and in the light of the identified objectives and strategic directions for health development in Oman (2006–2010), a number of priorities in different fields were defined. Following the prioritisation of important issues and problems, a framework for the Seventh Five-Year Plan for Health Development (2006–2010) was developed, through a consultative process, including ten proposed visions and the goals arising from these visions. The current Seventh Five-Year Health Development Plan (2006–2010) was developed at various levels and is monitored by outcome and performance indicators.

The seventh plan (2006–2010) has targeted the further development of the health services infrastructure, primary care and early prevention of diseases, and community involvement through health education promotion. This focus is an effort to face the challenges of the demographic, economic and social changes that have brought with them new epidemiological trends.

National Health Policy

Oman’s health policy is committed explicitly to the global Health For All (HFA) strategy, and accordingly, has laid down in broad terms the national strategy to achieve HFA based on Primary Health Care (PHC). In this context, national health policy rests on several basic principles, which govern health development in Oman:

1. Provision of comprehensive health services based on primary health care with its four components (curative, preventive, promotive and rehabilitative).

2. Equity in the distribution of health services among different population groups according to their health needs (with due consideration of the special needs of marginal and poor people, isolated villages, women, children, elderly and accessibility to health facilities).

3. Community involvement in planning and implementation of its health care aimed at developing community self-reliance for sustainable health development.

4. Inter-sectoral cooperation with other health-related sectors to ensure a positive impact on community health.

In order to ensure accelerated health development the government adopted several well thought out strategies to implement its health policy. First, the government declared health not only as a
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Evolution of the health system in Oman

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fundamental right of the citizen, but also committed itself to the provision of public health services for free.14 The government viewed this investment not only in the context of its contribution to provide financial protection against the cost of ill-health, but also because of the pivotal role of health development in economic and social development.15

Second, priority was given to the construction of a basic health infrastructure that would be universally accessible to the whole population. Today government local health services reach 100% of urban families and 90% of rural families.16 Health services are also provided, through mobile teams, to people living in very isolated areas. Third, with insufficient manpower, the MOH worked on a two-pronged human resource policy: importing health professionals from neighbouring countries of the Middle East and South Asia to meet the immediate need of the health system and, at the same time, developing its own indigenous human resources to achieve self-reliance in the long term.17 Fourth, from the early seventies, the MOH launched a series of vertical programmes targeted at the priority health problems based on their magnitude, prevalence and intensity as well as their associated burden of diseases.18 As an example, the rapid decline of malaria from 32,000 cases in 1990 to a few hundred per annum today (and these mostly imported)19 illustrates the success of Oman’s health care strategy.

Health Financing in Oman

Oman finances its health system largely through the Government budget, very limited cost-sharing, limited private payments for private sector expatriates through an “employer mandate”, and very small contributions from automobile accident insurance and social security taxes on private sector employees to cover work-related injuries.

Oman spends just 2.4% of gross domestic product (GDP) on health [Table 1].20 Governmental spending on health accounts for about 82.5% of total health expenditure. The government provides 93% of hospitals and about 97.3% of hospital beds. Public health services employ 77.2% of the doctors in the Sultanate, 91.6% of nurses [Table 2] and 85% of other paramedics.20 However, the private sector contribution in the health field has increased fairly rapidly over the last few decades as evidenced by the increasing numbers of private hospitals, clinics and pharmacies.4

The MOH is the main provider of health services in the country; currently MOH expenditure comprise 3.8% of total government expenditure.4 The MOH’s spending amounts to 80% of public sector spending, 47% of which is spent on inpatient care. The Ministry provides comprehensive coverage to all Omancitizens and expatriates working for the public sector and requires the annual purchase of a “health card” (for 1 Omani riyal = US$ 2.6) and a small co-payment for each facility visit (0.2 Omani riyals = US$ 0.50). The other public sector providers offer similar treatment benefits with very limited cost-sharing by those eligible to receive benefits. The MOH does provide coverage for treatment abroad, and funds treatment for around 350-400 individuals a year.21

Private spending is almost evenly split between employer-provided and out-of-pocket spending at 9% and 9.6% of total spending respectively. Types of services offered by the private sector vary: 2% for the most expensive services which are inpatients services, 59% for dental services, 51% for drugs and 19% for outpatient services.20

Table 1: Health expenditure indicators in Oman

<table>
<thead>
<tr>
<th>Indicators (reference year 2007)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Gross domestic product (GDP) per capita in US$</td>
<td>15,229</td>
</tr>
<tr>
<td>- Total expenditure on health per capita in US$</td>
<td>373</td>
</tr>
<tr>
<td>- Government expenditure on health per capita in US$</td>
<td>308</td>
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<tr>
<td>- Total expenditure on health as % of GDP</td>
<td>2.4</td>
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<tr>
<td>- General government expenditure on health (GGHE) as % of total health expenditure (THE)</td>
<td>82.5</td>
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<tr>
<td>- Out-of-pocket expenditure as % of THE</td>
<td>10.2</td>
</tr>
<tr>
<td>- General government expenditure on health as % of total government expenditure</td>
<td>5.2</td>
</tr>
<tr>
<td>- Ministry of Health budget as % of government budget</td>
<td>4.6</td>
</tr>
</tbody>
</table>

The Sultanate of Oman has entrusted the MOH with the responsibility of stewardship and coordination of the health sector, apart from being the principal health care provider. The MOH develops health policies, strategies and health programmes and plans for the sector and also bears the preventive, curative, and rehabilitative care workload.14 Services provided by the MOH are supplemented by other government hospitals/clinics including the Armed Forces Medical Services (AFMS), Royal Oman Police Medical Services (ROPMS), Petroleum Development Oman Medical Services (PDOMS) and the Sultan Qaboos University Hospital (SQUH). While the SQU Hospital serves mainly as a teaching hospital and provides tertiary care, the other public care providers cater mainly to their own employees and their families. The private hospitals and clinics, licensed by MOH through its Directorate of Private Health Establishments, and supervised by the respective regional directorates, play an increasingly important role in providing health care in Oman.4 Thus, policies decided by government are necessarily implemented to the full since there is no real alternative to the state health care system.

The MOH owns alone 49 hospitals (84.5% of the total), with 84.1% of hospital bed capacity in Oman. Four of these hospitals act as national referral hospitals, and 10 are regional hospitals providing tertiary plus secondary health care services (the last are also provided through 5 wilayat hospitals). In addition, MOH operates a network of 30 local hospitals and 167 health centers that provide PHC services.4 Table 2 presents the currently available information on the existing health infrastructure and human resources by provider.

<table>
<thead>
<tr>
<th>Provider</th>
<th>Hospitals</th>
<th>Hospital beds</th>
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<th>Clinics</th>
<th>Physicians</th>
<th>Nurses</th>
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<td>329</td>
<td>833*</td>
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<td>Royal Omani Police</td>
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<td>58</td>
<td>5,473</td>
<td>168</td>
<td>810</td>
<td>5,194</td>
<td>11,233</td>
</tr>
</tbody>
</table>


* Complete information currently unavailable.

Note: There are in addition 364 private pharmacies.

Source: Ministry of Health Statistics.4

### Table 2: Health infrastructure and human resources in Oman (2008)

Health System in Oman

The Sultanate of Oman has entrusted the MOH with the responsibility of stewardship and coordination of the health sector, apart from being the principal health care provider. The MOH develops health policies, strategies and health programmes and plans for the sector and also bears the preventive, curative, and rehabilitative care workload.14

Services provided by the MOH are supplemented by other government hospitals/clinics including the Armed Forces Medical Services (AFMS), Royal Oman Police Medical Services (ROPMS), Petroleum Development Oman Medical Services (PDOMS) and the Sultan Qaboos University Hospital (SQUH). While the SQU Hospital serves mainly as a teaching hospital and provides tertiary care, the other public care providers cater mainly to their own employees and their families. The private hospitals and clinics, licensed by MOH through its Directorate of Private Health Establishments, and supervised by the respective regional directorates, play an increasingly important role in providing health care in Oman.4 Thus, policies decided by government are necessarily implemented to the full since there is no real alternative to the state health care system.

The MOH owns alone 49 hospitals (84.5% of the total), with 84.1% of hospital bed capacity in Oman. Four of these hospitals act as national referral hospitals, and 10 are regional hospitals providing tertiary plus secondary health care services (the last are also provided through 5 wilayat hospitals). In addition, MOH operates a network of 30 local hospitals and 167 health centers that provide PHC services.4 Table 2 presents the currently available information on the existing health infrastructure and human resources by provider.

The Government has laid special emphasis on the role of private sector in the field of health care industry. It views the involvement of this sector as a contribution towards alleviating the increasing burden on the public health system, and creates an atmosphere of competition between public and private health sectors, thus improving the quality of health care provided in the country. Thus, the government has formulated a number of strategies to encourage the private sector to invest in health. The government gives financial support to the private health care sector through a law that treats them on an equal basis with those who invest in industry. They are given the same advantages and the same grants. In addition, the MOH provides the private sector with all the technical support they need to start their hospitals or clinics. Moreover, the MOH has privatised most of its support services in hospitals and health institutions, thus enabling the private sector to play an important role even for the
market segment of Omani nationals, government-employed staff, and their families who are generally eligible for free health care to the extent that this is feasible. The pharmaceutical sector and a large part of the dentistry services are almost exclusively left for the private sector to cover. The government provides soft loans (and free or subsidised sites in some cases) to private entrepreneurs desirous of setting up clinics/hospitals. Ministry of Health also extends other technical support to private establishments in numerous ways.21,22

Organisation and Management

Oman has a relatively small population of 2.9 million inhabitants4 who are scattered over large areas of sparsely populated settlements, many with 1,000 or fewer inhabitants.23

The MOH has made every effort to make health services easily accessible. More than 98% of the population19 now has access to primary health care services and the remaining 2% is served through mobile teams.6

The institutional organisation of the MOH is relatively centralised with three under-secretaries responsible for administrative/financial affairs, health services and planning reporting directly to the Minister.24 The MOH has, however, pursued a decentralisation process since 1990. A Directorate General of Health Services was established in each of the ten health regions (now eleven). Delegation of responsibilities, financial and administrative as well as decision-making was gradually devolved to health regions. Decentralisation has also been in effect at the wilayat (district) level since 1993.7 This approach to decentralisation has allowed the MOH to delegate necessary authorities and responsibilities to regional and wilayat levels. This has encouraged local initiatives and enabled local planning, and budget control.18 Furthermore, the wilayat health level, matching as it does the administrative level of local government, has a pivotal role in addressing determinants of health. It provides the ideal platform for inter-sectoral collaboration on a broader health agenda where the determinants of health need to be addressed by a multiplicity of agencies and the wider community. The Wilayat Health Committees, established in 1999 in all wilayats and chaired by the Wali (local governor) provide, in principle, the main forum for supporting the multi-sectoral and community-based activities of the MOH and inducting community support group volunteers, whose main orientation is towards health education.

### Table 3: Coverage and primary health care service indicators in Oman

<table>
<thead>
<tr>
<th>Indicators</th>
<th>%</th>
<th>Reference Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Population with access to local health services, total</td>
<td>98</td>
<td>2008</td>
</tr>
<tr>
<td>+ Population with access to local health services, urban</td>
<td>100</td>
<td>2008</td>
</tr>
<tr>
<td>+ Population with access to local health services, rural</td>
<td>95</td>
<td>2008</td>
</tr>
<tr>
<td>+ Antenatal care coverage</td>
<td>99</td>
<td>2007</td>
</tr>
<tr>
<td>+ Births attended by skilled health personnel</td>
<td>99</td>
<td>2007</td>
</tr>
<tr>
<td>+ Population with sustainable access to improved water source</td>
<td>75</td>
<td>2003</td>
</tr>
<tr>
<td>+ Population with access to improved sanitation</td>
<td>89</td>
<td>2003</td>
</tr>
<tr>
<td>- One year-old immunised in 2008 with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ BCG anti tuberculosis vaccine</td>
<td>99.9</td>
<td>2008*</td>
</tr>
<tr>
<td>+ DPT3 diphtheria, pertussis (whooping cough) and tetanus vaccine</td>
<td>99.2</td>
<td>2008*</td>
</tr>
<tr>
<td>+ OPV3 polio vaccine</td>
<td>99.9</td>
<td>2008*</td>
</tr>
<tr>
<td>+ Measles/MMR1 (MVC1) measles mumps and rubella vaccine</td>
<td>99.9</td>
<td>2008*</td>
</tr>
<tr>
<td>+ HBV3 hepatitis vaccine</td>
<td>99.2</td>
<td>2008*</td>
</tr>
</tbody>
</table>

Legend: * = Data updated from MOH statistics4
Source: World Health Organization, Oman Country Profile.29
Several community-based initiatives such as the Healthy Wilayat Project, Healthy Lifestyle Project, Healthy City and Healthy Village projects were recently implemented in order to help increase the awareness of the respective communities about environmental and health problems, and thus create active community involvement and ownership for health actions.

Recently, a number of regional referral hospitals and major wilayat hospitals were made autonomous and now are run, administratively and financially, by hospital management boards with a reasonable degree of decision-making authority. Plans to monitor performance of the autonomous hospitals are being developed. It is expected that the hospital autonomy initiative will ensure better and more cost-effective services in the future than ever before.

Health Workforce

In the early years of the Omani Renaissance, Oman imported its health workforce from other countries in large numbers, as its educational infrastructure was inadequate. It adopted that policy in order to accelerate health services development and fulfill the aspirations of the people of Oman. His Majesty Sultan Qaboos has advocated Omanisation as a national strategy for self-reliance, in order to sustain the social and economic development achieved in the country. The government attaches significant importance to human resources development as a strategy for achieving effective health services development.

Nevertheless, the issue of human resources for health (HRH) is complex in Oman as health workforce development strategies are governed by a multiplicity of stakeholders from within the MOH itself, but also from outside the ministry. Health professional associations and councils have only recently started to form, though with limited influence so far on manpower planning, management and development.

Of the 5,194 physicians now working in the health institutions, there are 1,323 Omanis representing a 25% Omanisation level. Physicians are trained by the Sultan Qaboos University College of Medicine and Health Sciences, the private sector Oman Medical College, and to a small extent by universities abroad. Sultan Qaboos University has increased its intake to the MD program to meet the increased need for graduate physicians and to promote the Omanisation of this category. In order to encourage medical education, the MOH permits the use of its Sohar Regional Hospital as a teaching hospital for the Oman Medical College. The MOH, in collaboration with Sultan Qaboos University, is sponsoring the Oman Medical Specialty Board to train physicians in a number of specialties.

The availability of local training in nursing and other paramedical professions has significantly contributed to Omanisation levels. In 1975, there were only 450 nurses working in Oman, mostly expatriates. By the end of 2008, there were a total of 11,233 nurses, 56% of them were Omanis. By the same date, training institutes had also graduated a total of 9,031 health professionals from different specialties (including the basic diploma nursing); among these were 543 laboratory technicians, 376 radiographers, 133 physiotherapists and 622 assistant pharmacists. These graduates have contributed to Omanisation levels of 49% for laboratory technicians, and 56% for the last three categories.

### Table 4: Health status indicators in Oman

<table>
<thead>
<tr>
<th>Indicators (reference year 2008)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Total life expectancy at birth (years)</td>
<td>71.6</td>
</tr>
<tr>
<td>- Newborns with low birth weight (%)</td>
<td>9.2</td>
</tr>
<tr>
<td>- Perinatal mortality rate (per 1,000 total births)</td>
<td>13.8</td>
</tr>
<tr>
<td>- Neonatal mortality rate (per 1,000 total births)</td>
<td>6.4</td>
</tr>
<tr>
<td>- Infant mortality rate (per 1,000 live births)</td>
<td>9.0</td>
</tr>
<tr>
<td>- Under five mortality rate (per 1,000 live births)</td>
<td>11.7</td>
</tr>
<tr>
<td>- Maternal mortality ratio (per 10,000 live births)</td>
<td>16.7</td>
</tr>
</tbody>
</table>

*Calculated as the number of stillborn infants of 24 completed weeks or more plus the number of deaths occurring under 7 days of life divided by the number of stillborn infants of 24 weeks or more gestation plus all liveborn infants in the same year.

**Calculated as the number of children dying under 28 days of age divided by the number of live births that year.

Source: Data updated from MOH statistics.
Health Care Delivery

Generally, the organisation of health care delivery in Oman is based on a primary health care (PHC) approach, with clearly delineated referral pathways between 3 levels of care: primary, secondary and tertiary. The MOH is now operating 167 health centers of which 74 have maternity beds and 21 are extended health centers. These health centers provide preventive, curative and promotive primary health care to the community. In addition, the extended health centers were established to provide specialty care in certain disciplines. Local hospitals, also, provide PHC services. The PHC system is based on the wilayat, or district, the unit of local administration that is the closest to the community. The central role of community health work to a primary health care approach was placed firmly on the international health agenda by World Health Organization Member States in the Declaration of Alma-Ata in 1978.

Secondary health care is provided through regional (mostly autonomous) and sub-regional (wilayat) hospitals. Tertiary care is provided through four national referral hospitals each specialising in a few fields. The MOH also extends the services of mobile medical teams to about 2% of the population living in remote mountainous areas.

Over the years, there has been a growing trend in the utilization of health services (PHC in particular). During 2008, patient visits to outpatient clinics in MOH institutions were about 11 million with an average of 3.9 visits per individual per year. About 253 thousand patients were discharged from MOH hospitals, the average number of inpatients per day being 2,513. The average occupancy rate for all MOH hospitals is 54.9%, indicating significant excess capacity.

Concerns for quality assurance and equity in health care availability, have dictated the Ministry’s health development plans and infrastructure development. Thus, the issue of quality moved high on the agenda of the MOH and was introduced in PHC in 2001, and then to hospitals as well. The Omani quality assurance and improvement programme aims to institutionalise quality in health care institutions with the ultimate goal of providing the highest quality standards of care and thus achieving user satisfaction.

Health Outcomes

Oman is one of the few countries worldwide that has achieved a dramatic transformation in its health status over a remarkably short span of time. Oman’s current health indicators compare well with those of many developed countries with a remarkable control of pregnancy related mortality and morbidity, preventable diseases of childhood and other communicable diseases of public health relevance. This is evident from the changes in the various health indicators.

Currently, the country’s health status indices show an average life expectancy of 71.6 years for males and females at birth. This has been achieved despite a relatively high fertility rate and the consequent large proportion of the population under age 15 years (35.19%). On the other hand, four indices for population coverage with basic health services are among the highest in the world. These include over 99% coverage rate for major vaccines, 99.2% antenatal care coverage (at least one visit during pregnancy), 98.6% of all deliveries taking place in hospitals, and 98% of the population now have access to primary health care services [Table 3].

Oman has also moved from a position amongst the countries in the region with the highest childhood mortality in 1970s, to be amongst the best performers and has even caught up with countries with a much earlier start in development and wealth [Table 4]. In less than 40 years, infant mortality rate has dropped to less than one tenth of its former level (9.0 per 1,000 live births in 2008, down from 118 in 1972), and the under-five mortality rate has dropped by a staggering 94% (11.7 per 1,000 live births in 2008, down from 181 in 1972). Such patterns reflects one of the fastest declines in under-five mortality ever recorded globally. This means that Oman has been successful in utilising all its available resources in order to achieve a satisfactory health status of the population.

These dramatic declines in mortality indicators were mainly because of achievements in reducing communicable diseases. Childhood diseases were highly prevalent during the 1970s; 103 cases of acute poliomyelitis, 102 cases of tetanus, and 43 cases of diphtheria were reported in 1975. Today no single case of poliomyelitis has been reported since 1993. The last case of diphtheria was reported...
in 1992 and only one case of tetanus neonatorum has been reported since 1991. The number of cases of measles, mumps and pertussis reported was very high in 1975: more than 16,000 cases of measles, 14,000 cases of mumps and 13,000 cases of pertussis; these dropped in 2008 to 6,995 and 58 respectively. Other communicable diseases have seen a similar reduction. There were 6,162 cases of pulmonary tuberculosis diagnosed clinically in 1975 compared to only 217 cases in 2007. About 5,000 cases of hepatitis and 24,000 of trachoma were reported in 1975 compared to only 772 and 72 cases respectively in 2008. Malaria, one of the most prevalent diseases in the past, is coming close to eradication. Only 965 cases of malaria were confirmed during 2008 compared to 32,720 during 1990. There were also 144 cases of leprosy and 39 cases of filariasis reported in 1975. Leprosy today is no longer a public health problem as the incidence is less than 1 per 100,000 of the population and no cases of filariasis have been reported.4

### International Recognition

Oman’s remarkable achievements in health developments during the recent past are well recognised and widely acclaimed both regionally and internationally. The country has been recognised for achieving record-breaking gains in population health status and health infrastructural development.31 In respect of its achievements, Oman has received the following international recognitions and appreciations in the last two decades:

1. According to the United Nations International Children's Emergency Fund (UNICEF) Progress of Nations 1993 report, Oman’s 65% decline in its child mortality rate in the 1980s was the second highest in the world, and the highest in the Middle East and North Africa (MENA) region.32

2. In 1993, and according to the previous report, Oman’s 97% measles immunisation rate was the highest in the MENA region, and one of the best five in the world. Oman was among the 12 countries which achieved and exceeded the Decade Goal of vaccinating 90% of children against measles by the year 2000.32

3. The Progress of Nations report, issued in 1997 by UNICEF, acknowledged the Omani achievements in child health and ranked Oman among the leading countries in the Middle East, Africa and even the whole world in controlling childhood diseases such as poliomyelitis, diphtheria and tetanus neonatorum.33

4. According to the Human Development Report 1997, Oman was the first in the world for its impressive achievements in under-5 mortality reduction and 99% immunisation coverage of infants, which led also to a marked reduction in...
in childhood morbidity. The report stated that Oman was a pioneer in the field of human development.18

5. In a study done by Harvard University and commissioned jointly by the Government of Oman, UNICEF and the WHO regional Office for the Eastern Mediterranean Region, health sector achievements in Oman were analysed and considered as a model to demonstrate health developments.1

6. In an analysis of health systems undertaken by the World Health Organization (WHO) in 2000, Oman's health system ranked first among all WHO Member States (191 countries) for its health financing efficiency. It was also ranked 8th using a composite index measuring performance of the health system, attainment of health goals, responsiveness to users and the fairness of its financing [Table 5].31

7. The World Bank Report on the Sultanate of Oman in 2001, Cost Effectiveness Review of the Health Sector, praised the health system in Oman and stated that it spent less money in percent of gross domestic product (GDP) "public and private" compared with countries at a similar income level. Per capita total health expenditure was well below that found in countries with similar income levels.22 It thus appears that Oman's investments in health have been both effective and efficient.22

8. The latest WHO report in 2008 acknowledged Oman's performance in the last four decades and commended it exclusively as an example of success in investing consistently in a national health service and sustaining that investment over time.28

Conclusion
Recent and ongoing efforts of the MOH guided by the national health policy have achieved impressive progress in the health status of Omani citizens as evidenced by high level health indicators that are comparable to those of developed countries. The attainment of what can be seen as a population health transition has taken place within a relatively short period of time and has been achieved at a comparatively modest cost.31 To learn from the experience, Oman's success could be attributed to the following factors.

It is believed that strong political commitment and national investment in the primary health care approach are the basis for the effective and efficient Omani health system. This was demonstrated not only in the assurance given by the government about free provision of health services to the people of Oman, but also in the keen interest that the Head of the Government, His Majesty Sultan Qaboos, has demonstrated towards health development. This is evidenced during His Majesty the Sultan's annual tours in various regions of Oman during which he meets his people, and personally advocates for health even touching upon such sensitive issues as birth spacing.

Historically, health transitions on a similar scale to that of Oman were widely attributed as much to the improvement of non-health conditions as to those related to the health system, for example, the level of income, education, transport, women's empowerment and access to information. However, the role of the health sector and the health delivery system in speeding health transition has been significantly boosted by advances such as potent technologies (i.e. vaccines), effective medicines, and the feasibility of wider coverage of populations by these and other far-reaching public health interventions.12 It is interesting to note that with the possible exception of hospital delivery care, almost all of these interventions are provided as ambulatory deliverables at the PHC outlets in Oman.12

Furthermore, the effectiveness of PHC delivery was considerably consolidated by decentralisation and adoption of the wilayat PHC health system. The strategy brought the PHC system closer to the community and led to a number of community-based initiatives spearheaded and supported by Wilayat Health Committees and Community Support Groups.12

Oman laid great emphasis, right from the start, on sound planning supported by an efficient health information system. Proper planning at all levels fostered successful linkage between health goals and main functions of Oman's national health system.

The Omani health sector also benefited from others' experiences by drawing on regional and international experiences in other countries, including the effective technical cooperation with international organisations such as UNICEF, WHO
and the World Bank. Thus, the country was able to develop programmes, the designs of which had already been tested successfully elsewhere.

In conclusion, Oman has achieved remarkable improvements in health indicators, including a rapid decline in communicable diseases during the past four decades. Increased expenditure on health has resulted in improved indicators of health services, health manpower development and health care. Planning has helped the government, policymakers, health care providers and all other stakeholders focus and work towards the set goals and objectives and work communally to achieve them.

References


Incidence and Determinants of Birth Defects and Enzyme Deficiencies among Live Births in Oman
A review of the 2005 National Register

*Rajiv Khandekar, 1 Yasmin Jaffer 2

Abstract: Objectives: In 2003, the Omani Ministry of Health Child Health Care Program initiated a national Birth Defects (BD) Register. This paper reviews the magnitude and risk factors of birth defects in children born and registered in 2005 using data from the BD Register. Methods:Pediatricians and neonatologists examined children with BDs found either during screening at birth or when attending clinics in their first year of their life. Clinical examination, laboratory, sonographic and radiological investigations were carried out. A pre-tested form was used to note personal details, type of birth defect including International Classification of Diseases-10 (ICD-10) codes of BD and selected risk factors. The incidence rates per 100 live births were calculated.

Results: The annual incidence of BD in Oman was 2.53% (95% CI 2.38–2.68). Males had a significantly higher risk of BD than females (relative risk (RR) = 2.0). The regional variation of BD was also significant (χ² = 363). The incidence of anemia due to enzyme disorders was 1.4%. BD of urogenital organs, hands and feet and Down’s syndrome were the main types of anatomical defects. Consanguinity among parents (RR = 0.85) and low birth weight (RR = 0.28) was negatively associated with birth defects. Mothers giving birth at gestational age of <37 weeks (RR = 1.89) had a higher risk of having children with BD. Maternal and paternal age were not associated to BD. Conclusion: The national Register for BD is an important evaluation tool. Both genetic and acquired risk factors seem to affect BD rates and types in Oman.

Keywords: Birth defects; Congenital anomalies; Oman.

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The United Nation’s Millennium Developmental Goal-4 to reduce child mortality by two-thirds from 1990 levels by 2015 will not be met unless the mortality from birth defects and preterm birth is recognised and addressed. Worldwide, the prevalence rates of all genetic birth defects combined range from a high of 82/1,000 live births in low-income regions to a low of 39.7/1,000 live births in high-income regions. Countries like Oman, which has undergone rapid socioeconomic development, are currently undergoing epidemiological transition. Communicable disease rates are declining, but chronic and non-communicable diseases are on the rise. The magnitude of genetic disorders is high in Omani children and it is likely to increase unless known risk factors like consanguinity, better survival of preterm babies due to improved child health care, and limited acceptance of therapeutic abortions are addressed.

The Maternal and Child Health Care Program as well as the programme for controlling genetic disorders in Oman has recognised this health problem and included it in the 6th Five Year Health Plan. A national BD Register was started in 2003 with BD defined as physical abnormalities or enzyme deficiency, mainly glucose-6-phosphate dehydrogenase deficiency (G6PD). Paediatricians provide the information for the Register and its programme managers improved its quality of Register in the initial years. The authors analysed the national BD Register for 2005 to estimate the incidence of BDs for live births and their epidemiological determinants. On this basis, public health related recommendations were proposed.

Methods

This was a review of the national BD Register. The Ethical and Research Committee of the Ministry of Health gave permission for the study. Paediatricians and neonatologists at ten regional hospitals were our study investigators. All babies born in the year 2005 in Oman were our total study population. Children with BDs, found either during screening at birth or when attending clinics in their first year of life, were our specific study population. Those identified with anatomical deformities were registered after detailed clinical examination. Blood tests were performed for children suspected to suffer from genetic blood disorders. Children with BDs also underwent radiological and sonographic evaluation to identify any other anomalies in addition to the principal defect. Personal information like date of birth, sex, area of residence, tribe, mother’s age at birth, father’s age, order of birth, birth weight, gestational age on birth, status of child in the first year of life (alive or dead), medical history and degree of consanguinity among parents were noted on a standardised pre-tested form. The principal BD as per the International Classification of Diseases-10 (ICD-10) code was also noted. All the children with Down’s syndrome had their condition confirmed by laboratory tests. The children were managed by paediatric services either in regional hospitals or with the help of a paediatric surgeon.
at tertiary hospitals. If treatment was possible, but facilities were not available within the country, the child’s treatment, in a reputed centre abroad, was paid for by the Omani government.

The BD Register was initiated in the year 2002. The first year was the pilot phase to strengthen the registration system. From 2003, a national data collection system was implemented by the national Health Information Management System (HIMS). The Department of Mother and Child Health (MCH) of the Ministry of Health (MoH) liaised with regions to monitor and follow the registration of children with BD. Neonatologists and other specialists like paediatric ophthalmologists, ear, nose and throat surgeons, cardiologists, etc, in regional and wilayat (district) MoH hospitals reported information on BD. The attending physician of the institution where such a child was first reported was labelled as the reporting person. As information in the Register was based on identity of the parent health institution, duplications were avoided. The national supervisor for MCH followed through with the attending physicians to ensure the completion of all relevant information in the BD Register.

The data on live births, children with low birth weights (< 2.5 kg) and the proportion of twin births, to determine plurality, was provided by the Department of Health Information and Statistics. The proportion of preterm babies in general population was 9.4% in a study in Saudi Arabia. We took it as reference for calculating preterm babies in the cohort of live births in 2005 in Oman.

The regional health information officers computed the data from the pre-tested forms by using Epi Info” 6 software (Center for Disease Control, USA). The statistician of the Oman Ministry of Health’s (MoH) Maternal & Child Health Care (MCH) Department compiled the national Register. After ensuring completion of information, univariate analysis was carried out using the parametric method and the Statistical Package for Social Studies (SPSS, Version 12). Frequencies and incidence of BDs nationally and of regional subgroups were calculated per 100 live births. The risk of BD was compared to the children born without BD in 2005 in Oman by calculating relative risk, 95% confidence intervals (CI) and P values (set at (< 0.05).

The identities of children with BD and their parents were de-linked from information on risk factors of BD and only the principal investigator had access to this information. The results of this study were shared with regional paediatricians and the staff of the programme for the control of genetic diseases. Policies for strengthening the BD Register and the care of children with BD were then proposed to the members of the national Mother and Child Health Care Committee.

Results

The BD Register of Oman had 1,393 children registered in 2005. Of them, 1,065 (76.5%) children were born in 2005. Fifty-seven (4.02%) children with BD died in the first year of life. The characteristics of children with BD were compared to all the Omani children born in 2005 [Table 1]. Five children with BD had undetermined gender on clinical examination.

The incidence of BDs was calculated for different epidemiological variables. Live births were used as the denominator to calculate the incidence of BD. Data on the birth cohort, number of children with BD, incidence per 100 live births, the relative risk, their 95% CI and the P values are given in Table 2. The incidence of BD in Oman during 2005

Table 1: Characteristics of the children born in 2005 and children with birth defects in Oman

<table>
<thead>
<tr>
<th>Region</th>
<th>Children born in 2005</th>
<th>Children with birth defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscat</td>
<td>9,861</td>
<td>184</td>
</tr>
<tr>
<td>Dhofar</td>
<td>4,115</td>
<td>66</td>
</tr>
<tr>
<td>Dhakhiliya</td>
<td>5,727</td>
<td>338</td>
</tr>
<tr>
<td>North</td>
<td>3,466</td>
<td>40</td>
</tr>
<tr>
<td>Sharqiya</td>
<td>4,088</td>
<td>105</td>
</tr>
<tr>
<td>South</td>
<td>6,856</td>
<td>190</td>
</tr>
<tr>
<td>Sharqiya</td>
<td>3,778</td>
<td>78</td>
</tr>
<tr>
<td>North Batinah</td>
<td>3,578</td>
<td>41</td>
</tr>
<tr>
<td>South Batinah</td>
<td>436</td>
<td>21</td>
</tr>
<tr>
<td>Dhahira</td>
<td>160</td>
<td>2</td>
</tr>
<tr>
<td>Musandam</td>
<td>96</td>
<td>2</td>
</tr>
<tr>
<td>Al Wusta</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>42,065</strong></td>
<td><strong>1,065</strong></td>
</tr>
</tbody>
</table>

Table 2: Incidence of BDs per 100 live births in 2005

<table>
<thead>
<tr>
<th>Region</th>
<th>Incidence of BDs per 100 live births</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscat</td>
<td>17.3</td>
</tr>
<tr>
<td>Dhofar</td>
<td>6.2</td>
</tr>
<tr>
<td>Dhakhiliya</td>
<td>31.7</td>
</tr>
<tr>
<td>North</td>
<td>3.8</td>
</tr>
<tr>
<td>Sharqiya</td>
<td>9.9</td>
</tr>
<tr>
<td>South</td>
<td>17.8</td>
</tr>
<tr>
<td>Sharqiya</td>
<td>7.3</td>
</tr>
<tr>
<td>North Batinah</td>
<td>3.8</td>
</tr>
<tr>
<td>South Batinah</td>
<td>2.0</td>
</tr>
<tr>
<td>Dhahira</td>
<td>0.2</td>
</tr>
<tr>
<td>Musandam</td>
<td>0.2</td>
</tr>
<tr>
<td>Al Wusta</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>15.0</strong></td>
</tr>
</tbody>
</table>
was 2.53 per 100 live births and was significantly higher in boys compared to girls. (RR = 1.98 (95% CI 1.72–2.27), P value = <0.001). The regional variation of reporting BD in children was significant. The Dhakhiliya region had significantly higher BD rates (5.90 per 100 live births; 95% CI 5.29–6.51), whereas the North Sharqiya and Dhahira regions had lower incidences of BD (1.15/100 live births). The types of BDs as per the ICD-10 codes with incidence per 100 live births are given in Table 3. Of the 1,065 children with BD, 589 (55.3%) had anaemia due to G6PD enzyme disorders. Deformities of hands and feet were noted in 106 children with an incidence of 0.25 per 100 live births.

The rate of BDs was compared among the different subgroups of children born in 2005; the frequencies, relative risks, 95% CI and P values are given in Table 4. We did not find a significant association between maternal age at birth and the presence of BD. The information on other variables was missing for nearly half of the participants.

### Discussion

This is the first attempt at national level in Oman to review the profile of children with BD. The infant mortality rate (IMR) in Oman of 10.28/1,000 live births is now mainly due to non-communicable diseases. The high rate of hospital deliveries in Oman, together with a nearly 100% immunisation rate of children against infectious diseases (including rubella) as well as free access to high standard, regional neonatal and child health care services have resulted in a marked decline in deaths due to avoidable conditions. Unfortunately, risk factors for genetic disorders such as the high rate of diabetes in women, consanguineous marriage practices, limited therapeutic abortions and mothers of older age are still present in Oman. In such a situation, knowledge of the incidence of BDs and their risk factors is crucial in order to formulate future prevention and intervention policies.

In 2005, the overall incidence of BD in Oman was 2.53% (95% CI 2.38–2.68), but a study in one of the regions of Oman showed a BD prevalence of 2.46%. The rate in Oman was more than that reported in Iran (1.01%), Kuwait (1.25%) and Bangladesh (2.3%) and the UAE (0.79%). It is worth noting that, in spite of variations in all these studies, the populations were all of Muslim religion. Apart from Bangladesh, the other study areas were in Middle Eastern countries, where the health services are accessible and of a high standard. Therapeutic abortion is also not widely accepted in these countries. Despite the similarities among these countries the differences in the rates cannot be explained. Perhaps the high incidence of diabetes in the >20 population in Oman and diabetes in mothers being a known risk factor of BD, could be a logical explanation for the higher incidence of BD in our study. Further studies of specific BDs in Oman are recommended to explain the reason for the higher incidence of BD in Oman compared to neighbouring countries. However, Oman has the following factors which militate against the higher incidence of BDs found in this study: 1) only 0.5% prevalence of smoking among females; 2) a religious taboo on the consumption of alcohol and controls on its availability; 3) low incidence of malnourishment and folic acid provision to females during antenatal period points at a lower risk of central nervous system congenital malformation; 4) universal immunisation against rubella, and 5) controlled prescription of medicines with teratogenic properties.

The incidence of BD was significantly higher in males compared to females in our study. This was also reported in Iran and in a study by Cui et

### Table 2: Incidence of Birth Defect (BD) per 100 live births in Oman in 2005.

<table>
<thead>
<tr>
<th>Variant</th>
<th>Live births</th>
<th>No. with BD</th>
<th>% of BD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21,264</td>
<td>799</td>
<td>2.74</td>
<td>2.52–2.96</td>
</tr>
<tr>
<td>Female</td>
<td>20,801</td>
<td>390</td>
<td>1.83</td>
<td>1.23–1.54</td>
</tr>
<tr>
<td>Region**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscat</td>
<td>9,861</td>
<td>184</td>
<td>1.87</td>
<td>1.60–2.13</td>
</tr>
<tr>
<td>Dhofar</td>
<td>4,115</td>
<td>66</td>
<td>1.60</td>
<td>1.22–1.99</td>
</tr>
<tr>
<td>Dhakhiliya</td>
<td>5,727</td>
<td>339</td>
<td>5.90</td>
<td>5.29–6.51</td>
</tr>
<tr>
<td>N. Sharqiya</td>
<td>3,466</td>
<td>40</td>
<td>1.15</td>
<td>0.80–1.51</td>
</tr>
<tr>
<td>S. Sharqiya</td>
<td>4,088</td>
<td>105</td>
<td>2.57</td>
<td>2.08–3.05</td>
</tr>
<tr>
<td>N. Batinah</td>
<td>6,856</td>
<td>190</td>
<td>2.77</td>
<td>2.38–3.16</td>
</tr>
<tr>
<td>S. Batinah</td>
<td>3,778</td>
<td>78</td>
<td>2.06</td>
<td>1.61–2.52</td>
</tr>
<tr>
<td>Dhahirah</td>
<td>3,578</td>
<td>41</td>
<td>1.15</td>
<td>0.80–1.49</td>
</tr>
<tr>
<td>Musundam</td>
<td>436</td>
<td>21</td>
<td>4.82</td>
<td>2.81–6.83</td>
</tr>
<tr>
<td>Wousta</td>
<td>160</td>
<td>2</td>
<td>1.25</td>
<td>0.47–2.97</td>
</tr>
</tbody>
</table>

Legend: RR = relative risk; *Validity: RR = 1.98, 95% CI = 1.72–2.27, P value = <0.001; **Validity: χ2 = 363, 95% CI = DF = 8, P value = <0.001
A study of opposite sex twins suggested that males had a 29% higher risk of BD compared to their sisters. A study with a large sample showed that a higher percentage of males was noted with obstructive cardiac defects while females were more likely to have all types of neural tube defects. Folic acid supplementation and high take-up rates of antenatal care in Oman may have resulted in a lower incidence of neural tube defects and less females with BD of these types.

The regional variation in BD was marked in Oman. Different tribes in different regions could explain this variation. Regional variation was noted in the prevalence of congenital heart defects in a study done in Saudi Arabia.

A maternal age of more than 25 years was associated with BDs in the United Arab Emirates. In our study also, younger mothers had children with BD. In contrast, mothers of >35 years of age had a significantly higher risk of having children with autism and heart defects BD. In another study in Oman, older aged mothers had a significant risk of giving birth to children with Down's syndrome. We cannot explain the reason for this negative association in the present study. We did not include stillborn and naturally aborted preterm infants when calculating the incidence and risk factor in our study. Multi-system genetic disorders could be higher in the group that died prematurely. Perhaps this could be the reason of the observed non-association in our study.

The influence of paternal age (>35 years) was associated with a higher incidence of Down's syndrome. Factors related to the father's occupation also have been attributed to incidence of BD.

In our study, we did not find such an association. Information on the father's age was missing for 29 children and these fathers are more likely to be in the >45 years age group. If we review the risk of BD on this assumption, then paternal age was a significant risk factor for BD in Oman.

Low birth weight and preterm babies are known risk factors for BD. Surprisingly, low birth weight was negatively associated to BD in our study. The non-inclusion of stillbirths with BD might be the reason for such an association. The risk of BD has been noted in twin and multiple pregnancies especially those arising from artificial reproductive techniques. Since there was no information on weight and plurality for a large number of children in our cohort, the association of BD with birth weight and plurality should be viewed with caution.

Given the fact that there were only seven pairs of twin children, we did not calculate the risk of BD to plurality. It should be noted that BD could be the reason for preterm deliveries and low birth weight of infants.

Consanguinity has been documented as a risk factor for many congenital anomalies. However, in our study, it was not found to be a risk factor for BD. Since we excluded still births and aborted fetuses, we may have found less multi-syndromic congenital anomalies with a strong genetic link. In addition, small and close-knit communities, such as the Kabila tribe in Oman, could have a long history of consanguinity; however, given better education

### Table 3: Birth Defect (BD) by type in Oman in 2005

<table>
<thead>
<tr>
<th>Type of BD</th>
<th>Children with BD</th>
<th>Incidence of BD</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia due to enzyme disorders</td>
<td>589</td>
<td>1.40</td>
<td>1.29–1.51</td>
</tr>
<tr>
<td>Deformities of hand &amp; feet</td>
<td>106</td>
<td>0.25</td>
<td>0.20–0.30</td>
</tr>
<tr>
<td>Urogenital anomalies</td>
<td>80</td>
<td>0.19</td>
<td>0.15–0.23</td>
</tr>
<tr>
<td>Anomalies of skull &amp; spine</td>
<td>41</td>
<td>0.10</td>
<td>0.07–0.13</td>
</tr>
<tr>
<td>Anomalies of heart &amp; great vessels</td>
<td>41</td>
<td>0.10</td>
<td>0.07–0.13</td>
</tr>
<tr>
<td>Down's syndrome</td>
<td>32</td>
<td>0.08</td>
<td>0.05–0.10</td>
</tr>
<tr>
<td>Musculoskeletal anomalies</td>
<td>23</td>
<td>0.05</td>
<td>0.03–0.08</td>
</tr>
<tr>
<td>Cleft palate/lip</td>
<td>21</td>
<td>0.05</td>
<td>0.03–0.07</td>
</tr>
<tr>
<td>Anomalies of alimentary canal</td>
<td>21</td>
<td>0.05</td>
<td>0.03–0.07</td>
</tr>
<tr>
<td>Malformations of eye &amp; ear</td>
<td>19</td>
<td>0.05</td>
<td>0.02–0.07</td>
</tr>
<tr>
<td>Respiratory anomalies</td>
<td>6</td>
<td>0.01</td>
<td>0.00–0.03</td>
</tr>
<tr>
<td>Other</td>
<td>86</td>
<td>0.20</td>
<td>0.16–0.25</td>
</tr>
<tr>
<td>Oman</td>
<td>1,065</td>
<td>2.53</td>
<td>2.38–2.68</td>
</tr>
</tbody>
</table>
in the younger generation, consanguinity, a known risk factor for BD, may now be less than in the past.

Migration to urban areas and the growth of the nuclear family has also been postulated to dilute the role of consanguinity and that could be the reason for the observed association of consanguinity with BD in our study. 34

Anaemia due to G6PD enzyme disorders was the main reported BD in Oman. This agreed with earlier observations in Oman. 35, 36 There were a significant number of BDs of the urogenital system, Down’s Syndrome children and deformities of the hands and feet in our study. Further studies with a larger sample of these BDs are recommended. The surveillance for BD in different countries as reported by International Center for Birth Defect Surveillance and Research (ICBDSR) suggested that rate of Down’s syndrome in our study matched that of Cuba and Italy. However, it was lower than USA, Canada and France. 37 Inclusion of BD among aborted fetuses in other countries could be the reason for the higher rate compared to our study. In these countries, the registration included BD among aborted fetus and paid special attention to factors during pregnancy associated to BD. In Oman, the BD Register included genetic blood disorders and excluded aborted fetuses therefore comparison of rates should be done with great caution.

As this study was a retrospective Register review, loss of data or incomplete data was an inherent limitation. In spite of communicating with regional programme managers to complete the Register as well as using indirect indicators from other sources like the child health registers at primary health institutions and records of infant deaths at regional hospitals, we still had missing information that could have introduced bias into our study especially while reviewing the association of risk factors to BD.

Our study suggested that the incidence of BD in surviving infants was high. The Maternal and Child Health Program should emphasise the

<table>
<thead>
<tr>
<th>Table 4: Risk factors for Birth Defects (BD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factor</td>
</tr>
<tr>
<td>---------------------------------------------</td>
</tr>
<tr>
<td><strong>Mother’s age</strong></td>
</tr>
<tr>
<td>&lt; 35 years</td>
</tr>
<tr>
<td>≥ 35 years</td>
</tr>
<tr>
<td>Missing</td>
</tr>
<tr>
<td><strong>Father’s age</strong></td>
</tr>
<tr>
<td>&lt; 45 years</td>
</tr>
<tr>
<td>≥ 45 years</td>
</tr>
<tr>
<td>Missing</td>
</tr>
<tr>
<td><strong>History of consanguinity in parents</strong></td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td><strong>Birth weight</strong></td>
</tr>
<tr>
<td>&lt; 2.5 kg</td>
</tr>
<tr>
<td>≥ 2.5 kg</td>
</tr>
<tr>
<td>Missing</td>
</tr>
<tr>
<td><strong>Gestational age at birth</strong></td>
</tr>
<tr>
<td>&lt; 37 weeks</td>
</tr>
<tr>
<td>≥ 37 weeks</td>
</tr>
<tr>
<td>Missing</td>
</tr>
<tr>
<td><strong>Plurality</strong></td>
</tr>
<tr>
<td>Single birth</td>
</tr>
<tr>
<td>Multiple births</td>
</tr>
<tr>
<td>Missing</td>
</tr>
</tbody>
</table>
need for improved quality of registration in order to ensure complete records. Both genetic and acquired factors seem to interact and result in a high incidence of BD in Oman. The health services at regional level should be well equipped to identify and manage children with BD. Some of the children with BD, even after successful management, will need long term follow-up and rehabilitation. Hence prevention, care and rehabilitation should be an integral component of the BD control programme. Further studies of important BDs and their risk factors would enable the programme to formulate a preventive and rehabilitative approach for each of them.

ACKNOWLEDGEMENTS

We would like to thank Mr Hamoud S Al-Gabri, Health Information Officer and Ms Flor Deliza of the Ministry of Health’s Maternal and Child Health Program for their help in interpreting the data related to maternal and child health care linked to the national Register for BD in Oman. We also acknowledge the contribution of health professionals in regions especially the paediatricians and neonatologists who examined the children with BDs. We thank Dr. Anna Rajab of the Genetics Unit at the Royal Hospital, Muscat, Oman, for advice in writing part of the discussion section. The cooperation and commitment of parents and relatives of children with BD are highly appreciated.

The preliminary results of this study were presented in 1st National Conference of Birth Defects held in Muscat, Oman, in 2007.

References

Incidence and Determinants of Birth Defects and Enzyme Deficiencies among Live Births in Oman: A review of the 2005 National Register

Validity of Cardiac Markers as Diagnostic and Prognostic Indicators of Complications in Patients undergoing Percutaneous Coronary Intervention

Hafidh A Alhadi1 and Keith A A Fox2

Objectives: The aim of this study was to assess the diagnostic and prognostic value of heart-type fatty acid-binding protein (H-FABP) in elective percutaneous coronary intervention (PCI) and compare it with standard cardiac markers. Methods: A prospective evaluation was done of 80 consecutive patients admitted for elective PCI. Serum cardiac troponin T (cTnT), cardiac troponin I (cTnI), creatine kinase-MB (CK-MB mass), myoglobin, and H-FABP were determined pre-angioplasty and 1, 2, 4, and 16–24 hours post-angioplasty. Elevated cardiac markers were correlated with demographic, angiographic and procedural variables. Patients were followed up for 20–26 months. Results: H-FABP peaked early at 2 hours and was useful for the early detection of evolving AMI within 1–3 hours after angioplasty. Cardiac-TnI, myoglobin, H-FABP, CK-MB mass, and cTnT concentrations were elevated in 46.25%, 17.5%, 13.3%, 11.25%, and 7.5% respectively. Cardiac-TnI was the most sensitive marker for detecting complications and was superior to all other markers. Elevated cardiac markers were correlated with old age (P < 0.02); chest pain + ECG changes of ischaemia (P < 0.003); use of stents (P < 0.019) and major complications such as major dissection (P < 0.004); transient vessel closure (P < 0.022); bail out stent (P < 0.003), and AMI (P < 0.042). Elevated cardiac markers were associated with a reduction of event-free survival (16.92 versus 20.67 months, P < 0.03). Conclusion: Heart-type-FABP measurements at 1 hour (or thereafter) post-PCI may offer an early chance of detecting evolving AMI; cTnT was the most sensitive marker for the detection of major complications in patients undergoing PCI. Measurements of cTnI 16–24 hours post-PCI should be part of the routine management of patients following elective PCI.

Keywords: Percutaneous coronary intervention; PCI; Acute coronary syndrome; Heart-type fatty acid-binding protein; Cardiac markers; Cardiac troponins; Complications.

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PERCUTANEOUS CORONARY INTERVENTION (PCI) is widely used in the treatment of many patients with stable angina, unstable angina (UA), recurrent angina after coronary artery bypass grafting (CABG), and acute myocardial infarction (AMI).1-3 PCI is, in general, a safe procedure; however, occasionally complications occur, including AMI (3–5%),1-2 emergency CABG (3–7%),4 and death (0.9%).5 These events are usually caused by extensive arterial dissection, intracoronary thrombosis, or both, with resultant vessel occlusion. Acute closure occurs in 2–8% of patients undergoing PCI.6 In 75% of patients with abrupt closure, it occurs within minutes, in the other 25% it usually occurs within 24 hours.7 Ultrasound imaging has shown that dissection of the arterial wall is detected in 50–80% of patients who have undergone successful PCI.8 Other complications of PCI include coronary vessel rupture or injury, re-stenosis, arrhythmias, coronary artery spasm/elastic recoil, and embolism.9 Side branch occlusion occurs in 5% of side branches that are adjacent to a dilated coronary stenosis.10

Uncomplicated angioplasty is not associated with any significant release of cardiac markers;11 however, more sensitive cardiac markers have increased the numbers of patients diagnosed with myocardial injury after PCI. These infarcts have been associated with increased risk of future complications.12-14 Minor increases of creatine kinase-muscle and brain (CK-MB) after an apparently successful coronary intervention have been reported in 11.5–26% of cases, and have been associated with an increased risk of cardiac death and AMI during follow-up.12,15 Serum cardiac troponin I (cTnI) and cardiac troponin T (cTnT) elevations have been detected in 13–44% of patients undergoing PCI.14,16-17 An increased cTnT concentration post-PCI has been correlated with a higher incidence of complex lesion morphology during angioplasty.18

Heart-type fatty acid-binding protein (H-FABP) has been found to be a useful early marker for the detection of myocardial injury.19 The value of H-FABP as an early marker for the identification of myocardial damage during PCI has not yet been studied. The aims of the study were to examine the relation between elevations of cardiac markers post-PCI and complication rates during and after PCI and to determine whether elevated cardiac markers post-PCI are related to demographic, angiographic or procedural variables.

**Methods**

The study population consisted of a consecutive series of 80 patients recruited from the Cardiology Unit at the Royal Infirmary of Edinburgh over an eight month period in 2002. Ethical approval for the study was obtained from the local ethical committee and written informed consent was obtained from each patient. Thereafter, five serial blood samples were collected from each patient at 0 hour (baseline concentration, pre-angioplasty) and at 1 hour, 2 hours, 4 hours and 16–24 hours after angioplasty. The study group consisted of patients who were referred for elective angioplasty for both stable angina pectoris and UA. Patients who had a non-elective angioplasty (e.g. rescue angioplasty, primary angioplasty, salvage angioplasty, or emergency angioplasty) were excluded from this study. Patients were categorised into two main groups according to the presence (cTnI positive) or absence (cTnI negative) of elevated cTnI concentrations ≥ 0.18 µg/L. The two groups were compared with respect to demographic, angiographic and procedural variables.
variables, and the frequency of complications during PCI and the in-hospital period. Patients were followed-up for 20–26 months after discharge from hospital and the numbers of cardiac events in each group were compared. Angiographic success was defined according to the European Society of Cardiology Task Force Guideline on Angioplasty as < 20% residual diameter stenosis and thrombolysis in myocardial infarction (TIMI) 3 flow.20 Clinical success was defined as angiographic success without in-hospital complications (death, AMI, emergency CABG, or ischaemia driven repeat PCI).

Cardiac-TnI, CK-MB mass, and myoglobin were analysed on a Stratus CS analyser machine (Dade Behring, Germany), using commercially available test materials. The coefficients of variations for cTnI were 6.8%, and 6.7% at concentration range 0.24–0.36µg/L, and 4.6–6.9 µg/L respectively. Heart-type-FABP was analysed by an enzyme linked immunosorbent assay method using commercially available assays (Hycult,
Cambridge, UK). The analytical sensitivity of H-FABP mean ± SD was 0.206 ± 0.047 µg/L. Cardiac-TnT was analysed on Elecsys 2010 using commercial assays (Roche, Germany). The reference ranges quoted by the manufacturer for CK-MB mass, cTnI, myoglobin, cTnT, and H-FABP assays were validated by assaying the reference ranges of 20 healthy blood donors samples (10 males and 10 females, mean age ±SD = 63.8 ±8.01, range 53–75 years, median = 65 years). The mean ± SD concentrations of these markers were CK-MB mass =1.52 ± 0.8 µg/L, cTnI = 0.015 ± 0.006 µg/L, myoglobin = 41.5 ± 13.3 µg/L, cTnT = 0.011 ± 0.002 µg/L, and H-FABP = 6.86 ± 2.21 µg/L. The optimal cut-off concentrations of cardiac markers were based on receiver operating characteristic (ROC) curve analysis between patients with and without complications after PCI, and also considerations of cardiac markers concentrations in the normal healthy blood donor group, the control group, and the basal or pre-angioplasty concentrations. The following cut-off concentrations of cardiac markers were used to indicate myocardial injury following angioplasty (cTnI ≥ 0.18 µg/L; cTnT ≥ 0.1 µg/L; CK-MB mass ≥ 5 µg/L; myoglobin ≥ 95 µg/L, and H-FABP ≥ 16 µg/L). All these cut-off concentrations were associated with statistically significant areas under the curve (P < 0.0005).

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS™, Pittsburgh, statistical software, Version 12). Continuous variables were presented as mean ± SD. Comparisons between cTnI positive and negative groups demographic, angiographic and procedural variables were conducted by the Mann-Whitney U test for continuous variables and chi-square or Fisher’s exact test for categorical variables. Comparison of the mean concentrations of serial cardiac markers changes at 0 hour (before angioplasty) and at 1, 2, 4, and 16–24 hours after angioplasty was conducted by the Friedman test. Significance was defined as a P value ≤ 0.05. The rate of event-free survival was estimated from the Kaplan-Meier survival method and was compared with the log rank test.

Results

The study group included 21 females (26%) and 59 males (74%). The mean age of the group was 61.1 ± 7.5 years. The control group (who had an angiography procedure alone without angioplasty) consisted of 12 patients, 5 females and 7 males with a mean age 61.9 ± 8.7 years. There were no significant releases of any of the cardiac markers in the control group (data not shown). This provides evidence that excludes diagnostic procedure as the cause of cardiac trauma and supports angioplasty as the primary cause of cardiac markers release. Cardiac-TnI was the most frequent abnormal marker and was therefore chosen for comparison in this study. In 37 out of 80 patients (46.25%), the cTnI concentration was ≥ 0.18 µg/L. An increase in cTnI concentration (> 0.06– ≤ 0.17 µg/L) was observed in 22 patients (27.5%). The area under the curve (AUC) for cTnI was greater than that for other markers. Myoglobin was increased in 14 (17.5%) patients, H-FABP in 13.3%, and CK-MB mass in 11.25%. In all cases where CK-MB mass, cTnT, H-FABP or myoglobin were elevated, cTnI was also elevated.
As compared with cTnI, cTnT was increased above the cut-off concentration in only 6 (7.5%) patients, and five of them had significant complications. Cardiac-TnT was elevated to concentrations between 0.01–0.06 µg/L in 36 patients, and between ≥ 0.06 – < 0.1 µg/L in 4 patients. The complications reported in these two groups were in 10 and 3 patients respectively. All 6 patients with cTnT > 0.1 µg/L and the 13 patients in the last two groups had cTnT ≥ 0.18 µg/L. In the cTnI negative group (43 patients, 53.75%), no increase in cTnT or CK-MB mass above the cut-off concentration was observed. Myoglobin was elevated in two patients, and H-FABP (concentration = 21 µg/L) in one.

### Table 2: Procedural variables in patients with and without elevated cardiac troponin I (cTnI). Continuous variables are presented as mean ± SD and categorical variables are presented as percentages (in brackets).

<table>
<thead>
<tr>
<th>Procedure data</th>
<th>cTnI positive group (n = 37)</th>
<th>cTnI Negative group (n = 43)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain ± ECG changes of ischaemia</td>
<td>19 (51.4)</td>
<td>6 (13.9)</td>
<td>0.004</td>
</tr>
<tr>
<td>Procedure information</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of lesions dilated (per patient)</td>
<td>46 (1.24)</td>
<td>41 (1.24)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of vessels dilated (per patient)</td>
<td>41 (1.11)</td>
<td>40 (1.21)</td>
<td>NS</td>
</tr>
<tr>
<td>Balloon diameter (mm)</td>
<td>3.3 ± 0.56</td>
<td>3.12 ± 0.45</td>
<td>NS</td>
</tr>
<tr>
<td>Total number of balloon inflation (n)</td>
<td>6.4 ± 4.6</td>
<td>4.81 ± 2.8</td>
<td>NS</td>
</tr>
<tr>
<td>Total time of balloon inflation (minutes)</td>
<td>5.77 ± 4.18</td>
<td>3.41 ± 2.86</td>
<td>NS</td>
</tr>
<tr>
<td>Maximum inflation time (seconds)</td>
<td>50.12 ± 26</td>
<td>55.24 ± 24.34</td>
<td>NS</td>
</tr>
<tr>
<td>Maximum inflation pressure (Pa)</td>
<td>11.21 ± 3.34</td>
<td>10.45 ± 3.56</td>
<td>NS</td>
</tr>
<tr>
<td>Total duration of procedure (minutes)</td>
<td>56.9 ± 38.3</td>
<td>42.31 ± 19.2</td>
<td>NS</td>
</tr>
<tr>
<td>Major complications during PCI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major dissection</td>
<td>10 (27)</td>
<td>1 (2)</td>
<td>0.004</td>
</tr>
<tr>
<td>Side branch occlusion</td>
<td>5 (13.5)</td>
<td>2 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>Transient vessel occlusion</td>
<td>7 (19)</td>
<td>1 (2)</td>
<td>0.022</td>
</tr>
<tr>
<td>Major technical failure</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>Bail out stent</td>
<td>7 (19)</td>
<td>0 (0)</td>
<td>0.003</td>
</tr>
<tr>
<td>Minor complications during PCI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor dissection</td>
<td>8 (21.6)</td>
<td>7 (16)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary spasm/ elastic recoil</td>
<td>2 (5.4)</td>
<td>5 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Minor technical failure</td>
<td>1 (3)</td>
<td>2 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>Post-procedural complications (24h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td>3 (8)</td>
<td>0 (0)</td>
<td>0.042</td>
</tr>
<tr>
<td>Angina with re-catheterisation</td>
<td>5 (13.5)</td>
<td>1 (2)</td>
<td>NS</td>
</tr>
<tr>
<td>Angina without re-catheterisation</td>
<td>1 (3)</td>
<td>2 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>Emergency CABG.</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>Total number of stents</td>
<td>42</td>
<td>32</td>
<td>0.019</td>
</tr>
<tr>
<td>Reason for stenting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent for dissection</td>
<td>15 (40.5)</td>
<td>8 (17)</td>
<td>0.05</td>
</tr>
<tr>
<td>Stent for sub-optimal result</td>
<td>12 (32.4)</td>
<td>15 (35)</td>
<td>NS</td>
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<tr>
<td>Elective stent</td>
<td>3 (8)</td>
<td>6 (14)</td>
<td>NS</td>
</tr>
<tr>
<td>Bail out stent</td>
<td>7 (19)</td>
<td>0 (0)</td>
<td>0.003</td>
</tr>
<tr>
<td>Use of IVUS during PCI</td>
<td>6 (16)</td>
<td>1 (2)</td>
<td>0.045</td>
</tr>
<tr>
<td>Post-procedural treatment</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>11 (30)</td>
<td>20 (47)</td>
<td>NS</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>8 (22)</td>
<td>7 (16)</td>
<td>NS</td>
</tr>
<tr>
<td>Abciximab + Ticlopidine</td>
<td>3 (8)</td>
<td>2 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>Abciximab + Clopidogrel</td>
<td>3 (8)</td>
<td>1 (2)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Legend: cTnI = cardiac troponin I; P = probability value; ECG = electrocardiogram; NS = not significant; mm = millimetre; Pa = Pascal; PCI = percutaneous coronary intervention; AMI = acute myocardial infarction; CABG = coronary artery bypass grafting
The release patterns of cardiac markers in the cTnI positive group are shown in Figure 1. The peak concentrations of H-FABP, myoglobin, cTnI, cTnT, and CK-MB mass were achieved at 2 hrs, 4–16 hrs, 16–24 hrs, 16–24 hrs, and 16–24 hrs respectively. Eighteen patients had an increase in cTnI concentration alone. Eight patients had some complications during PCI, whereas in 6 patients no specific complications were reported. However, in these patients the angioplasty was described as technically difficult and prolonged or the lesion was complex, and three patients had failure of stent deployment, sudden drop of blood pressure after sheath removal, and limb ischaemia post-procedure. Two patients in this group had total occlusion of the vessels and two had ostial lesions. In four patients with cTnI elevations (range 0.18–0.65 µg/L), no specific complications were reported to explain this rise.

The use of newer and potent antiplatelets treatment after PCI was liberal in this group of patients. Fifty-five patients (68%) received a combination of ticlopidine and/or clopidogrel and/or abciximab antiplatelets after stenting. The demographic and angiographic data of the cTnI positive and negative groups are shown in Table 1. Patients in the cTnI positive group were older (P < 0.02). Clinical and angiographic successes were reported more frequently in the cTnI negative group (95% versus 73%, P < 0.013), and (95% versus 81%, P < 0.04) respectively. Table 2 illustrates the procedural variables. There was a significant increase of the following in the cTnI positive group: chest pain ± ischaemic ECG changes during PCI (51.4% versus 13.9%, P < 0.004); numbers of stents used (42 versus 32, P < 0.019); and use of intravascular ultrasound during PCI (16% versus 2%, P < 0.045). There was no difference between the groups related to the total duration of PCI, the total numbers of balloon inflations per procedure, the number of lesions treated, balloon size, inflation time and pressure, or the antiplatelet regimes after PCI. The frequency and types of complications reported during and after PCI were significantly increased in the cTnI positive group. Out of the 37 patients in this group, 23 (62%) had complications compared to only 14 out of the 43 patients (32.5%) in the cTnI negative group (P < 0.03).

<table>
<thead>
<tr>
<th>Event</th>
<th>cTnI (+) group (n = 37)</th>
<th>cTnI (-) group (n = 43)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina control post-procedure</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Worse</td>
<td>10 (27)</td>
<td>10 (23)</td>
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<tr>
<td>Better</td>
<td>20 (54)</td>
<td>30 (70)</td>
<td>NS</td>
</tr>
<tr>
<td>Unchanged</td>
<td>7 (19)</td>
<td>2 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac event(s) during follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admitted with angina</td>
<td>5 (14)</td>
<td>3 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>Admitted with UA</td>
<td>5 (14)</td>
<td>2 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>Admitted with AMI</td>
<td>1 (3)</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Admitted with Heart failure</td>
<td>1 (3)</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Target vessel revascularisation</td>
<td>6 (16)</td>
<td>7 (16)</td>
<td>NS</td>
</tr>
<tr>
<td>Non-target vessel revascularisation</td>
<td>5 (14)</td>
<td>4 (9)</td>
<td>NS</td>
</tr>
<tr>
<td>Referred for CABG</td>
<td>3 (8)</td>
<td>3 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>Death</td>
<td>1 (3)</td>
<td>2 (5)</td>
<td>NS</td>
</tr>
<tr>
<td>Total No. with uncontrolled angina</td>
<td>17 (46)</td>
<td>12 (28)</td>
<td>NS</td>
</tr>
<tr>
<td>Total No. of patients with events</td>
<td>17 (46)</td>
<td>12 (28)</td>
<td>NS</td>
</tr>
<tr>
<td>Total No. of events per group</td>
<td>29 (78)</td>
<td>21 (48)</td>
<td>NS</td>
</tr>
<tr>
<td>Average duration of follow-up (months)</td>
<td>22.6 ± 1.5</td>
<td>23 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>Patients lost to follow-up</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Legend: cTnI = cardiac troponin I; P = probability value; NS = not significant; UA = unstable angina; AMI = acute myocardial infarction; CABG = coronary artery bypass grafting.
stents (19%, \( P < 0.003 \)); AMI (8%, \( P < 0.042 \)); side branch occlusion (SBO) (13.5%, \( P = \text{NS} \)); major technical failure of equipment during angioplasty (3%, \( P = \text{NS} \)); angina requiring re-catheterisation (13.5%, \( P = \text{NS} \)); and minor dissection (21.6%, \( P = \text{NS} \)).

Forty-two stents were used in this group compared to 32 stents in the cTnI negative group. The increased frequency of stents in this group was mostly to treat dissections (40.5% versus 17%, \( P = 0.05 \)). Thirteen stents (31%) were used mostly on a bail-out basis to treat major dissection ± acute vessel closure. The use of stents for sub-optimal angioplasty results was slightly more in the cTnI negative group (49% versus 40.4%). Three patients developed AMI after PCI (1 Q wave and 2 non-Q wave AMI). The concentrations of cardiac markers in these patients were significantly elevated. H-FABP was the first marker to appear in significant concentrations after AMI. Peak concentrations of H-FABP, myoglobin, CK-MB mass and troponins occurred at 2 hours, 4 hours, 16–24 hours, and 16–24 hours respectively after angioplasty. The release patterns of cardiac markers were similar to the release patterns seen in Figure 1. H-FABP reached diagnostic concentrations for AMI 1–2 hours post-angioplasty. The diagnosis of AMI based on myoglobin, CK-MB mass, and troponins was established at 2–4, 4–16, and 4–16 hours respectively. Five patients had SBO during angioplasty. In 3 patients, this complication followed an extensive dissection. Out of the 5 patients, two developed AMI, two had considerable chest discomfort and ST segment depression ± T wave inversion, and in one patient the SBO was asymptomatic. Cardiac-Tn concentration was elevated in all patients. The mean cTnI increase in these three groups was 14.7 µg/L, 1.73 µg/L, and 0.18 µg/L respectively. Creatine kinase-MB mass, and myoglobin were increased in three patients, whereas H-FABP and CTnT were increased in two patients only. In the cTnI negative group, two patients had asymptomatic SBO, but there was no increase in cardiac markers in any of them. Forty-three patients had cTnI < 0.18 µg/L. Fourteen patients (32.5%) in this group developed complications during PCI; however, the frequency and severity of complications in this group were considerably lower than the cTnI positive group. These complications included one patient with major dissection, two patients with transient SBO, and one patient with transient vessel closure. The types of complications reported in the remaining 10 patients were minor dissections, coronary spasm, elastic recoil, and minor technical problems.

After discharge, clinical follow-up was possible in 79 out of 80 patients (98.75%). The mean follow-up period was 22.3 ± 1.7 months (range 20–26 months). The incidence of adverse clinical events is summarised in Table 3. Patients who had cTnI elevation post-PCI had a non-significant higher incidence of complications (angina pectoris, UA, and non-target vessel revascularisation). The total number of clinical events per group in the cTnI positive and cTnI negative group was 29/37 (78%) versus 21/43 (48%) respectively, \( P = \text{NS} \).
The various subgroups of patients with SBO. These cTnI and other markers and different symptoms in AMI. There were different rises of concentrations of proteins after PCI. Heart-type-FABP was the earliest marker that could detect evolving AMI post-PCI, despite uneventful PCI. Their cTnI concentration was between 0.08–0.11 µg/L. Surprisingly, cTnT was highly predictive of the need for CABG on long-term follow-up. Fifty percent of patients with elevated cTnI after PCI were referred for CABG compared to only 4% of patients with normal cTnT after PCI (P < 0.004). There were no other statistical differences between the cTnT positive and negative groups when other cardiac events were compared between the two groups. The time-dependent effect of post-procedural cTnI elevation on late clinical outcome was assessed using the Kaplan-Meier survival analysis. There was a significant decrease in event-free survival with more recurrent angioplasty, repeat PCI, and CABG in the group of patients who had cTnI elevations during angioplasty [Figure 2]. The mean event-free survival for the group with cTnI elevation and those without cTnI elevation was 16.92 months (standard error (SE) = 1.66, 95% confidence interval (CI) = 13.67–20.18, median = 23 months) versus 20.67 months (SE = 1.64, 95% CI = 17.46–23.88, median = 27 months) respectively (P < 0.03). Event-free survival was also decreased in cTnI and H-FABP positive groups. There were no event-free survival differences when CK-MB mass or myoglobin positive and negative groups were compared.

Discussion

The frequency of cTnI increases post-PCI in patients with complications was much higher than that seen with myoglobin, CK-MB mass, H-FABP, and cTnT. Cardiac-TnI was the most useful marker for the detection and quantification of PCI related complications. This reflects the superior sensitivity of cTnI for the detection of small releases of myocardial proteins after PCI. Heart-type-FABP was the earliest marker that could detect evolving AMI post-PCI within 1–2 hours and the concentration had returned to normal within 16–24 hours. H-FABP may be a potential early marker that can help select patients with chest pain, in the early post-PCI period, for early investigations to ascertain the diagnosis of AMI. There were different rises of concentrations of cTnI and other markers and different symptoms in the various subgroups of patients with SBO. These differences may be related to the size of the side branch vessel, the extent of collaterals, and the duration of the occlusion. The occurrence of asymptomatic SBO, and also the absence of the rise of concentration of cardiac markers following documented SBO has been reported by others.10,13 Cardiac markers were also increased in the groups that had more stents and intravascular ultrasound investigations. Cardiac marker concentrations are elevated in some patients after PCI procedures involving stenting.21 However, this increase indirectly reflects more complications, for example dissection in this group. It is not clear whether the use of intravascular ultrasound during PCI contributes to myocardial injury or merely reflects underlying complications.

Cardiac-TnI was increased in a small numbers of patients who had no complications reported during PCI. This may be due to: 1) the formation of small thrombi at the angioplasty site that may subsequently embolise to small distal arteries leading to small areas of focal necrosis; 2) the inability of contrast angiography to detect complications (indeed, intravascular ultrasound has been shown to be much more sensitive for the detection of coronary dissection after PCI compared with contrast angiography: 83% versus 27.% 3) the variability of observers reporting complications and 4) mechanical trauma to the heart caused by guide wires manipulations within the coronary arteries. In our study, we found no apparent explanations for cTnI increases in 27% of patients, which was comparable to data published by Garbarz et al, who reported a 34% increase in cTnI concentrations in their study, which was not accounted for by complications during PCI.22 The increases in cTnI, cTnT, CK-MB mass in the group with SBO was in agreement with Genser et al., who reported an increase in these markers in patients with SBO even when this complication was asymptomatic.13

The total frequency of cTnI rise (46.25%) in this study was slightly higher than that reported elsewhere in the literature. This could be explained by the use of cTnI sensitive assays with a relatively low cut-off concentration (≥ 0.18 µg/L) to indicate myocardial injury post-PCI. The frequency of CK-MB mass elevation in our study (11.25%) was lower than that reported previously (15–26%). This could be related to differences in assay methods used. Kugelmass et al. reported elevated CK-MB in 11.5% of patients following elective PCI, with no clinical sequels over
two years follow-up. However, in a small subset with a greater elevation of CK-MB, there was a trend towards decreased late survival compared to patients without CK-MB elevation. They also reported common CK-MB elevation after coronary stenting. An increased frequency of cardiac events on long-term follow-up (angina, PCI, CABG) was noticed in some patients who had very small increases of cTnI concentration (0.08–0.1 µg/L), which suggests that even small increases of cTnI may have a significant prognostic value and may reflect more diffuse or extensive CAD.

Long-term complications in patients with elevated cardiac markers post-PCI have been suggested by Abdelmeguid et al., who reported more frequent and more serious complications (e.g. death and AMI). These differences could be related to several factors. First, the follow-up period in our study was relatively short compared to the study by Abdelmeguid (3–5 years, in some patients up to 8.5 years). Second, the use of stents was more frequent in the group of patients with elevated cardiac markers concentrations, which may alter the short-term risk of further progression to more serious complications.

Third, the use of newer and more potent antiplatelets regimes (clopidogrel, abciximab) was also high in our study. The clinical benefit of these antiplatelets compounds in reducing the progression to AMI and death in patients with myocardial injury is well-established. Despite the fact that there were no statistically significant differences between the numbers of events, there was still a significant difference with respect to event-free survival between groups with and without elevations of these markers after angioplasty.

Increases in cTnI after PCI had been described previously. Ravkilde et al. found moderate increases in CK-MB mass in 6 of 23 patients (26%) undergoing visually successful PCI, whereas only 3 (13%) showed cTnI elevation. In this study, the percentage of positive cTnI results after PCI was only 7.5% using a third generation cTnI assay that was very sensitive (< 0.01 µg/L) and specific. Some of the previous studies used a lower cut-off concentrations e.g. ≥ 0.04 µg/L or ≥ 0.06 µg/L, to indicate the presence of myocardial injury post-PCI.

Increased cTnT ≥ 0.06 µg/L has also been found to be associated with increased risk of death and AMI (10.5%) compared to cTnT ≤ 0.06 µg/L. Based on ROC curve analysis, a cut-off concentration of cTnT ≥ 0.06 µg/L was slightly more sensitive and equally specific to cTnT ≥ 0.1 µg/L for the detection of complications. Depending on whether the cut-off concentration used was ≥ 0.1 µg/L or ≥ 0.06 µg/L, the frequency of abnormal cTnT elevations was 7.5% and 12.5% respectively. Despite the low sensitivity of cTnT, the specificity and positive predictive value for the detection of complications was very high. Event-free survival of patients with elevated cTnT concentrations was significantly lower than those without cTnT elevations after angioplasty. Cardiac-TnT was also associated with increased risk of CABG on long-term follow-up thus validating the prognostic significance of cTnT elevations post-PCI.

Measurements of cardiac markers post-PCI will be a useful adjunct to angioplasty and will help detect patients with subtle myocardial damage and may guide further management. Twelve patients (32%) with elevated cTnI in our study did not receive any form of antiplatelets (other than aspirin) during or after PCI. The cTnI concentrations range in these patients were 0.18–2.12 µg/L. Eight out of these 12 patients had worsening of their angina or further cardiac events during follow-up.

**Conclusion**

Heart-type-FABP measurements at 1 hour (or thereafter) post-PCI in patients with suspected complications may offer the best early chance of detecting evolving AMI. Cardiac-TnI has emerged as the most sensitive marker for the detection of major complications in patients undergoing PCI. It offers a reliable detection of myocardial damage that is sometime not obvious by visual assessment alone. The adjunctive measurements of cardiac markers post-PCI could help identify certain groups with elevated cardiac markers concentrations that might benefit from long-term treatment with newer antiplatelets therapy. Measurements of cTnI 16–24 hours post-PCI should be part of the work-up management of patients following elective PCI.

**CONFLICT OF INTEREST**

The authors report no conflict of interest.

**References**

1. Parisi AF, Folland ED, Hartigan P. A comparison of angioplasty with medical therapy in the treatment of


Heart-Type Fatty Acid-Binding Protein in the Early Diagnosis of Acute Myocardial Infarction

The potential for influencing patient management

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**ABSTRACT:** Objectives: The objective of this study was to evaluate the diagnostic value of heart-type fatty acid-binding protein (H-FABP) in patients with acute chest pain and compare it with standard cardiac markers. Methods: We undertook a prospective evaluation of 100 consecutive patients admitted with acute chest pain suggestive of acute coronary syndromes (ACS). Serum cardiac troponin I (cTnI), cardiac troponin T (cTnT), creatine kinase-MB (CK-MB) mass, myoglobin, and H-FABP were determined at presentation and 2, 4, 8–10, and 16–24 hours after presentation. The main outcome measure was the best sensitivity value within 6 hours after symptom onset. Results: H-FABP peak concentration occurred at 8 hours after symptoms onset and was the most sensitive early marker with 79.9% and 98% of patients with AMI identified at presentation and 2 hours after presentation respectively. The sensitivity of all other cardiac markers (CK-MB mass, cTnI, cTnT, and myoglobin) at presentation was < 62%. The negative predictive value of H-FABP (94%) was also superior to other markers within the first 2 hours of presentation. Myoglobin was the second most sensitive early marker at presentation. Peak sensitivity of cTnI, CK-MB mass, and cTnT were present at 4, 8–10, and 8–10 hours respectively after presentation. Conclusion: Combined measurement of H-FABP and cTnI on two occasions during the first 8 hours after symptom onset was sufficiently sensitive and specific for the early diagnosis of most patients with acute MI and may provide advantages over other cardiac marker combinations.

Keywords: Acute myocardial infarction; Acute coronary syndromes; Heart-type fatty acid-binding protein; Cardiac markers.
Heart pain is a non-specific complaint and is the most frequent reason for patients to seek urgent medical attention.\(^1\) A proportion of these patients will be in the process of evolving acute myocardial infarction (AMI) and, of these, about 25% lack the diagnostic features of infarction at presentation despite subsequently evolving Q wave infarcts. Current diagnostic and triage systems based on clinical history and electrocardiogram (ECG) results lack both sensitivity and specificity. Between 2 and 10% of patients with AMI may be inadvertently discharged from accident and emergency (A&E) departments leading to serious health and legal consequences. Conversely, inappropriate admissions of a large number of patients without acute coronary syndromes (ACS) will have substantial cost implications.\(^2\) Cardiac markers are critical in making the diagnosis of AMI but, thus far, their role has mainly been for retrospective confirmation of AMI, 12–24 hours after admission. Creatine kinase (CK), CK muscle and brain (CK-MB) and troponins lack sufficient precision within the first 6 hours of presentation. Myoglobin is an early marker of myocardial injury, but has poor specificity.\(^3\)

Heart-type fatty acid-binding protein (H-FABP) is a novel marker with the potential for the early diagnosis of AMI within 6 hours of symptoms onset.\(^4\) Its sensitivity for the diagnosis of AMI is comparable with myoglobin; however, the specificity of H-FABP for myocardial tissue is significantly better than that of myoglobin.\(^5\) This early release of H-FABP coupled with relative cardiac tissue specificity are potential advantages that may be valuable for the early diagnosis, triage, and management of patients with AMI.\(^6,7\) To date, there have been few studies comparing the value of these markers for the early diagnosis of AMI.\(^8\) The aim of the current study is to compare the value of H-FABP for the early diagnosis of AMI with other cardiac markers such as myoglobin, creatine CK-MB mass, serum cardiac troponin I (cTnI), and cardiac troponin T (cTnT) in a standardised setting.

### Methods

Included in the study, over a seven months period in 2002, were 100 consecutive patients with acute chest pain admitted within 6 hours of symptoms onset through the A&E Department at the Royal Infirmary of Edinburgh. Ethical approval was obtained from the local ethical committee, the Lothian Health Board, Edinburgh, UK. Informed consent was obtained from each patient before beginning the study. All enrolled patients were evaluated by the A&E Department physician. The evaluation included a brief history and physical examination and a recording of a 12-lead ECG. The time of onset of symptoms was carefully recorded for each patient at presentation. Five serial blood samples beginning at 0 hour (at presentation), 2 hours, 4 hours, 8–10 hours, and 16–24 hours after presentation and cTnI, cTnT, CK-MB mass, myoglobin, and H-FABP were measured at each time interval. All sequential patients were included in this study if they presented within 6 hours after the onset of symptoms, and had prolonged ischaemic chest pain (≥ 10 minutes in duration) suggestive of ACS, with or without ECG changes suggestive of ischaemia. Patients were excluded from the study if they had: 1) repeated intramuscular injection; 2) cardiac arrest at presentation; 3) recent surgery, coronary artery bypass graft (CABG) or AMI (< 1month); 4) any evidence of renal impairment or hypothyroidism.

The diagnosis of ST elevation myocardial infarction (MI) was based on the revised definition of MI and had to include at least two of the following three findings: 1) clinical history of prolonged ischaemic chest pain ≥ 30 minutes in...
Table 1: Demographic and clinical data of patients in the various study groups. Continuous variables are presented as mean ± SD and categorical variables are presented as percentages (in brackets).

<table>
<thead>
<tr>
<th>Demographic &amp; clinical data</th>
<th>STEMI Group 1</th>
<th>Non-STEMI Group 2</th>
<th>UA Group 3</th>
<th>Angina/atypical Group 4</th>
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</thead>
<tbody>
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<td>14</td>
<td>20</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>66.58 ± 11.74</td>
<td>67.36 ± 11.34</td>
<td>67.45 ± 12.31</td>
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<td>9 (64)</td>
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<td>12 (57)</td>
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<td>16 (36)</td>
<td>5 (36)</td>
<td>4 (20)</td>
<td>9 (43)</td>
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</tr>
<tr>
<td>Time to presentation (hrs)</td>
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<td>10 (50)</td>
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<td>4 (19)</td>
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</tr>
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</tr>
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<tr>
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<td>9 (45)</td>
<td>13 (62)</td>
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</tr>
<tr>
<td>FHx of IHD</td>
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<td>3 (21)</td>
<td>1 (5)</td>
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<td>Admission</td>
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<tr>
<td>HR</td>
<td>72.97 ± 17.14</td>
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<td>66.92 ± 11.18</td>
<td>77.0 ± 16.35</td>
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<tr>
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<tr>
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<td>ECG changes at admission</td>
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<tr>
<td>Persistent ST elevation</td>
<td>39 (87)</td>
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<td>1 (7)</td>
<td>5 (25)</td>
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Legend: SD = standard deviation; STEMI = ST elevation myocardial infarction; UA = unstable angina; AMI = acute myocardial infarction; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; DM = diabetes mellitus; HTN = hypertension; FHx of IHD = family history of ischaemic heart disease; HR = heart rate; BP = blood pressure; ST, T, Q, = ST segment, T wave segment, Q wave segment of electrocardiogram (ECG); NS = not significant.
duration; 2) evolution of typical changes in at least two adjacent leads of the ECG, appearance of ST segment elevation > 2 mm 0.08 seconds after J point persisting for at least 24 hours with or without Q waves, defined as ST elevation MI; 3) a time-dependent rise in concentration of CK-MB or troponins and a subsequent fall. Unstable angina was diagnosed when patients had two or more of the following criteria without clear-cut ECG changes of infarction or cardiac markers (troponins or CK-MB) elevations diagnostic of AMI: 1) ischaemic chest pain ≥ 10 minutes in duration; 2) transient ST segment elevation ≥ 1 mm 0.08 seconds after J point less than 30 minutes in duration; 3) transient or persistent ST segment depression ≥ 1 mm 0.08 seconds after J point in two adjacent leads; 4) symmetrical or asymmetrical T wave inversion ≥ 1 mm excluding T wave inversion in leads III, AVR, and V1 only. Patients were diagnosed as having non ST elevation MI if they had one or more of the criteria listed above and in addition, they had evidence of myocardial necrosis as reflected by CK-MB or troponin elevation and a subsequent fall. Patients were diagnosed as having atypical or anginal chest pain if they had all the following criteria: 1) typical or atypical presentation of chest pain; 2) none of the above listed ECG changes and 3) no rise in CK-MB or cTnI.

Patients were divided into four main groups for comparison: Group 1 included patients with ST elevation MI, the ‘STEMI group’; Group 2 included patients with non ST elevation MI, the ‘Non-STEMI’ group; Group 3 included patients with unstable angina (UA), the ‘UA group’; Group 4 included a heterogeneous population of patients with mixed medical diagnoses other than the above. Patients in Group 4 were referred to as ‘atypical/anginal chest pain group’. The selected diagnostic cut-off concentrations were based on receiver operator characteristic (ROC) curve analysis [Figures 1A and 1B] between patients with MI (STEMI and non-STEMI groups, n = 59) and controls (atypical/anginal chest pain group, n = 21 and healthy blood donor controls, n = 20). These cut-off concentrations were CK-MB mass ≥ 5 µg/L (sensitivity = 86.3%, specificity = 99%); cTnI ≥ 0.18 µg/L (sensitivity = 90.8%, specificity = 99%); cTnT ≥ 0.1 µg/L (sensitivity = 76.4%, specificity = 99%); H-FABP ≥ 12.5 µg/L (sensitivity = 91.4%, specificity = 86%), and myoglobin ≥ 95 µg/L (sensitivity = 81.2%, specificity = 99%).

The laboratory analysis of cTnI, CK-MB mass, and myoglobin was done on a Stratus CS analyser machine (Dade Behring, Germany), using commercially available test materials. The coefficients of variations for cTnI were 6.8%, and 6.7% at concentration range 0.24–0.36 µg/L, and 4.6–6.9 µg/L respectively. H-FABP was analysed by an enzyme linked immunosorbent assay method using commercially available assays (Hycult, Cambridge, England).

Figures 1A and B: Receiver operator characteristic (ROC) curves that were used to derive the cut-off concentrations for A) the various cardiac markers (blue = CK-MB mass concentrations; green = cTnI concentrations; red = cTnT concentrations; black = myoglobin concentrations); and B) H-FABP. See text for sensitivity and specificity values.
The analytical sensitivity of H-FABP (mean ± 2SD) was 0.206 ± 0.047 µg/L. The coefficient of variation for H-FABP measurements was always < 10%. Cardiac-TnT was analysed on Elecsys 2010 using commercial assays (Roche, Germany). The reference ranges quoted by the manufacturer for CK-MB mass, cTnI, myoglobin, cTnT, and H-FABP assays were validated by assaying the normal ranges of 20 healthy blood donor samples (10 males and 10 females). The mean ± SD concentrations of these markers were CK-MB mass = 1.52 ± 0.8 µg/L; cTnI = 0.015 ± 0.006 µg/L; myoglobin = 41.5 ± 13.3 µg/L; cTnT = 0.011 ± 0.002 µg/L, and H-FABP = 6.86 ± 2.21 µg/L.

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS™, Pittsburgh, statistical software, Version 12). Variables were expressed as mean ± SD. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were measured for each marker at each time interval after presentation and compared. Chi-square tests were used to explore the group differences with respect to categorical variables. The Kruskal–Wallis H-test was conducted to compare continuous variables and mean cardiac markers concentrations differences in the four groups. Significant results are indicated by probability values less than or equal to 0.05.
Panel A: Patients with ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (Non-STEMI)

Panel B: Patients with unstable angina and atypical/anginal pain

Legend: CK-MB = creatine kinase-muscle & brain; cTnI = serum cardiac troponin I; H-FABP = heart-type fatty acid-binding protein

Figure 2: Illustrates the release pattern (time-concentration profile) of the different cardiac markers at each time after presentation in patients in the various study groups. The data for cTnT were omitted from the graph because they were on a different scale, but were similar to those of cardiac troponin I.
Results

Out of 100 consecutive patients presenting with acute chest pain, 45 patients (45%) had ST elevation MI (Group 1), 14 patients (14%) had non-STEMI (Group 2), 20 patients (20%) had UA (Group 3). The last 21 patients (21%) constituted Group 4. The demographic and clinical data of the patients in these four groups is shown in Table 1. The study group consisted of 66% males. The mean age, percentage of males/females, the prevalence of risk factors, and the prevalence of previous cardiac disease (CABG, PCI) were not significantly different between the groups. The prevalence of previous angina ($P < 0.05$), systolic blood pressure ($P < 0.024$) and type of chest pain at presentation ($P < 0.027$) were statistically different. Figure 2 illustrates the release characteristics of cardiac markers in the four groups. For the STEMI group, myoglobin and H-FABP were the earliest makers of myocardial injury. The peak concentrations of myoglobin and H-FABP were reached in samples taken 2 hours after presentation (8 hours after symptoms onset). The peak concentrations of CK-MB mass and cTnI occurred at 8–10 hours after presentation (14–16 hours after the onset of chest pain). The peak concentrations of cTnT occurred at 16–24 hours after presentation (24–30 hours after onset of symptoms). H-FABP and myoglobin concentrations decreased significantly at 16–24 hours, whereas CK-MB mass, cTnI, and cTnT were still present in high concentrations. For the non-STEMI group, H-FABP and myoglobin peak concentrations were achieved at 2 hours and the concentrations of these markers had decreased to normal levels at 16–24 hours after presentation. For CK-MB mass, the peak concentration occurred at 8–10 hours. The maximum increase in cTnI and cTnT occurred late at 16–24 hours. The concentrations of CK-MB mass, cTnI, and cTnT were still present in significant levels at 16–24 hours.

Figure 3 is a line chart representation of the sensitivity values of cardiac markers for the diagnosis of MI in the STEMI only group, n = 45 patients. H-FABP was the most sensitive marker at presentation (75.5%), and it remained elevated with a sensitivity of 100% for the next 2–8 hours after presentation. H-FABP sensitivity was also superior to other markers within the first two hours of presentation. Myoglobin and CK-MB mass sensitivity were similar in the first 2 hours (93%). However, the peak sensitivity of myoglobin (93%) and CK-MB mass (100%) were reached at 2 hours, and 8–10 hours respectively. Cardiac-TnI reached higher sensitivity (97.7%) earlier (2 hours) than myoglobin, CK-MB mass, and cTnT. The sensitivity of cTnT gradually increased from a low level at presentation (24%) to the highest level (100%) at 8–10 hours after presentation [Figure 3].

The overall sensitivity, specificity, PPV, and NPV were determined for the whole group (n = 100 patients). Table 2 shows the percentages of these values for the different cardiac markers at each time interval after presentation. H-FABP still had the
Heart-Type Fatty Acid-Binding Protein in the Early Diagnosis of Acute Myocardial Infarction

The potential for influencing patient management

The highest sensitivity at presentation (79.9%). Almost all patients (98%) with MI were diagnosed within 2 hours after admission (8 hours after onset of symptoms). The specificity of H-FABP at 2 hours was 93.3%. Compared to other markers, H-FABP had the highest NPV (94%) at 2 hours. The PPV of H-FABP was also high (98%). Myoglobin had the second highest sensitivity at 0 hour (59.4%) rising to 87.5% two hours after presentation. The corresponding specificity, PPV, and NPV were 93.75%, 98.24%, and 65.22% respectively. All other cardiac markers had low sensitivities at 0 hr (i.e. at presentation) 32.8%, 42%, 56% for cTnT, CKMB mass and cTnI respectively. The specificity, PPV, and NPV by CK-MB mass, cTnI, myoglobin, and H-FABP respectively. Most of the cardiac markers had high PPV (92–100%). The performance of cTnI was better than cTnT in terms of overall sensitivity, specificity, PPV, and NPV. Reliable sensitivity, specificity, PPV, and NPV by CK-MB mass and cTnI were observed at 4 hours after presentation. Reliable sensitivity (96.9%), specificity (93.75%), PPV (98.4%), and NPV (88.23%) of cTnT were evident at 8–10 hours after presentation.

Discussion

In patients presenting with AMI, H-FABP appeared to be a reliable cardiac marker indicator 6 hours after symptom onset, peaked at 8 hours and had decreased significantly towards normal concentrations by 16-24 hours after presentation. These two features of H-FABP, early concentration peak following myocardial injury and rapid return to normal base line concentration, differentiate this marker from the troponins and CK-MB. They suggest the potential of H-FABP for early detection of myocardial injury and early detection of re-infarction. The sensitivities of H-FABP (75.5% and 79.7%) for the detection of AMI, observed within the first 6 hours after symptoms onset in this study, was in agreement with some previously published data. In our study, H-FABP was the most sensitive marker at presentation and within the first two hours after presentation (i.e. 8 hours after symptom onset) and demonstrated the highest NPV (94%). This was consistent with other previously published data. A study by Alansari et al. showed that myoglobin and H-FABP provide little clinical value when measured on admission in patients presenting with chest pain. Most of the standard cardiac markers in Alansari’s study had limited diagnostic value at presentation. The overall NPV of all cardiac markers was low < 52% within the first 6 hours after symptom onset. The sensitivity of these markers for the early diagnosis of AMI was < 62%. Bakker et al. reported low sensitivity (< 64%) and low NPV of routine cardiac markers CK-MB mass, cTnT, myoglobin, CK-MB activity, and CK to allow early exclusion of AMI. This study highlights two important facts: 1) H-FABP was more sensitive than myoglobin and 2) H-FABP had higher NPV than myoglobin. High sensitivity is essential for the early ‘rule in’ of patients with AMI, and high NPV is important for the early ‘rule out’ of AMI, since more than 90% of patients who present with acute chest pain to an A&E department do not have AMI. This superiority of H-FABP over myoglobin may be attributable to the fact that 1) the myoglobin content of skeletal muscle is twice that of the heart (hence interference from skeletal muscle injury i.e. less specific) whereas the H-FABP content of skeletal muscles is only 10–50% of that of the heart and 2) the normal plasma concentration of H-FABP (< 5 µg/L) is 10–15 fold lower than that of myoglobin (20–80 µg/L). Hence, the differing features of myoglobin and H-FABP allow the use of lower, but more discriminate, cut-off concentrations of H-FABP thus improving the sensitivity. The limitation of the enzyme-linked immunosorbent assay (ELISA) method, which produces results in around 90 minutes, could be overcome by using the new rapid bed-side H-FABP tests. However, as it is solely excreted by the kidney, this cardiac marker has limitations in patients with renal impairment and skeletal muscle injury.

Conclusion

The main conclusions of this study are, first, that H-FABP was superior to myoglobin (and other markers) for the early diagnosis of AMI within 6 hours after symptom onset. Second, the diagnostic window for H-FABP is relatively prolonged (up to 14 hours after symptom onset). This diagnostic window provides sufficient opportunity for the detection of AMI and initiation of appropriate therapy. Third, cTnI, as measured on the Stratus CS machine, was highly sensitive supporting its use for
the early detection of patients with AMI. Fourth, measurement of H-FABP and cTnI at two intervals during the first 8 hours after symptom onset was sufficiently sensitive and specific for the early diagnosis of most patients with AMI. We propose an alternative: that H-FABP should be combined with a specific marker like cTnI. The combination of H-FABP and cTnI improves specificity for a definitive diagnosis of AMI. We also propose that this combination should be tested in a larger-scale study and, if the current findings are confirmed, H-FABP and cTnI may constitute the standard combination for early diagnosis of MI.

ACKNOWLEDGMENTS
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CONFLICT OF INTEREST
The authors report no conflict of interest.

References
Antenatal Care Seeking Behaviour among Slum Mothers
A Study of Rajshahi City Corporation, Bangladesh

Mahfuzar Rahman,*Rafiqul Islam and Mosfequr Rahman

OBJECTIVES: The study aimed to identify the important effects of some selected variables in antenatal care (ANC) seeking behaviour among slum mothers.

METHODS: The data for the study were collected in 2006 from 700 mothers in the slum areas of Rajshahi City Corporation (RCC), Bangladesh. Results: The results indicate that tetanus toxoid (TT) is relatively widespread in slum areas of RCC. Serious health implications were observed for the mothers and their children who lived in the study areas because more than half of the respondents (56.1%) were not assisted at their last childbirth by any health professional. The respondents were too poor to buy iron tablets/syrup and vitamin tablets/syrup during their last pregnancy. The application of a logistic regression model suggested that demographic and socio-economic factors were associated with ANC seeking behaviour among slum mothers.

CONCLUSION: Respondents’ education, place of treatment, husband’s occupation, family’s income, and exposure to mass media had highly significant effects on mothers seeking medical checkups during their last pregnancy.

Key words: Care, prenatal; Mothers; Slums; Logistic regression; Immunization program; Tetanus toxoid; Bangladesh.

Advances in Knowledge
1. This study found that the following demographic and socio-economic factors were associated with antenatal care-seeking behaviour among slum mothers of Rajshahi City Corporation in Bangladesh: respondent’s education, husband’s occupation, family income, and exposure to mass media.

2. These factors should be increased in order to boost antenatal care and reduce fertility, morbidity as well as mortality not only in slum areas of Bangladesh, but also in all underprivileged regions of the world.

Application to Patient Care
1. Government and non-governmental organisations should accelerate medical facilities to increase antenatal care for women in the slum area of Rajshahi City Corporation in Bangladesh.

2. Mass media has a great role to play in creating awareness about antenatal care among women in the slum areas as well as among underprivileged populations elsewhere.
Bangladesh is a small South Asian country which became independent in 1971 after a bloody war. Rapid urbanisation in Bangladesh (26% of the 147.1 million inhabitants live in urban areas) is fuelling a growth in urban poverty, particularly in the urban slums where the quality of life is extremely poor. \(^1\) The average population density in slums was reported in 2005 as 831 persons per acre or 205,415 people per square kilometre. \(^2\) Despite significant improvements, the maternal mortality ratio and infant mortality rate remain high (380 and 50 per thousand respectively). \(^1\)

Antenatal care (ANC) is the medical supervision given to a pregnant woman and her baby starting from the time of conception up to the delivery of the baby by a physician, midwife or obstetrician or a combination of these professionals. It includes regular monitoring of the mother and her baby throughout pregnancy by a variety of routine regular examinations and tests (some routine and some for special circumstances). It also includes planning for pregnancy and continues into the early neonatal and postpartum period. Only 9% of births in Bangladesh take place at a health facility, while almost all others are home deliveries and only 55.9% of mothers receive some form of ANC. \(^3\) Ideally, all pregnant women should have regular antenatal checkups either by a paramedic or by a doctor. The Bangladesh Demographic and Health Survey (BDHS) reported that about 44% of the pregnant women, who gave birth during the five years prior to the 2004, did not receive any ANC visit, while 16.1% received only one visit. In rural Bangladesh, the majority (81.6%) of the women had only one ANC visit, while 14.6%, 3% and 0.8% had two, three and more than three visits respectively. The median gestational age at the first antenatal visit was 7 months; 74.3% of the first antenatal visits took place between the sixth and the eighth month of pregnancy. The midwife was present around the time of labour and/or delivery in the case of 3,909 (40.7%) of the women who received ANC compared to only 748 (11.1%) of the women not receiving it (relative risk = 3.73, \(P = 0.000\)). About one quarter (26.5%) of the women who received ANC experienced a labour or delivery complication, including the 21 women who died as a consequence of pregnancy. \(^4\)

A study showed that the odds of having a live birth is 11.807 times higher among women who had good ANC and good health than those who lacked good health and had no ANC services. \(^5\) Another study on syphilis in the antenatal period also showed that completed treatment was significantly associated with age of gestation at first visit (\(P = 0.029\)), with women attending later in pregnancy less likely to receive all three doses of treatment. \(^6\) More recently, the potential of the antenatal period as an entry point for HIV prevention and care, in particular for the prevention of HIV transmission from mother to child, has led to renewed interest in access to and use of ANC services. \(^7,8\)

In 2001, the WHO published the conclusions of a randomised controlled trial of a new model of ANC [Figure 1] and also carried out a systematic review of other randomised trials that looked at the effectiveness of different models of ANC. \(^9\)

Pregnancy and childbirth related complications are the leading causes of maternal morbidity and mortality in Bangladesh. This exploratory study was important because it gave a picture of the state of ANC in the slum areas and will help to indicate necessary changes in customs and laws to improve existing ANC programmes with a view to reducing maternal morbidity and mortality in Bangladesh.

Therefore, the main aim and objective of this study was to determine the effects of some selected variables on ANC seeking behaviours among slum mothers.

Methods

The data for this study were collected in 2006 from 8 different slums of 3 wards of RCC, Bangladesh. Seven hundred married women, aged 15-49 years, were selected using a purposive sampling technique and took part in face-to-face interviews. Those women who had no child less than five years of age at the time of the interview were not included in this study. Taking an antenatal check-up, coded as 1 if the mothers took any medical checkup during last pregnancy or 0 if otherwise, was taken as the dependent variable in the logistic regression analysis. The following explanatory variables were considered in this study: type of births, respondent’s education, access to mass media, family’s monthly income, electricity supply in the home, husband’s occupation, household asset index, place of treatment and type of latrine. The 700 respondents
were selected from 8 different slums of 3 wards, as shown in the Table 1.

The linear logistic regression model was employed to determine the factors associated with ANC seeking behaviour among the women in the study area and the relative effects of various characteristics on ANC seeking. The independent variables used in the logistic regression model are shown in Table 5.

The city of Rajshahi stands on the bank of the river Padma. It is basically an administrative centre having a population of 489,514 in 2005 spread over 51.3 square kilometers. There are 641 slum clusters in the city with a population of 156,793 (32% of the total city population). Most of the slum dwellers originate from the immediate vicinity of the city, and were driven to the slums by, among other things, erosion along the river Padma. The large slums are located on the left bank of the river in the city protection embankment.

The people of Rajshahi city get health services from different hospitals like Rajshahi Medical College Hospital (RMCH), the Christian Mission Hospital, and the T.B. Hospital etc. Other general hospitals are Bangladesh Rifles (BDR) Hospital, Combined Military Hospital (CMH), and the Prison Hospital where there is no access for general public. Non-government (NGO) services addressing health issues of the poor are limited. The RCC is conducting an Asian Development Bank-Government of Bangladesh (ADB- GOB) financed project, the NGO Services Delivery Program (NSDP), within the RCC area with a view to improving the health of the urban poor and reducing preventable mortality and morbidity by increasing access to primary health care. These projects are run by two NGOs, namely Anannya and Tilottoma, under an agreement with RCC. The services provided by these NGOs mainly focus on maternal and infant health care, growth monitoring and feeding, supply of family planning materials etc. and take Taka 10 (= $0.143) as a consultation fee.

Moreover, the Bangladesh Rural Advancement Committee (BRAC) is one of the remarkable NGOs working for the health promotion of the urban poor in Rajshahi. The women can receive pregnancy check up services from BRAC’s health unit by paying Taka 15 (= $0.215). The RCC is also operating the City Hospital to provide preventive, curative and promotional health care services to the poor and taking Taka 5 (= $0.072) as a consultation fee.

Under the Support for Basic Services in Urban Area (SBSUA) project, RCC also provides health services to the urban poor in the form of immunisation against six Expanded Program on Immunization (EPI) diseases to children under one year of age; tetanus toxine (TT) vaccination of women aged 15-49; maternal and infant care; growth monitoring; prevention and treatment of diarrhoea etc. The slum dwellers tend not to choose government facilities as government dispensaries are probably not near their locality and they are

Figure 1: The new WHO antenatal care (ANC) model (2001)
often unaware of these facilities. Even when they have heard about government facilities, they do not know what type of treatment is provided and are not sure whether they will get the treatment they require. In addition, there are several private clinics, but due to their higher costs low-income people cannot afford their services. They mainly go to local, traditional, mostly untrained, but cheaper, practitioners and sometimes use NGO facilities.

Results

**TETANUS TOXOID (TT) VACCINATION**

The TT vaccine is given to women during their childbearing age (15–49 years) to protect them from tetanus during their whole reproductive life and their newborns from neonatal tetanus. Neonatal tetanus is a fatal disease, caused by a pathogen transmitted during or after childbirth in unhygienic delivery. A woman needs a total of five TT doses for the protection of the whole reproductive period, and these should be administered according to the following schedule recommended by WHO: TT1, the first dose, at the age of 15 years; TT2 four weeks or more, after TT1; TT3 six months or more, after TT2; TT4 one year or more after TT3; and TT5 one year or more, after TT4. For minimum protection, it is recommended that the pregnant women should receive at least two doses of the toxoid.

Table 2: Percentage distribution of women aged 15-49 by TT vaccine

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<tr>
<td>TT4</td>
<td>83.4</td>
</tr>
<tr>
<td>TT5</td>
<td>72.0</td>
</tr>
</tbody>
</table>

Table 2 presents the percentage distribution of women who received the TT1, TT2, TT3, TT4, and TT5 vaccines or not between age of 15 and the data collection period. From the Table 2, we see that the proportion of women who received TT1 dose was 92.6% although nationwide the TT1 dose coverage rate is higher (95%). This proportion drops to 83.4 and 72.0 percent for TT4 and TT5 doses respectively [Table 2]. The data indicates that TT coverage is relatively widespread in Bangladesh. Although there has been no change in recent years in ANC coverage, the proportion of women receiving TT injections has risen substantially.

**ASSISTANCE DURING LAST DELIVERY**

From the standpoint of child survival and maternal health, the first priority is a safe and clean delivery. Experience in both developed and developing countries shows that babies delivered under proper medical supervision are significantly less subject to health hazards. Safe delivery is an important element in reducing the health risks for mothers, especially in the case of births to younger mothers. These are often first births which carry higher risks than second, third or fourth births. Proper delivery with the assistance of a trained medical practitioner and hygienic conditions reduce the risk of infection and facilitate management of obstetric complications that can endanger the life of the mothers and their newborn. In this context, the respondents were asked about the assistance during their last delivery. We classified the respondents who were helped either by a health worker or nurse, or a doctor with Bachelor of Medicine and Bachelor of Surgery (MBBS), or a traditional birth attendant (TBA) or a combination of these, as ‘taking help from health professionals’ and we identified the remainder as taking help from non-health professionals/untrained birth attendants (UTBA).

Table 3 shows that more than half (56.1%) of the respondents did not receive professional help during their last delivery i.e. they received help from a UTBA or from people outside the health profession. So, we can say that there are serious
health implications for the mothers and their children who live in the study areas. This means that the importance of mothers going to a health facility for their childbirth is not properly promoted in the study areas.

TAKING IRON TABLETS/SYRUP AND VITAMIN TABLETS/SYRUP

Iron tablets/syrup and vitamin tablets/syrup are supplements necessary during pregnancy for the health of mothers and their unborn babies. Table 4 shows the percentage distribution of mothers according to whether they took iron tablets/syrup and vitamin tablets/syrup during their last pregnancy period, related to their family’s monthly income. For this purpose, we classified the respondent’s total family income into three groups as Taka ≤2000, Taka 2001–2500 and Taka 2501+ per month (US$ 28.5, $30–36 and over $37 per month respectively)

Although the percentage taking iron tablets/syrup and vitamin tablets/syrup during their last pregnancy increased somewhat with the increase of family’s monthly income, the overall percentage of those taking iron tablets/syrup and vitamin tablets/syrup is only 41.6% and 31.4% respectively, which is unsatisfactory [Table 4]. So, we can say that, irrespective of their level of income, well under half the respondents of the study areas do not take iron tablets/syrup and vitamin tablets/syrup during their pregnancy. This is no doubt because low monthly incomes prevent many from purchasing iron tablets/syrup and vitamin tablets/syrup.

MULTIVARIATE ANALYSIS

The results of the logistic regression analysis, presented in Table 5, show that the respondents’ education, place of treatment, husband’s occupation, family income, and exposure to mass media were significantly associated with going for an ANC checkup during the last pregnancy. Table 5 shows that education was the key factor among slum area mothers in seeking medical checkups during pregnancy; large and statistically significant differences were observed here despite having controlled for other variables. The relative odds ratio for literate mothers was found to be 1.994 indicating that the likelihood of medical checkup during the last pregnancy of literate mothers was 1.994 times higher than for illiterate ones. Husband’s occupation was another significant factor influencing medical checkup during pregnancy. The logistic co-efficient indicated that the highest occurrence of medical checkup during last pregnancy was among wives of service sector workers, followed by businessmen. These women were 1.214 and 1.078 times respectively more likely to go to medical checkup than the wives of labourers [Table 5].

Family income was also significantly associated with antenatal checkups in the last pregnancy. The results shows that women with a monthly family income of TK 2001–2500 and TK 2501+ (US$30–36 and over $37 per month respectively) were 1.052 times and 1.402 times respectively more likely to go for an antenatal medical checkup than the women with a monthly family income of TK ≤2000 (US$ 28.5) [Table 5]. Types of toilet facility had an effect on antenatal medical checkups; mothers with hygienic toilet facilities were 1.699 times more likely to go for antenatal medical checkups, but this effect is not statistically significant.

The result reveals that the mothers who go to hospitals and clinics for general health related
Discussion

The study indicates that the proportion of pregnant women in the study area who take TT injections is very high, but is still not 100% despite various measures taken by different authorities against this disease which is fatal to mothers and children. More than half of the births in slum areas take place without the assistance of any health professional. This may indicate that births take place in unhygienic conditions putting both mothers and their new borns at risk. As far as taking iron tablets/syrup and vitamin tablets/syrup is concerned, monthly income plays an important role. The results of the logistic regression indicated that medical checkups increased as the level of mothers’ education increased, as they come to realise the importance of antenatal medical checkups. Place of treatment is an important factor that may strongly affect whether mothers go for antenatal checkups. For this reason, the place of treatment is classified into two categories. In the first category, homeopathic, kabiraj (Bangladeshi medical practitioners without a degree in medical sciences) and others are included, followed by hospital and clinic. The results show that hospital and clinic is more likely to have medical checkups compared to homeopathic, kabiraj and others.

Table 5: Logistic regression estimates of regression coefficient and relative odds associated with medical checkup during last pregnancy.

<table>
<thead>
<tr>
<th>Background Characteristics</th>
<th>Coefficient (β)</th>
<th>Standard Error of β</th>
<th>Odds Ratio [Exp β]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respondent’s education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>Literate</td>
<td>0.690***</td>
<td>0.183</td>
<td>1.994</td>
</tr>
<tr>
<td>Husband’s occupation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labourer</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>Business</td>
<td>0.076</td>
<td>0.297</td>
<td>1.078</td>
</tr>
<tr>
<td>Service sector</td>
<td>0.194**</td>
<td>0.315</td>
<td>1.214</td>
</tr>
<tr>
<td>Family’s monthly income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2000</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>2001–2500</td>
<td>0.051**</td>
<td>0.555</td>
<td>1.052</td>
</tr>
<tr>
<td>2501+</td>
<td>0.388***</td>
<td>0.365</td>
<td>1.402</td>
</tr>
<tr>
<td>Types of latrine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unhygienic</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>Hygienic</td>
<td>0.530</td>
<td>0.301</td>
<td>1.699</td>
</tr>
<tr>
<td>Place of treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homeopathic, kabiraj and other</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>Hospital and Clinic</td>
<td>0.506***</td>
<td>0.169</td>
<td>1.659</td>
</tr>
<tr>
<td>Type of birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>2+</td>
<td>-0.070</td>
<td>0.178</td>
<td>0.932</td>
</tr>
<tr>
<td>Electricity in household</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>0.758</td>
<td>0.277</td>
<td>2.134</td>
</tr>
<tr>
<td>Household asset index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>Middle</td>
<td>0.350</td>
<td>0.598</td>
<td>1.419</td>
</tr>
<tr>
<td>Upper</td>
<td>0.581</td>
<td>0.444</td>
<td>1.788</td>
</tr>
<tr>
<td>Exposure to mass media</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not exposed</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>Exposed</td>
<td>0.812***</td>
<td>0.472</td>
<td>2.253</td>
</tr>
</tbody>
</table>

Legend: * = reference category; * = indicate P < 0.001 (highly significant); ** = P < 0.01 (significant); *** = P < 0.05 (less significant) respectively; Kabiraj = Bangladeshi medical practitioners without a degree in medical sciences.
while the secondly category is hospital and clinic. The results showed that the odds are higher for the mothers who go to hospitals and clinics for antenatal medical checkups. Mass media is also shown by this study to play a strong role by creating awareness about the pregnancy related complications and the negative effect these complications can have on the future health of mothers and their new born babies. Therefore, the role of mass media should be enhanced to reduce the overall pregnancy related morbidity and mortality in Bangladesh.

POLICY RECOMMENDATIONS
Effective policies are needed to improve existing ANC seeking behaviour in the slum areas of RCC. The specific recommendations are as follows:

1. ANC services such as childbirths need the assistance of health professionals; TT vaccination among the women should be enhanced in the study areas. Government, the private sector or NGOs, or all three should do this by increasing their funds and facilities.

2. The people of the study areas should be made aware of the available local health facilities and pregnant women should be encouraged to have antenatal medical checkups. This could be done by creating awareness among the slum people, especially among women, through mass media campaigns, and the education and employment sectors.

CONFLICT OF INTEREST
The authors report no conflict of interest.

References


Comparison of Ketorolac Tromethamine and Prednisolone Acetate in Preventing Surgically Induced Miosis during Cataract Surgery

Yusuf M Suleiman, Najwa F Krdoghli, *Aksam J Ahmad

Abstract: Objectives: The aim of this study was to compare the efficacy and safety of topical prednisolone acetate 1% and topical ketorolac tromethamine 0.5% in the maintenance of pupillary mydriasis during cataract surgery. Methods: Fifty patients were enrolled in this prospective, partially masked and randomised study. They were assigned to receive topical treatment with either prednisolone acetate (n = 25) or ketorolac tromethamine (n = 25), starting 24 hours before cataract extraction (either routine extracapsular cataract extraction or phacoemulsification). One drop of the study medication was instilled every 6 hours for a total of 4 drops. No epinephrine was used in the starting 24 hours before cataract extraction (either routine extracapsular cataract extraction or phacoemulsification). Results: The mean pupil diameter change from the time of the pre-incision until after cortical irrigation and aspiration and lens implantation was significantly less with ketorolac than with prednisolone (P = 0.003). Consequently, mean pupil diameter after cortical irrigation and aspiration and lens implantation was significantly greater with ketorolac than with prednisolone (P < 0.0001). No significant differences between groups were observed in the pupil diameter before the first incision (P = 0.244), nor after administration of a miotic agent (P = 0.505). Safety variables were comparable and no drug-related adverse events were reported. Conclusion: Ketorolac tromethamine 0.5% and prednisolone acetate 1% solutions were equally well tolerated without related adverse events, but ketorolac was better in preventing surgically induced miosis. Keywords: Ketorolac tromethamine; Prednisolone acetate; Cataract extraction; Miosis; Mydriasis.

Advances in Knowledge

1. Ketorolac tromethamine and prednisolone acetate are well tolerated when applied topically before cataract extraction.

2. Ketorolac tromethamine is very effective in preventing surgically induced miosis, while prednisolone acetate is not, despite the fact that both drugs inhibit the liberation of prostaglandins which are believed to be the main cause of surgically induced miosis and postoperative inflammation during cataract surgery.

3. Many previous studies have demonstrated that both drugs are equally effective in preventing and treating postoperative inflammation.

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Techniques for extracapsular cataract extraction (ECCE) have improved tremendously in the past few decades, with small-incision surgery nowadays being the standard treatment. Nevertheless, ocular tissue is traumatised during surgery leading to the activation of phospholipase A2, and the liberation of two groups of lipid molecules: arachidonic acid (AA) metabolites, and platelet-activating factors (PAFs). Arachidonic acid forms the substrate for further reactions mainly by the cyclo-oxygenase and the lipoxygenase pathways. The main products of the cyclo-oxygenase pathway are prostaglandins (PGs), and the main products of the lipoxygenase pathway are leukotrienes (LTs). Endogenous PGs produce many effects such as: miosis during surgery, postoperative inflammation, increased permeability of the blood-ocular barriers, conjunctival hyperaemia and change in intraocular pressure. Platelet-activating factors induce an impressive repertoire of responses in vitro and seem to be a major regulator of cell adhesion and vascular permeability in many forms of acute inflammation, trauma, shock, and ischaemia, but their precise role is still under investigation.

The decrease in pupil diameter can make cataract removal more difficult and increases the risk of surgical trauma, postoperative ocular inflammation, and posterior capsule rupture. Thus, maintaining adequate pupil dilation is considered an important part of ensuring that cataract removal proceeds smoothly.

Inhibition of PGs’ biosynthesis inhibits intraoperative miosis during cataract surgery, reduces the vascular permeability of the blood-ocular barrier, and modifies inflammation.

Non-steroid anti-inflammatory drugs (NSAIDs) inhibit the cyclo-oxygenase enzyme, so inhibiting the biosynthesis of PGs but not LTs. Topical ophthalmic NSAIDs have been shown to be effective in treating a variety of conditions in which prostaglandins are believed to play a causative role, including surgically induced miosis, postoperative inflammation, treatment and prevention of cystoid macular oedema (CME), and control the pain of refractive surgery. The NSAID ketorolac tromethamine has demonstrated efficacy in the prevention of surgically induced miosis, in the treatment of postoperative ocular pain, in the treatment of chronic aphakic and pseudophakic CME and in the prevention and suppression of ocular inflammation after cataract surgery.

Glucocorticoids inhibit the phospholipase A2 enzyme and consequently inhibit the biosynthesis of both platelet-activating factors and arachidonic acid. This results in the inhibition of the biosynthesis of both PGs and LTs. Topical steroids like prednisolone acetate have been the standard regimen postoperatively for many years and are known to prevent inflammatory reactions after cataract extraction.

Previous studies have not mentioned the role of corticosteroids in preventing surgically induced miosis, despite that corticosteroids inhibit PGs liberation. However, important side effects of topical steroids are increased intraocular pressure (IOP), impairment of wound healing and postoperative ocular infection.

The present study compared the efficacy and safety profile of ketorolac tromethamine 0.5% ophthalmic solution with that of prednisolone acetate 1% ophthalmic solution in maintaining pupillary mydriasis during cataract surgery. The primary efficacy variable was the change in pupil diameter.

Methods

This prospective, partially masked and randomised study was performed in the Ophthalmology Department, Al-Assad Hospital, Tishreen University, Latakia, Syria during the period March 2008 to March 2009. Patients who were scheduled to undergo unilateral cataract surgery (either routine ECCE or phacoemulsification) and posterior
chamber-intraocular lens (PC-IOL) implantation were enrolled in the study. The study protocol was approved by the appropriate institutional review board and written informed consent was obtained from all patients before enrollment in the study. Some cases were excluded according to the study protocol. Patients were not enrolled if they had any of the following features: were pregnant or lactating; only one eye with good visual acuity; any uncontrolled systemic or ocular disease; a history of uveitis or glaucoma; pseudoexfoliation syndrome; a history of any ocular disorder or surgery that might interfere with the surgical procedure or interpretation of the study results; a known sensitivity to any of the components of the study medication; use of systemic steroids or NSAIDs within 2 weeks before study entry, or topical ophthalmic drugs in the eye to be operated within 1 month before study entry. After this process, fifty patients were enrolled in the study. Randomly, 25 patients were given ketorolac tromethamine 0.5% solution (ROLAC Oubari Pharma, Aleppo, Syria) or prednisolone acetate 1% solution (PRED-ALPHA-FORT® ALPHA-Ind., Aleppo, Syria) according to a randomisation schedule, starting 24 hours before surgery. One drop of study medication was instilled every 6 hours, for a total of 4 drops.

Topical pupillary dilating agents (tropicamide 0.5% and phenylephrine 10%) were used, starting one hour before surgery, to induce operative mydriasis. Antimicrobial agents were used starting 24 hours before surgery, and retrobulbar anaesthesia was used in all patients. The intraocular irrigating solutions did not contain epinephrine, rather viscoelastics were used by all surgeons. A miotic agent (carbachol) was used after intraocular lens (IOL) implantation, only when the pupil was still markedly dilated, to study the effect of ketorolac and prednisolone on the carbachol efficacy. Any non-study medications that could interfere with interpretation of the study results (e.g. affect pupil diameter) were specifically prohibited by the study protocol. The surgery then proceeded as scheduled and all patients received a subconjunctival dexamethasone plus gentamycin injection at the end of the surgery.

Intraoperative pupil diameter was measured at three different times during surgery using a Castroviejo caliper and standard microscope at 10x magnification under full illumination. The first measurement (preincision [pre-I]) provided the baseline value and was taken immediately before the first incision. The second measurement was

<table>
<thead>
<tr>
<th>Table 1: Patients characteristics of the two study groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisolone group n = 25</td>
</tr>
<tr>
<td>Ketorolac group n = 25</td>
</tr>
<tr>
<td><strong>P value</strong></td>
</tr>
<tr>
<td>Age by Year</td>
</tr>
<tr>
<td>Mean ± SD 70.56 ± 8.39</td>
</tr>
<tr>
<td>Range 47–84</td>
</tr>
<tr>
<td>Prednisolone group n = 25</td>
</tr>
<tr>
<td>Ketorolac group n = 25</td>
</tr>
<tr>
<td><strong>P value</strong></td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Female 13 (52%)</td>
</tr>
<tr>
<td>Male 12 (48%)</td>
</tr>
<tr>
<td>Prednisolone group n = 25</td>
</tr>
<tr>
<td>Ketorolac group n = 25</td>
</tr>
<tr>
<td><strong>P value</strong></td>
</tr>
<tr>
<td>Pre-surgery IOP (mmHg)</td>
</tr>
<tr>
<td>Mean ± SD 13.88 ± 3.47</td>
</tr>
<tr>
<td>Right 14 (56%)</td>
</tr>
<tr>
<td>Left 11 (44%)</td>
</tr>
<tr>
<td>Prednisolone group n = 25</td>
</tr>
<tr>
<td>Ketorolac group n = 25</td>
</tr>
<tr>
<td><strong>P value</strong></td>
</tr>
<tr>
<td>Operated eye</td>
</tr>
<tr>
<td>Right 14 (56%)</td>
</tr>
<tr>
<td>Left 11 (44%)</td>
</tr>
<tr>
<td>Prednisolone group n = 25</td>
</tr>
<tr>
<td>Ketorolac group n = 25</td>
</tr>
<tr>
<td><strong>P value</strong></td>
</tr>
<tr>
<td>Procedure</td>
</tr>
<tr>
<td>ECCE 15 (60%)</td>
</tr>
<tr>
<td>Phaco 10 (40%)</td>
</tr>
<tr>
<td>Prednisolone group n = 25</td>
</tr>
<tr>
<td>Ketorolac group n = 25</td>
</tr>
<tr>
<td><strong>P value</strong></td>
</tr>
</tbody>
</table>

Legend: *= Analysis of variance test; ** = χ² test.; IOP = intraocular pressure; ECCE = extra capsular cataract extraction; Phaco = phacoemulsification
Comparison of Ketorolac Tromethamine and Prednisolone Acetate in Preventing Surgically Induced Miosis during Cataract Surgery

Table 2: Angiographic characteristics of both groups

<table>
<thead>
<tr>
<th></th>
<th>Ketorolac group n = 25</th>
<th>Prednisolone group n = 25</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-I pupil diameter (Mean ± SD)</td>
<td>7.72 ± 0.54</td>
<td>7.52 ± 0.65</td>
<td>0.244*</td>
</tr>
<tr>
<td>Post I/A pupil diameter (Mean ± SD)</td>
<td>6.28 ± 0.74</td>
<td>5.34 ± 0.72</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>Change in pupil diameter from pre-I to post I/A (Mean ± SD)</td>
<td>1.44 ± 0.96</td>
<td>2.18 ± 0.70</td>
<td>0.003*</td>
</tr>
<tr>
<td>Patients needing mydriatic agent during surgery</td>
<td>4 (16%)</td>
<td>14 (56%)</td>
<td>&lt; 0.005**</td>
</tr>
<tr>
<td>Patients who received carbachol</td>
<td>21 (84%)</td>
<td>13 (52%)</td>
<td>&lt; 0.025**</td>
</tr>
<tr>
<td>Post M pupil diameter (Mean ± SD)</td>
<td>3.76 ± 0.77</td>
<td>3.92 ± 0.49</td>
<td>0.505*</td>
</tr>
<tr>
<td>Change in pupil diameter from post I/A to Post M (Mean ± SD)</td>
<td>2.55 ± 1.18</td>
<td>1.61 ± 0.96</td>
<td>0.014*</td>
</tr>
</tbody>
</table>

Legend: * = Analysis of variance test; ** = χ² test; Pre-I = preincision; Post I/A = Post irrigation & aspiration; post M = post miotic
Note: Post M pupil diameter and change in pupil diameter from post I/A to Post M concerns only the eyes which received carbachol at the end of surgery.

taken at the end of surgery, after cortical irrigation and aspiration, and PC-IOL implantation, before postoperative administration of a miotic agent (post-irrigation and aspiration [post-I/A]). The final measurement was taken at the end of surgery, but only for the patients who had postoperative administration of a miotic agent (postmiotic [post-M]). Care was taken to avoid the presence of viscoelastic in the anterior chamber prior to measurements. The change in pupil diameter during the most traumatic part of the surgical procedure was determined by subtracting the post-I/A value from the pre-I value. The change in pupil diameter caused by the postoperative use of a miotic agent was determined by subtracting the post-M value from the post-I/A value. The safety variables included the results of slit-lamp biomicroscopy and ophthalmoscopy, intraocular pressure, and visual acuity (Snellen chart). Adverse events were recorded and graded for severity.

Microsoft Excel (2003 Version) was simply used to manipulate the data and the available analysis of variance test was used to analyse the continuous variables (such as pupil diameter, changes in pupil diameter, intraocular pressure and age). Treatment differences in nominal categorical variables (such as sex, operated eye and surgical procedure) were analysed using (χ²) test. All tests were two sided, and the probability values of ≤0.05 were considered as statistically significant.

Results
The efficacy analysis revealed the following results with the mean pupil diameter during the three stages and the changes in pupil diameter shown in Table 2. The (mean ± SD) pre-I pupil diameter was (7.72 ± 0.54 mm) in the ketorolac group and (7.52 ± 0.65 mm) in the prednisolone group. No significant differences in pre-I pupil diameter were observed between the two groups (P = 0.244). The (mean ± SD) Post I/A pupil diameter was greater in the ketorolac group (6.28 ± 0.74 mm) than in the prednisolone group (5.34 ± 0.72 mm) and the difference was statistically significant (P < 0.0001). The mean pupil diameter change from pre-I to post I/A and PC-IOL implantation was significantly less (P = 0.003) in the ketorolac group (1.44 ± 0.96 mm) than in the prednisolone group (2.18 ± 0.70 mm). The number of patients requiring additional mydriatic medication during surgery was significantly greater (P < 0.005) in the prednisolone group (n = 14) than in the ketorolac group (n = 4). The number of patients who received a miotic agent at the end of surgery was significantly greater (P < 0.025) in the ketorolac group (21) than in the prednisolone group (13). The (mean ± SD) post-M pupil diameter was (3.76 ± 0.77 mm) in the ketorolac group and (3.92 ± 0.49 mm) in the prednisolone group. The difference was not significant (P = 0.505). The mean change in the pupil diameter from post I/A to post-M was significantly greater (P = 0.014) in the ketorolac group (2.55 ± 1.18 mm) than in the prednisolone group (1.61 ± 0.96 mm).

The safety analysis revealed no significant differences between groups in slit-lamp biomicroscopy and ophthalmoscopy results, intraocular pressure or visual acuity. In addition, no
treatment-related adverse events occurred. Adverse events occurred in 12% of patients in each group, but no event was considered to be related to the study medication.

Discussion

Surgically induced miosis is a well known event during cataract surgery and believed to be related to the stimulation of PGs release following surgical trauma. The first NSAIDs approved by the FDA for use as intraoperative inhibitors of miosis during cataract surgery were 0.03% flurbiprofen and 1% suprofen. They decrease the synthesis of PGs in the ocular tissues by inhibiting the cyclo-oxygenase pathway, thus reducing miosis. All commercially available topical NSAIDs appear to share this therapeutic benefit.1

One previous study has demonstrated the efficacy and safety profile of 0.5% ketorolac compared with its vehicle on maintaining intraoperative mydriasis.18 The results showed that the mean pupil diameter after cortical irrigation and aspiration was significantly greater (P = 0.03) with 0.5% ketorolac than with its vehicle. Many other previous studies have demonstrated the efficacy of ketorolac in preventing surgically induced miosis.12-19 In addition, many previous studies have compared the efficacy of NSAIDs and corticoids in ocular inflammation after cataract surgery, 8,9, 20-23 but the role of corticoids, which inhibit the biosynthesis of both PGs and LTs, in preventing surgically induced miosis seems not to have been investigated.

Our study demonstrated that ketorolac was significantly better than prednisolone in maintaining mydriasis during surgery. Patients in the ketorolac group had smaller mean decreases in pupil diameter than did patients in the prednisolone group. Many previous studies have demonstrated no significant differences between ketorolac and prednisolone in controlling postoperative inflammation. These findings, considering the fact that both study medications inhibit the biosynthesis of both PGs and LTs, in preventing surgically induced miosis seems not to have been investigated.

Our study also demonstrated no significant differences between ketorolac and prednisolone in the response to the mydriatic agents applied preoperatively, or to the miotic agent applied at the end of surgery. Previous studies have demonstrated that no differences between ketorolac and its vehicle were observed in the response to miotic agents administered at the end of surgery, or in the response to the mydriatic agents applied preoperatively,18 suggesting that neither ketorolac nor prednisolone has direct antimiotic or mydriatic properties.

In our study, the number of patients requiring additional mydriatics was significantly greater in the prednisolone group (P < 0.025) compared to the ketorolac group, while others demonstrated that no differences between ketorolac and its vehicle were observed in the need for additional mydriatics during surgery.18 This means that patients in the prednisolone group in our study required more additional mydriatics than patients in ketorolac vehicle group in the other comparable study. These findings support more the hypothesis that there are other factors responsible for reducing miosis which are altered by prednisolone, and that ketorolac decreases surgically induced miosis through inhibition of routes other than inhibition of prostaglandin synthesis.

A previous study showed that ketorolac had significantly greater efficacy than the glucocorticoids against blood-aqueous barrier breakdown at day 5 and week 2, as demonstrated by the difference in fluorescein concentration between the operated and nonoperated eyes. That is the median fluorescein concentration in the anterior chamber in the glucocorticoid-treated eyes was significantly elevated during the first two weeks after surgery and then began to decrease.20 Another previous study also demonstrated comparable results.24 That is during the first two postoperative weeks, the fluorescein leakage was significantly greater in the steroid-treated eyes than in the indomethacin+steroid-treated eyes. After the second postoperative week, the fluorescein leakage in the steroid-treated eyes continued to decrease. These findings suggest that prednisolone takes more time to act than ketorolac thereby having less efficacy in the intraoperative period.

However, these two studies, and others,21,22 have demonstrated that prednisolone and ketorolac were equally effective in regard of cells and flare in the anterior chamber during the early postoperative period. Another previous study demonstrated
that fluorescein concentration in placebo-treated eyes was significantly elevated during the first two postoperative weeks (comparable to fluorescein concentration in prednisolone-treated eyes in other studies) then began to decrease and the anterior chamber reaction (cells and flare) was also intensive. This means that prednisolone seems to be similar to the placebo regarding the effect on fluorescein leakage. Moreover the decrease in fluorescein concentration after the second postoperative week in the prednisolone-treated eyes seems not to be related to a delayed prednisolone efficacy. This means that prednisolone is also effective in the early postoperative period as regards the clinical anterior chamber reaction. It appears that although fluorescein is the most sensitive technique for demonstrating breakdown of blood-aqueous barrier (BAB), it may not always be an indicator of large molecule permeability. These findings disprove the hypothesis that prednisolone takes more time to act than ketorolac and suggest that ketorolac is effective against even small-molecule permeability (fluorescein) while prednisolone is effective only against large molecule permeability (cells, protein).

The differences in the efficacy between ketorolac and prednisolone may be due to their differing effects on platelet activating factors, which are inhibited by glucocorticoids, but not by NSAIDs; however, this hypothesis needs to be verified.

In the present study, the use of ketorolac and prednisolone was not associated with any significant adverse effects. This is consistent with previous studies that have documented the comparable tolerability of ketorolac and prednisolone in the treatment of postoperative ocular inflammation.

**Conclusion**

Ketorolac tromethamine 0.5% ophthalmic solution seems to be more effective in preventing surgically induced miosis during cataract surgery compared to prednisolone acetate 1% ophthalmic solution. Consequently, topical ketorolac administered 24 hour before cataract surgery, reduces the complications of miosis during surgery and the need for intraoperative epinephrine which has been linked to CME. We therefore advise to apply ketorolac 24 hours before cataract surgery.

**ACKNOWLEDGEMENTS**

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**CONFLICT OF INTEREST**

The authors report no conflict of interest.

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Phenomenological Explanation of Cell Inactivation Cross Section in Terms of Direct and Indirect Action

*Faika A Azooz*¹ and Suaad A Meerkhan²

OBJECTIVES: The aim of this study was to use survival curves data for the inactivation of V79 cells and CHO-K1 cells by protons, neutrons, C²³ ions and He³ ions to study the role of direct and indirect action in cell inactivation. METHODS: A large number of survival curves for the inactivation of V79 cells by protons, neutrons, and C²³ ions and for CHO-K1 cells inactivated by He³ ions over a wide energy range were taken from published references. Experimental data points were extracted from the published survival curves using MATLAB (Version 7.0) and fitted to the linear quadratic equation. The fit parameters were used to calculate the inactivation cross section (σ) at the initial slope, the 2Gy dose and at 10% survival for each particle type separately. RESULTS: The results, in general, showed that the inactivation cross section decreases nearly exponentially when increasing the mean free path for primary ionisation (λ), except in the case of protons, and to some extent neutrons, where the cross section takes a constant value at specific λ values. The cross section increased with increasing linear energy transfer (LET) and also became independent of LET at specific LET values. CONCLUSION: The results indicate that the cell damage due to the double strand breaks of DNA caused by indirect action is much larger than that caused by the direct action.

KEYWORDS: Cell inactivation; Damage mechanism; Radiation; DNA.

**ADVANCES IN KNOWLEDGE**
1. Indirect action is the main cause of damage to living cells.
2. Direct action is seen only in proton irradiation. This is what makes protons so effective in clinical radiotherapy.

**APPLICATION TO PATIENT CARE**
1. Differentiation between the direct and indirect action of cell inactivation helps to improve treatment methods for tumours.
2. Understanding inactivation mechanisms can help minimise the dose required when treating patients with radiation.
3. Accelerated protons and light ions have already proved their usefulness in clinical radiotherapy. To take the advantage of their possible benefits, and to optimise treatment procedures in individual cases, detailed understanding of the underlying radiobiological mechanism is necessary.

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**REFERENCES**

1. Accelerated protons and light ions have already proved their usefulness in clinical radiotherapy. To take the advantage of their possible benefits, and to optimise treatment procedures in individual cases, detailed understanding of the underlying radiobiological mechanism is necessary.
It is generally accepted that DNA is the principle target of radiation action and DNA double strand breaks (DSB) are the main cause of damage to living cells. DNA damage may occur either via direct action in which particulate radiation strikes the DNA molecules directly, or via indirect action in which radiation interacts with the water molecules in the cell to form free radicals which in turn damage the DNA strands. Depending on the type of radiation dose, and the cells involved, the effects can occur relatively fast or may take years to be observed. It is believed that the direct damage mechanism accounts for a tiny proportion of biological effects caused by overall radiation. Since direct observation of damage mechanism is impossible, physical quantities, such as inactivation cross sections, based on experimental observations are used to make prediction about these mechanisms. Watt et al. in a series of publications, have shown that maximum damage occurs when the mean free path for primary ionisation $\lambda$ matches the mean chord length ($\approx 2$ nm) in the DNA. In fact, very few researchers agree with this opinion.

The aim of this study was therefore to find out the role of direct and indirect action for protons, neutrons, He$^3$ ions and C$^{12}$ ions.

**Methods**

Multiple survival curves measurements from two common cell lines: V79 (Chinese hamster) and CHO-K1 (Chinese hamster ovary) were used for this study. Published survival curves data for cell inactivation were taken from references, scanned as image files and digitised to obtain the sets of experimental data points using the MATLAB computer program (MATLAB 7.0, The Mathworks, Inc., Natick, MA, USA). Forty seven survival curves (20 for protons, 13 for neutrons, 7 for He$^3$ ions and 7 for C$^{12}$ ions) were fitted to the linear quadratic (LQ) equation using the curve fitting tool (cftool) facility in the MATLAB system.

The $\alpha$ and $\beta$ values obtained from the fit were used to calculate the inactivation cross section $\sigma$. Although neutrons and other heavy ions are usually fitted to the linear term ($\alpha$) of the LQ equation, we found that a better fit is obtained when fitting the data to both terms. The goodness of fit was measured depending on many statistical parameters and distributions. The criteria for the goodness of fit were that the data points coincided very well with the fitted curve; the residual distribution (residual = data - fit) was either symmetric around zero or the residual value for individual points was nearly zero; the adjusted R-square value (R-square is the best indicator of the fit and can take on any value between 0 and 1, with a value closer to 1 indicating a better fit) should be very close to 1, and the sum of squares due to error (SSE) should approach zero.

The cross section relationships to the mean free path $\lambda$ and the linear energy transfer (LET) were studied at three radiobiologically important points: initial slope of cell survival curve, 2Gy fraction dose typical for radiotherapy and at 10% survival dose for protons, neutrons, helium and carbon ions. The adjusted R-square values for each fit are shown in Tables 1 to 4.

**CROSS SECTION CALCULATIONS**

The linear quadratic equation is given by:

$$\ln S = (-\alpha D - \beta D^2)$$ (1)

Where $S$ is the survival fraction, $D$ is the dose and $\alpha$ and $\beta$ are the fit parameters.

Deriving this equation with respect to $D$ represents:

$$\frac{d \ln S}{d D} = \alpha + 2\beta D$$ (2)

$\frac{d \ln S}{d D}$ represents the slope of the survival at any dose $D$.

For the initial slope:

$$\lim_{D \to 0} \frac{d \ln S}{d D} = \alpha$$ (3)

The cross section is related to the slope of the survival curve as: \[ \sigma(\mu m^2) = \frac{\text{slope/Gy} \cdot \text{L(keV/\mu m)}}{6.25 \cdot \rho (\text{g/cc})} \] (4)

Where $\rho$ is the density of the medium (g/cc) and $L$ is the track average linear energy transfer in (keV/\mu m).

The $\alpha$ and $\beta$ parameters obtained from the fit were used in equation (4) to calculate the cross section at:

a) the initial slope, slope = $\alpha$

b) at 2Gy dose since it is relevant in radiotherapy

$$\text{slope} = \alpha + 4\beta$$

c) At 10% survival, this is usually used for data...
comparison.

\[ \text{slope} = \alpha + 2\beta D \]

where D represent the dose at 10% survival.

**Results**

The \(\alpha\) and \(\beta\) values obtained from the fit and the calculated cross section values for each survival curve at the initial slope for protons, neutrons, He\(^3\) ions, and C\(^{12}\) ions are presented in Tables 1 to 4.

**\(\sigma - \lambda\) dependence on particle type**

The proton inactivation cross section \(\sigma\) of V79 cells, measured at the initial slope, 2Gy dose and at 10% survival is plotted against the mean free path \(\lambda\) in Figures 1a to 1c respectively. A distinguished feature of these figures is that the cross section decreases sharply below \(\lambda \approx 8.7\) nm and then takes a constant value at the initial slope and at 2Gy dose in the region between \(\lambda = (8.7-14)\) nm before it starts to decrease again at \(\lambda > 14\) nm, but this flat region has nearly vanished at 10% survival.

The neutron cross section \(\sigma\) versus the mean free path \(\lambda\) in the same regions selected for protons is plotted in Figures 2a to 2c in the same order as above. A sharp decrease of cross section is seen in all these figures. It is nearly exponential in shape, but still one can notice a very small flat region at the initial slope [Figure 2a] which lies between \((1.56<\lambda<2.5)\) nm.

In general, the proton and neutron cross section at 2Gy dose are somewhat higher than those at the initial slope.

The inactivation cross section of CHO-K1 cells by He\(^3\) ions at the initial slope, 2Gy dose and at 10% survival is shown in Figures 3a to 3c respectively, and the corresponding figures for the inactivation of V79 cells by C\(^{12}\) ions are shown in [Figures 4a to 4c]. Both groups of figures show that the cross section decreases in an exponential shape without any structure. The cross section values are very close to each other in the three selected regions.

**\(\sigma - \text{LET dependence on particle type}\)**

The inactivation cross section for the particles involved in this study is plotted against the linear energy transfer LET in the same regions of the survival curve mentioned above.

For protons, the cross section at the initial slope [Figure 5a] and at 2 Gy dose [Figure 5b] increases nearly linearly with LET up to LET = 16.8 keV/\(\mu\)m,
then takes a constant value between LET = 16.8 keV/μm and LET = 23.6 keV/μm, followed by a linear increase. The flat region is not very clear at 10% survival [Figure 5c].

A similar behaviour is also seen for neutrons, where the flat region occurs between LET = 32.4 keV/μm and LET = 48 keV/μm [Figures 6a at the initial slope and Figure 6b at 2Gy dose]. Again the flat region is not very clear at 10% survival [Figure 6c]. In the case of He3 ions, the cross section increases up to LET =133 keV/μm then starts to decrease sharply. This is the case for all regions under consideration in this study [Figures 7a to 7c].

The inactivation cross section for C12 ions increases up to LET = 339.1 keV/μm at the initial slope [Figure 8a] and then starts to decrease very slowly, but it reaches saturation at this value of LET in the 2Gy dose [Figure 8b] and the 10% survival [Figure 8c].

Discussion

It is believed that DSB are the main cause of cell damage and this damage is either due to direct action, in which the energy is directly deposited in the target molecule of biological interest, without the intervention of radical species derived from water analysis, or due to indirect action which is defined as the outcome of the radiolytic products of water on the target of biological importance.

As mentioned above, the inactivation cross section decreases with an increasing mean free path λ. This decrease takes an exponential shape in the case of He3 ions [Figure 3a to 3c] and C12 ions [Figure 4a to 4c], but the exponential shape is interrupted by a flat region in the case of protons [Figure 1a to 1c] and to a lesser extent neutrons [Figure 2a to 2c]. The cross section values at their maximum are about 3.5, 10, 30, 40 μm² for protons, neutrons, He3 ions and carbon ions respectively. These values are not outside the range of cross section values found by Watt21 and Belloni et al.22 The difference in cross section values for different particles is due to the dependence of ionisation density on particle type. For example, Tables 1, 2, and 3 that: 1.07 MeV protons have LET = 27.6 keV/μm, while 1 MeV neutrons have LET = 32.39 keV/μm, and 1.08 MeV He3 ions have LET = 138 keV/μm. This means that neutrons are able to produce more secondary particles than protons of the same energy and this applies to He3 ions and C12 ions. The result is higher cell damage or a higher cross section.

Usually the exponential shape refers to random events such as the exponential decay law. Assuming
that the indirect action of radiation is a stochastic process in which single strand breaks (SSB) happen by the effect of secondary radicals produced at random along the particle track, these radicals are highly reactive and are able to change the structure of a DNA biologically important molecule (a molecule that carries genomic information), and this may lead to cell inactivation. A radical can hit a single strand of DNA only and there is a probability that the SSB may undergo a repair process, but, since these radicals are large in number, it is very probable that the other strand is hit by another radical leading to DSB which is the main cause of damage to living cells. The breakage of each strand of the DNA separately is a totally random process and, as mentioned before, random processes take an exponential shape depending on the action that causes them. In this case, it is the strength of the ionisation density. This phenomenology applies to He\(^+\) ions [Figures 3a to 3c] and C\(^{12}\) ions [Figures 4a to 4c] at the three regions of interest in this study since these particles are highly ionising radiations and are able to produce a large numbers of free radicals.

Protons and neutrons at low \(\lambda\) values have large ionisation density and are able to produce many radicals, but not as large as that for heavier ions. This is reflected in the lower cross section values at the lower end of the \(\sigma – \lambda\) curve for each of them. So the cell inactivation by protons up to \(\lambda = 8.7\) nm and that for neutrons up to \(\lambda = 1.56\) nm is dominated by indirect action. The small flat region between \((8.7 < \lambda < 14)\) nm for protons [Figure 1a] and between \((1.56 < \lambda < 2.5)\) nm for neutrons [Figure 1b] means a different mechanism is in action. We think it is the direct action process in which the two DNA strands are hit by the incident particle itself at the same time and not by its secondary radicals. Observing a flat region at these specific values of \(\lambda\) means that there is some kind of relation between \(\lambda\) and the DNA structure which enhances the direct action. This relation is not yet well understood and needs more investigations. The reasons for this observation of the direct action of protons and not observing it in the case of neutrons, He\(^+\) ions, and C\(^{12}\) ions is that the competitiveness between direct and indirect action for cells inactivated by protons is not as large as that for cells inactivated by one of the other three particles under study because of the small indirect action cross section in the case of protons compared to that for He\(^+\) ions, C\(^{12}\) ions and neutrons. The direct action of heavy ions, such as He\(^+\) ions and C\(^{12}\) ions, is missed because of the large indirect action. Moreover, the high \(\lambda\)- edge of the

![Figure 5: Inactivation cross section of V79 cells by protons versus linear energy transfer: a) at the initial slope; b) at 2Gy dose; c) at 10% survival.](image)

![Figure 6: Inactivation cross section of V79 cells by neutrons versus linear energy transfer: a) at the initial slope; b) at 2Gy dose; c) at 10% survival.](image)
proton curve is not asymptotic as for other particles; this means that there are still some direct action events taking place. These observations explain why protons have a wide usage in radiotherapy and are regarded as having the ability to concentrate the dose in more discrete target volumes. They would deposit all their energy in the cells of the target, without irradiating normal cells that may be in the target since they produce less indirect effects which are randomly distributed. 23

The proton inactivation cross section at 2Gy dose [Figure 1b] shows similar behaviour to that at the initial slope and the flat region can still be seen since protons, unlike other particles, are not heavily ionising. Hence they produce a lower number of radicals, but the flat region in the case of neutrons at 2Gy dose [Figure 2b] has vanished because neutrons are heavy ionising particles compared to protons and are able to produce more radicals which enhance the indirect action and cause the direct action effect to disappear. The higher cross section values obtained at the low λ edge of the σ–λ curve for protons and neutrons at 2Gy dose as compared to those at the initial slope, are because of the higher number of secondary radicals produced by a 2Gy dose than lower doses.

The flat region in the proton inactivation cross section at 10% survival [Figure 1c] is not as clear as that at the initial slope or at 2Gy dose. This is because that the 10% survival may occur at any dose larger than one gray depending on the energy of the particle, so we expect a large mixture of direct and indirect action in this region, but the direct action still plays a major role in the inactivation of cells. The neutron cross section at 10% survival [Figure 2c] shows an exponential shape which means that the indirect action dominates.

The direct–indirect action mechanism is seen also in the σ–LET relationship for protons [Figures 5a to 5c]. At low LET values, which correspond to the high λ-edge of the σ–λ curve, the increase of cross section with increasing LET up to LET=16.8 keV/µm indicates the dominance of indirect action and the flat region at (16.8 ≤ LET ≤ 23.6) keV/µm, which corresponds to (14 ≥ λ ≥ 8.7) nm, is attributed to direct action, where it occurs purely in this specific region. Then, the cross section increases nearly linearly with increasing LET to resume the indirect action phase.

The same thing can be said about the neutron cross section at the initial slope [Figure 6a], but there are very few data points in the flat region since there is not much published data for the inactivation of V79 cells by neutrons. The flat region is better

![Figure 7](image7.png)  
**Figure 7:** Inactivation cross section of CHO-K1 cells by 3He ions versus linear energy transfer: a) at the initial slope; b) at 2Gy dose; c) at 10% survival.

![Figure 8](image8.png)  
**Figure 8:** Inactivation cross section of V79 cells by 12C versus linear energy transfer: a) at the initial slope; b) at 2Gy dose; c) at 10% survival.
seen in the $\sigma$ – LET curve for neutrons at 2Gy dose [Figure 6b] and at 10% survival [Figure 6c] than that in the $\sigma$ – $\lambda$ curve.

No flat region can be seen in $\sigma$ – LET curve for He$^3$ ions [Figures 7a, 7b and 7c) and C$^{12}$ ions [Figure 8a, 8b and 8c] since the direct action is negligible compared to the indirect action, but the cross section increases nearly linearly to reach a maximum value at $\text{LET} = 133 \text{ keV/\mu m} = \lambda = 0.82 \text{ nm}$ in He$^3$ ions. It is less obvious, but can still be distinguished to have its maximum at $\text{LET} = 339.1 \text{ keV/\mu m} = \lambda = 0.13 \text{ nm}$ in C$^{12}$ ions at the initial slope and takes a saturation shape at 2Gy dose and 10% survival. These peaks or saturations indicate that an overkill process is taking place.

**Conclusion**

Inactivation cross section due to ionising radiations provides a good tool to study damage mechanisms since it takes different shapes for different particles when plotted against physical parameters as the mean free path or the LET.

In this study, we have found that the inactivation
cross section $\sigma$ in general decreases with increasing mean free path $\lambda$; this decrease takes an exponential shape in the inactivation of CHO-K1 cells by He$^3$ ions and V79 cells by C$^{12}$ ions. The exponential shape is attributed to the interaction of secondary radicals with DNA to produce DSB which are the main cause of cell damage. This process is described as an indirect action process. The inactivation cross section of V79 cells by protons and neutrons also decreases nearly exponentially with increasing $\lambda$ and this decrease is due to indirect action, but the semi-exponential shape in the case of protons, and to some extent neutrons, is interrupted by a flat region at specific $\lambda$-values. We believe this flat region is due to the interaction of the incident particle itself with the DNA strands, and the process is a direct action process. This gives protons the ability to concentrate the dose in more discrete target volumes which is very useful in radiotherapy treatments.

The $\sigma$-LET curves for the particles under study have shown that the cross section increases nearly linearly with LET and the flat region is also seen in

Table 2: Survival curve parameters for the inactivation of V79 cells by neutrons

<table>
<thead>
<tr>
<th>E (MeV)</th>
<th>LET (kev/µm)</th>
<th>$\lambda$ (nm)</th>
<th>$\alpha$ (Gy$^{-1}$)</th>
<th>$\beta$ (Gy$^{-2}$)</th>
<th>$\sigma$ (µm$^2$)</th>
<th>$R^2$</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.11</td>
<td>51.64</td>
<td>1.21</td>
<td>0.82</td>
<td>0.28</td>
<td>8.67</td>
<td>0.9968</td>
<td>Hall$^{13}$</td>
</tr>
<tr>
<td>0.176</td>
<td>55.32</td>
<td>1.23</td>
<td>0.804</td>
<td>0.003</td>
<td>8.5</td>
<td>0.9995</td>
<td>Leenhout$^{14}$</td>
</tr>
<tr>
<td>0.22</td>
<td>55.06</td>
<td>1.266</td>
<td>0.795</td>
<td>0.21</td>
<td>8.4</td>
<td>0.9988</td>
<td>Hall$^{13}$</td>
</tr>
<tr>
<td>0.34</td>
<td>51.2</td>
<td>1.43</td>
<td>0.776</td>
<td>0.15</td>
<td>8.2</td>
<td>0.9999</td>
<td>Hall$^{13}$</td>
</tr>
<tr>
<td>0.43</td>
<td>48.15</td>
<td>1.55</td>
<td>0.653</td>
<td>0.26</td>
<td>6.9</td>
<td>0.9995</td>
<td>Hall$^{13}$</td>
</tr>
<tr>
<td>0.433</td>
<td>48.02</td>
<td>1.56</td>
<td>0.558</td>
<td>0.15</td>
<td>5.9</td>
<td>0.9955</td>
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<tr>
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<td>42.74</td>
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<td>0.485</td>
<td>0.11</td>
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<td>0.996</td>
<td>Leenhout$^{14}$</td>
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<tr>
<td>0.66</td>
<td>40.53</td>
<td>1.26</td>
<td>0.501</td>
<td>0.136</td>
<td>5.3</td>
<td>0.9995</td>
<td>Hall$^{13}$</td>
</tr>
<tr>
<td>1</td>
<td>32.39</td>
<td>2.5</td>
<td>0.47</td>
<td>0.058</td>
<td>5.0</td>
<td>0.9995</td>
<td>Hall$^{13}$</td>
</tr>
<tr>
<td>2</td>
<td>20.7</td>
<td>4.317</td>
<td>0.24</td>
<td>0.022</td>
<td>2.55</td>
<td>0.9999</td>
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</tr>
<tr>
<td>6</td>
<td>9.05</td>
<td>11.72</td>
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<td>0.057</td>
<td>0.65</td>
<td>0.9989</td>
<td>Hall$^{13}$</td>
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<tr>
<td>13.6</td>
<td>3.7</td>
<td>26.16</td>
<td>0.02</td>
<td>0.39</td>
<td>0.23</td>
<td>0.9986</td>
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<tr>
<td>15</td>
<td>3.4</td>
<td>28.84</td>
<td>0.016</td>
<td>0.05</td>
<td>0.17</td>
<td>0.9994</td>
<td>Hall$^{13}$</td>
</tr>
</tbody>
</table>

Legend: LET = linear energy transfer

Table 3: Survival curve parameters for the inactivation of CHO-K1 cells by He$^3$ ions

<table>
<thead>
<tr>
<th>E (MeV)</th>
<th>LET (kev/µm)</th>
<th>$\lambda$(nm)</th>
<th>$\alpha$ (Gy$^{-1}$)</th>
<th>$\beta$ (Gy$^{-2}$)</th>
<th>$\sigma$ (µm$^2$)</th>
<th>$R^2$</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.84</td>
<td>133</td>
<td>0.82</td>
<td>1.487</td>
<td>------</td>
<td>31.6</td>
<td>0.9995</td>
<td>Muller$^{16}$</td>
</tr>
<tr>
<td>1.13</td>
<td>138</td>
<td>0.92</td>
<td>1.359</td>
<td>------</td>
<td>29.5</td>
<td>0.9994</td>
<td>Muller$^{16}$</td>
</tr>
<tr>
<td>1.22</td>
<td>140</td>
<td>0.95</td>
<td>1.245</td>
<td>0.00004</td>
<td>27.9</td>
<td>0.9999</td>
<td>Muller$^{16}$</td>
</tr>
<tr>
<td>1.38</td>
<td>142.6</td>
<td>0.988</td>
<td>1.23</td>
<td>------</td>
<td>28.06</td>
<td>0.9992</td>
<td>Muller$^{16}$</td>
</tr>
<tr>
<td>2.3</td>
<td>121.5</td>
<td>1.46</td>
<td>1.24</td>
<td>------</td>
<td>26.8</td>
<td>0.9997</td>
<td>Muller$^{16}$</td>
</tr>
<tr>
<td>4.6</td>
<td>77.8</td>
<td>2.78</td>
<td>0.684</td>
<td>------</td>
<td>8.7</td>
<td>0.9953</td>
<td>Muller$^{16}$</td>
</tr>
<tr>
<td>10.7</td>
<td>41</td>
<td>6.5</td>
<td>0.284</td>
<td>0.030</td>
<td>2.6</td>
<td>0.9991</td>
<td>Muller$^{16}$</td>
</tr>
</tbody>
</table>

Legend: LET = linear energy transfer
the proton and neutron cross section, but not in He\textsuperscript{3} ions or C\textsuperscript{12} ions.

**CONFLICT OF INTEREST**
The authors report no conflict of interest.

**References**


Optimum Anthropometric Criteria for Ideal Body Composition Related Fitness

Hashem Kilani, and Asem Abu-Eishah

ABSTRACT: Objectives: The three aims of this study were to establish equations for ideal body composition related fitness to be used by adults willing to gain optimum body composition related fitness; to predict the possible symmetrical major muscle circumference, and to compute the ideal body fat percentage (BFP) with ideal body weight (IBW) based on the body mass index (BMI). Methods: Twenty-four athletes were intentionally selected, with heights of 166–190 cm and aged 20–42 years, according to a judging committee that used modified International Federation criteria for the Mr. Fitness competition “super body category”. Common anthropometric and body composition measurements were taken for the following independent variables: body height, upper limb length, lower limb length, thigh length, arm length, shoulder width, forearm length, shank length, and wrist girth; and for the following dependent variables: circumferences of shoulder, thigh, waist, hip, chest, biceps, forearm, shank, and neck. Skin fold thickness was measured at three sites by a Harpenden caliper to calculate BFP. Results: The findings indicate that there was a predictive correlation between major independent variables and body circumferences. The mean range used to find out the ideal BFP percentage which was 5.6–6.7%. A common anthropometric and body composition model was used to find the IBW and the following dependent variables: circumference, arms, shoulder, and body fat percentage. Conclusion: It is suggested that the above equations, the ideal BFP percentage and the IBW be used as criteria in training sessions to achieve ideal body composition related fitness.

Keywords: Body Composition; Anthropometric; Resistance training.

Advances in Knowledge
1. This is the first study that establishes prediction equations to achieve ideal body composition related fitness.
2. The results of this study will help novices in developing their own resistance training programme based on the equations.

Application to Patient Care
1. In order to maintain good health status, patients need to follow a regular physical activity regime based on this study’s equations.
2. Patients with posture abnormality may apply these prediction formulas to achieve body alignment and correct posture through a rehabilitation program.

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Fitness club participants have different goals when they plan to workout. Some people would like to reduce weight, others to increase cardiovascular endurance, and the rest would like to develop muscle mass. For the first two groups, sufficient standards and criteria exist for the design and monitoring of an appropriate physical training programme that would lead to beneficial changes in body composition, such as reductions in body fat and increases in cardiovascular fitness. The third group, bodybuilders, compete on the size, definition, symmetry and shape of their muscular body composition. The ideal body composition related fitness represents the actual lean body mass symmetry combined with a low fat percentage that leads to a high level of health-related fitness.

However, before aiming to achieve ideal body composition related fitness, people need to follow a well-balanced diet with a regular physical activity regime early in their lives in order to maintain a good health status. Not only is regular physical activity essential for normal growth and development, but physical activity habits established early in life tend to carry over into adulthood.1,2 Although activities that enhance cardiorespiratory fitness are generally recommended for all, research increasingly suggests that resistance training can offer unique benefits for children, adolescents, and for patients having osteoporosis, diabetics, arthritis and most non-communicable diseases, especially when appropriately prescribed and supervised.2,4,5

Physical fitness requirements for body builders have recently evolved away from only developing bulky muscle. Physical fitness is a term that is used interchangeably with cardiorespiratory fitness, musculoskeletal fitness and health related physical fitness. Recently, resistance training and weight training with cardio drills were developed to allow people to achieve multiple physical fitness objectives. Thus, the relationship between cardio and muscular functioning is enhanced by virtue of multiple intervention training leading to a healthier lifestyle.5 The American College of Sport Medicine (ACSM) recommends that young adults, who have no medical problems that may limit their acceptable level of activity, should engage in moderate intensity aerobic exercise for a minimum of 30 minutes at least 5 days a week. In addition to the recommendations for aerobic exercise, the guidelines also specify that healthy adults should engage in moderate resistance (strength) training at least twice per week and should aim to work all of the major muscle groups.6 The available evidence suggests that muscular strength and power also prevent the risk of cardiovascular mortality, independent of cardiovascular fitness, and their development might be considered as prophylaxis for non-communicable diseases.1,2

In the context of promoting muscular strength and power, the International Body Fitness Federation (INBF), the non-profit amateur affiliate of the World National Bodybuilding Federation (WNBF), organises the Mr. Fit Body Contest where health fitness and body symmetry are demonstrated by contestants executing certain manoeuvres.9 Planning, predicting, and monitoring changes in body symmetry and health fitness are critical for this calibre of bodybuilders. Anthropometrically based prediction equations designed to detect body composition changes, have not been rigorously tested in athletes. Several reports have commented on the inadequacy of various skin-fold-thickness equations to predict changes in body composition, whether modest10,11 or large.12,13,14 Most previous studies predicted BMI or body fat percentages from either anthropometric measures only, or with other correlation methods to body segment circumferences. To date, standard or predictive equations that would assess the relationship between body parts and the symmetrical composition of the desired ideal body composition are not available for practical application. The purpose of this study is to establish equations for ideal body composition related fitness that can be used by adults wanting to gain optimum body composition related fitness to predict the possible symmetrical major muscle circumference, and to compute the ideal body fat percentage (BFP) with ideal body weight (IBW) based on the body mass index (BMI). In this

3. Using the equations from this study, weight reduction can be achieved through resistance training that would optimise body composition and fitness level.
4. The knowledge obtained from this study will encourage young people to initiate an active lifestyle early in their lives thus preventing the occurrence of non-communicable diseases.
context, the following questions were raised: 1) What is the ideal fat percentage for optimum body composition? 2) What is the ideal body weight for optimum body composition? 3) Which are the most predictive variables derived from this study?

Methods

Twenty-four Jordanian male athletes participated in this study. They were 20–42 years old and their height ranged between 166 and 190 cm. They were selected from a total of 84 athletes from 91 clubs by a judging committee using modified International Fitness Federation criteria for the Mr. Fit Body contest. The “Super Body” category was used as the standard for the ideal bodies for this study. They reported to have been drug-free for the previous seven years. Although, the sample size is not large, it was sufficient for the classical statistics used in this analysis as shown in the tables. The Statistical Package for the Social Sciences (SPSS) software, Version 15, was used for statistical analysis. All participants gave informed consent to participate in the study.

Common anthropometric and body composition measurements were taken for the following independent variables: body height (BH), upper limb length (ULL), lower limb length (LLL), thigh length (TL), arm length (AL), shoulder width (SW), forearm length (FL), shank length (SL), and

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>Max value</th>
<th>Min value</th>
<th>SD</th>
<th>M</th>
<th>SE</th>
<th>The confidence interval 95% of the sample Minimum–Maximum</th>
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</thead>
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<tr>
<td>Age (yr)</td>
<td>25.79</td>
<td>42</td>
<td>20</td>
<td>4.83</td>
<td>25.00</td>
<td>0.99</td>
<td>23.75–27.83</td>
</tr>
<tr>
<td>Height (cm)</td>
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<td>190</td>
<td>166</td>
<td>6.32</td>
<td>173.25</td>
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<td>Weight (kg)</td>
<td>73.50</td>
<td>88.7</td>
<td>64.8</td>
<td>6.21</td>
<td>72.85</td>
<td>1.27</td>
<td>70.87–76.12</td>
</tr>
<tr>
<td>BMI</td>
<td>23.78</td>
<td>24.8</td>
<td>22</td>
<td>0.62</td>
<td>23.80</td>
<td>0.13</td>
<td>23.51–24.04</td>
</tr>
<tr>
<td>Fat %</td>
<td>6.17</td>
<td>9</td>
<td>4</td>
<td>1.33</td>
<td>6.00</td>
<td>0.27</td>
<td>5.60–6.73</td>
</tr>
<tr>
<td>Neck circum (cm)</td>
<td>39.69</td>
<td>44</td>
<td>37</td>
<td>1.78</td>
<td>39.75</td>
<td>0.36</td>
<td>38.94–40.44</td>
</tr>
<tr>
<td>Chest circum (cm)</td>
<td>101.81</td>
<td>110</td>
<td>96</td>
<td>3.57</td>
<td>102.0</td>
<td>0.73</td>
<td>100.31–103.32</td>
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<td>84</td>
<td>72</td>
<td>3.23</td>
<td>78.50</td>
<td>0.66</td>
<td>76.87–79.59</td>
</tr>
<tr>
<td>Hip circum (cm)</td>
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<td>99</td>
<td>85</td>
<td>3.36</td>
<td>91.00</td>
<td>0.69</td>
<td>90.21–93.04</td>
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<td>Shoulder circum (cm)</td>
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<td>129</td>
<td>111</td>
<td>4.90</td>
<td>119.0</td>
<td>1.00</td>
<td>117.89–122.03</td>
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<td>Arm circum (cm)</td>
<td>35.04</td>
<td>38.5</td>
<td>32</td>
<td>1.76</td>
<td>35.00</td>
<td>0.36</td>
<td>34.30–35.78</td>
</tr>
<tr>
<td>Forearm (cm)</td>
<td>29.77</td>
<td>32</td>
<td>28</td>
<td>1.29</td>
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<td>0.26</td>
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<td>62</td>
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<tr>
<td>Shank circum (cm)</td>
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<td>39</td>
<td>31</td>
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<td>36.25</td>
<td>0.40</td>
<td>35.25–36.92</td>
</tr>
<tr>
<td>Arm length (cm)</td>
<td>33.02</td>
<td>38</td>
<td>30</td>
<td>1.93</td>
<td>33.00</td>
<td>0.39</td>
<td>32.21–33.83</td>
</tr>
<tr>
<td>Shank length (cm)</td>
<td>42.65</td>
<td>48.5</td>
<td>38.5</td>
<td>2.51</td>
<td>42.00</td>
<td>0.51</td>
<td>41.59–43.71</td>
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<tr>
<td>Wrist girth (cm)</td>
<td>17.61</td>
<td>19</td>
<td>17</td>
<td>0.63</td>
<td>17.50</td>
<td>0.13</td>
<td>17.34–17.87</td>
</tr>
<tr>
<td>Upper extremity length (cm)</td>
<td>80.98</td>
<td>89</td>
<td>76</td>
<td>2.77</td>
<td>81.25</td>
<td>0.57</td>
<td>79.81–82.15</td>
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<tr>
<td>Upper extremity length (cm)</td>
<td>94.02</td>
<td>103</td>
<td>85</td>
<td>4.64</td>
<td>95.00</td>
<td>0.95</td>
<td>92.06–95.98</td>
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<tr>
<td>Forearm length (cm)</td>
<td>28.17</td>
<td>30</td>
<td>25</td>
<td>1.38</td>
<td>28.50</td>
<td>0.28</td>
<td>27.58–28.75</td>
</tr>
<tr>
<td>Thigh length (cm)</td>
<td>43.40</td>
<td>48</td>
<td>38</td>
<td>2.80</td>
<td>44.00</td>
<td>0.57</td>
<td>42.21–44.58</td>
</tr>
<tr>
<td>Shoulder width (cm)</td>
<td>37.77</td>
<td>43</td>
<td>34</td>
<td>2.01</td>
<td>37.75</td>
<td>0.41</td>
<td>36.92–38.62</td>
</tr>
</tbody>
</table>

Legend: SE = standard error; SD = standard deviation;
wrist girth (WrG); and the following dependent variables: circumferences of shoulder (Sh), thigh (T), waist (W), hip (H), chest (Ch), biceps (Bi), forearm (F), shank (S), and neck (NK). Skin fold thickness was measured at three sites with a Harpenden caliper to ascertain the subject’s body fat percentage (BFP). Based on a previous pilot study and other research, all measures were reliable and valid.

**Results**

The descriptive anthropometric statistics mean, median, standard deviation, and minimum and maximum values for the 24 participants are presented in Table 1. The 95% confidence interval for each variable is also shown in the table. Values falling beyond this confidence interval were assumed as outliers. With respect to the first and second research questions, Table 1 illustrates 95% confidence interval for the ideal fat percentage and the ideal body weight for the optimum body composition. The formula applied to determine BMI, which uses the BW over square height in metres, can be applied inversely to predict the ideal body weight using either the mean or the values falling within the 95% confidence interval. Thus, the acceptable values used to find out the ideal BFP %, which are between 5.6 and 6.7%, can be used to determine the (IBW) which is \( H^2 \times 23.77 \pm 2SE \). Table 2 also showed that the highest significant coefficient correlation was between shoulder circumference and total body height. In addition, shoulder circumference was the dependent variable that significantly correlated with all independent variables except wrist girth. In order to determine the best prediction equation for each dependent variable, an analysis was conducted using SPSS software which uses several independent variables and one dependent variable. Stepwise multiple linear regressions were used. In addition, regression variance analysis was used to explore the explanation power for the predicted equations. Wrist girth was the independent variable most often derived as a predictor whether in isolation or combined with other independent variables. The total body height came next as shown in Table 3. The following predictive equations were derived from the statistical manipulation:

1. Neck circumference = -3.882 + 0.349 (ULL) + 0.868 (WrG)
2. Shoulder circumference = -6.221 + 0.943 (BH) + 1.031 (TL) – 0.889 (LLL)
3. Chest circumference = 57.083 + 0.476 (LLL)
4. Waist circumference = 25.772 + 0.459 (BH) – 1.581 (WrG)
5. Hip circumference = 34.212 + 0.425 (BH) – 0.442 (TL) + 0.881 (AL) - 1.528 (WrG)
6. Biceps circumference = 23.776 + 0.26 (TL)
7. Forearm circumference = 9.406 + 1.157 (WrG)
8. Thigh circumference = 30.632 + 0.574 (TL)
9. Shank circumference = 6.666 + 1.671 (WrG)

Discussion
Since the statistical analyses were run for variable values falling within the 95% confidence interval, the above equations would apply for a sample of men aged between 24 and 28 years, height between 172 and 178 cm, and body fat percentages between 5.6 and 6.7%. The ideal homogenous weight can be predicted using the formula of BMI inversely which is \( H^2 \times 23.77 \pm 2SE \). This equation offers an advantage over other methods such as measures of BMI or weight, body composition, and fat distribution in assessing body composition related fitness.13 Body weight is not a suitable measure for assessing ideal body composition related fitness because an increase in weight due to an increase in fat-free mass (FFM) can be misinterpreted as an increase in body fatness. BMI measure can not be valid for all people; hence, we should be cautious when this index is applied to the extremes of physical types such as elite athletes, the physical frail, pregnant women, and children.15 Direct measures of percentage body fat and FFM are currently impractical for widespread use in screening for general health and fitness standards. Indirect or clinical methods usually rely on estimation of body composition from easily measured variables such as circumferences or skinfold thicknesses and use of prediction equations. Fridel et al. suggest that anthropometry can provide better estimates of fatness than body mass index, but it is still relatively insensitive to short-term alterations in body composition.10

In order to identify changes correctly and to provide positive and correct feedback, it is necessary to be able to assess progress without the use of expensive equipment or technically complex procedures. Kilani indicated that on average, fat percentages are 12 to 15% and 18 to 22% for males and females respectively. For most elite athletes, these percentages are lower and might reach 3% for bodybuilders.15 Three percent is the lowest level of essential body fat needed for males to survive without hazardous health problems. Fat loss is well represented by a simple decrease in the abdominal girth measurement, even for the leanest men.10 Not surprisingly, the circumference equation that includes the wrist girth and height length instead of arm and thigh lengths proved to be the most reliable to follow as shown in Table 2. Using all nine equations before enrolling into an exercise programme will lead to an optimisation of the symmetry of body segment circumferences and an ideal body weight and body fat percentage related health status.

In addition, the above equations can also be used for non-athletes, including patients, when they want to exercise in a scientific manner. In general, if patients have posture abnormalities, they may...
apply these formulae to achieve body alignment and correct posture. If obesity is the major health problem, weight reduction can be achieved through resistance training that would optimise body composition and fitness level. The use of the previous equations can also be prescribed to patients in rehabilitation programmes. Finally, young people need to work out based on these equations to achieve fitness and to prevent non-communicable diseases since the effective application of the equations works as prophylaxis for patients with arthritis, obesity, diabetes, and hypertension.

Conclusion
This analysis provides a thorough study of multiple anthropometric and body composition measures and their association with ideal body shape related fitness in a population highly involved in achieving muscle symmetry outcomes. The study has identified the equations for the most predictive criteria in order to achieve ideal body shape related fitness. A training programme can therefore be planned based on the initial anthropometric measurements and then predict the homogeneity of muscle bulk, definitions, and shape with fairly accurate efficiency and effectiveness. The above equations can be used to predict ideal BFP % and IBW as criteria in the training sessions to achieve ideal body composition. However, further research is still needed to confirm the validity of implementing the above predictive formulas for any active person initiating a training programme.

CONFLICT OF INTEREST
The authors report no conflict of interest.

References
Clinically-Defined Maturity Onset Diabetes of the Young in Omanis
Absence of the common Caucasian gene mutations

*Nicholas JY Woodhouse,1 Omayma T Elshafie,2 Ali S Al-Mamari,2 Naji HS Mohammed,2 Fatma Al-Riyami,2 Sandy Raeburn3

Objectives: We are seeing a progressive increase in the number of young patients with clinically defined maturity onset diabetes of the young (MODY) having a family history suggestive of a monogenic cause of their disease and no evidence of autoimmune type 1 diabetes mellitus (T1DM). The aim of this study was to determine whether or not mutations in the 3 commonest forms of MODY, hepatic nuclear factor 4α (HNF4α), HNF1α and glucokinase (GK), are a cause of diabetes in young Omanis. Methods: The study was performed at Sultan Qaboos University Hospital (SQUH), Oman. Twenty young diabetics with a family history suggestive of monogenic inheritance were identified in less than 18 months; the median age of onset of diabetes was 25 years and a median body mass index (BMI) 29 at presentation. Screening for the presence of autoimmune antibodies against pancreatic beta cells islet cell antibody (ICA) and glutamic acid decarboxylase (GAD) was negative. Fourteen of them consented to genetic screening and their blood was sent to Prof. A. Hattersley's Unit at the Peninsular Medical School, Exeter, UK. There, their DNA was screened for known mutations by sequencing exon 1-10 of the GCK and exon 2-10 of the HNF1α and HNF4α genes, the three commonest forms of MODY in Europe. Results: Surprisingly, none of the patients had any of the tested MODY mutations. Conclusion: In this small sample of patients with clinically defined MODY, mutations of the three most commonly affected genes occurring in Caucasians were not observed. Either these patients have novel MODY mutations or have inherited a high proportion of the type 2 diabetes mellitus (T2DM) susceptibility genes compounded by excessive insulin resistance due to obesity.

Keywords: Diabetes Mellitus, Type II; Diabetes mellitus, maturity onset; MODY; mutations; Diabetes, familial; Young adults; Oman.

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Diabetes mellitus (DM), both types I and II, is common worldwide and now affects more than 5% of all obese adolescents; however, optimal investigation and management is still unclear. Doctors often struggle to provide the best therapy, especially in regions where lifestyle changes in the last one or two generations have contributed to the diabetogenic risk.

In Oman, as in other countries of the Arabian Peninsula, type 2 diabetes (T2DM) especially and other complex, multifactorial disorders have reached epidemic levels. We are now seeing a progressive increase in the number of young Omani diabetics (<25 years) with a family history indicating a monogenic cause of their disease and who have no evidence of type 1 diabetes mellitus (T1DM). These patients have clinically defined maturity onset diabetes of the young (MODY), a disorder resulting from mutation in 6 different genes causing deficient insulin secretion. They are often misdiagnosed as T1DM and treated with insulin. However, some patients have mutations in the genes encoding HNF1α or β-cell potassium adenosine triphosphate (K-ATP) channels both of which respond well to low dose sulphonylurea (SU) therapy. To date, we have identified three such families (not included in the present study) who were able to discontinue insulin and continue on SU therapy alone. Clearly therefore, MODY exists in Oman and in this study we have screened an additional 14 patients for common MODY mutations.

Methods

Twenty young diabetics with a family history suggesting monogenic inheritance [Figure 1], and whose antibodies against pancreatic beta-cells islet cell antibodies (ICA) and glutamic acid decarboxylase (GAD)) were negative, were identified in less than 18 months. Of these 14 patients, whose characteristics are shown in Table 1, consented to genetic screening and their blood was sent to the Molecular Genetics Laboratory at the Peninsular Medical School, Exeter, UK. There, their DNA was screened for known mutations by sequencing exon 1-10 of the glucokinase gene and exon 2-10 of the HNF1α and HNF4α, the commonest forms of MODY in Europe using the DNA ABI PRISM® 3100 Genetic Analyzer.

Results and Discussion

In this small group of young Omani diabetics, we expected to find several with known MODY mutations, particularly as we have already identified 3 different MODY families responsive to SU therapy. Surprisingly, this was not the case and mutations in the three commonest forms of MODY were not observed, although all had family histories suggestive of a monogenic cause of their disease and no evidence of T1DM. How might this be explained? Either these patients had novel MODY mutations or have inherited one or more of the T2DM susceptibility genes. Novel mutations cannot be ruled out as, in a recent and larger Danish study, mutations were found in only half the patients with clinically defined MODY, as ours. Interestingly, patients with clinically defined MODY in Mexico and China have few of the documented mutations occurring in Caucasians which suggests that our Omani MODY patients may have novel gene mutations as well. However, we suspect that early onset T2DM is more likely, particularly as the median BMI in our study group was 29, an additional factor associated with early onset disease.

MODY is a familial monogenic form of diabetes with autosomal dominant inheritance and high penetrance of 80–95%. In contrast to type 1 and type 2 diabetes, MODY usually develops below 25 years [Figure 2]. Currently there are 6 identified gene mutations, three of them, HNF1α, HNF4α and glucokinase, are common and account for >80% of MODY cases in Europe and North America, while others are rare (HNF1β, insulin promoter factor 1 and neurogenic differentiation factor 1). Some of the MODY patients will not
Clinically Defined Maturity Onset Diabetes of the Young in Omani

Absence of the common Caucasian gene mutations

 Clinically Defined Maturity Onset Diabetes of the Young in Omani

Absence of the common Caucasian gene mutations

With young patients, the clinician should distinguish between T1DM (with autoimmune destructions of the beta-cells and insulin dependence), monogenic defects due to the maturity onset of diabetes in the young (MODY) and T2DM which is multifactorial. With their early age of onset, patients with single gene disorders such as MODY are often misdiagnosed as T1DM and inappropriately treated with insulin. This is unfortunate as patients with glucokinase deficiency (GKD) have few complications and rarely require treatment. Furthermore, patients with transcriptions factor mutations (such as HNF1α and neonatal Kir6.2) respond dramatically to sulphonylurea medication. Recently, we have successfully switched diabetics, from three families, from insulin of many years duration to oral SUs. Although monogenic DM in the UK is only estimated to occur in 1–2% of the diabetic population (i.e. up to 40,000 patients), in Oman the incidence of monogenic disease is probably much higher due to the higher rate of consanguinity.

Mutagenesis screening is expensive so we are now actively screening candidate patients using a trial of SU therapy. Screening is carried out in patients aged <30 years who are taking insulin, have a positive family history and no GAD or ICA antibodies. Of the 10 patients studied so far 3 have gratifyingly responded to low dose SU therapy. This trial is currently in progress, together with screening of the patients for the T2DM susceptibility genes which are currently known to be associated with T2DM.

### Table 1: Details of the 14 patients with a family history suggesting a monogenic cause of their disease. Shown is the median and range of age and BMI at diagnosis. Four were taking insulin alone and 10 oral hypoglycaemic agents.

<table>
<thead>
<tr>
<th>Age at diagnosis/Yr Median</th>
<th>Sex</th>
<th>BMI</th>
<th>Therapy</th>
<th>GAD / ICA</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 (12-40)</td>
<td>10  M</td>
<td>29</td>
<td>INS</td>
<td>Negative</td>
</tr>
<tr>
<td>4 F</td>
<td>20-41</td>
<td>OHA</td>
<td>Negative</td>
<td></td>
</tr>
</tbody>
</table>

**Legend:** BMI = body mass index; GAD = glutamic acid decarboxylase; ICA = islet cell antibody; INS = insulin; OHA = oral hypoglycaemic agents

### References


A Rare Presentation of Attention Deficit/Hyperactivity Disorder
A recommendation to be more alert!

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ABSTRACT: We report the case of a 7-year-old Omani girl with tuberous sclerosis (TS), attention deficit hyperactivity disorder (ADHD) and bipolar disorder (BD), at Sultan Qaboos University Hospital (SQUH), Oman. For a year she had been suffering from hyperactivity, aggression, over talkativeness, insomnia, risk-taking behaviour, distractibility, poor attention and seizures. This clinical picture evolved slowly, but was progressive in nature. Before the consultation at her local health centre, she was given four drugs without being properly investigated; she continued to deteriorate. In SQUH, she showed hyperactive-impulsive behaviour, elation, flight of ideas, preoccupation with self and high self-confidence. The physical examination revealed multiple hypomelanotic patches all over the body and a shagreen patch at the sacral area. The electroencephalogram showed generalised epileptic discharges, while brain imaging showed multiple parenchymal calcified foci in both cerebral hemispheres. Other investigations were normal. She was given valproate, and then a psychostimulant, methylphenidate, that controlled her state. Our aim in reporting this case is not only because it is unique, given its rare comorbidity (ADHD, TS and BD), but also to remind our junior colleagues to be alert to the possibility of an underlying neuropathology when performing clinical examinations and investigations of children presenting with neuropsychiatric symptoms.

Keywords: Attention deficit hyperactivity disorder; Tuberous sclerosis; Bipolar disorder; Children; Mania; Physical examination; Investigation; Case report; Oman.

ATTENTION DEFICIT HYPERACTIVITY disorder (ADHD) is the most common neuropsychiatric disorder encountered in children and adolescents, whether in the community or in the clinic. It can be mild, moderate or severe. The prevalence rate of ADHD in Oman is 5.1% in schoolgirls and 7.8% in schoolboys, which are comparable to the rates found in other studies.1,2,3,4 Boys are affected more than girls in a ratio of 3–4:1. The three main symptoms of ADHD are: attention problems, hyperactivity and impulsivity, occurring in variable proportions, giving rise to three main subgroups: mainly inattentive (20%), mainly hyperactive-impulsive (12%) and the combined subgroup (68%).5,6 In addition, ADHD children have low self-esteem, emotional instability and...
poor memory. Often the age of onset is 3 years of age; however, symptoms must appear during the first seven years of life, and should persist at least for six months, to fulfill the diagnostic criteria. The disorder may continue even after adolescence in about half of the cases.7 Many family studies suggest that genes play a large role in causation, possibly through polygenic inheritance. Like many other psychiatric illnesses, ADHD probably results from an interaction between both genetic and environmental factors such as: cigarette smoking, alcohol, malnutrition, and infection during pregnancy; hypoxia and brain injuries during labor.8,9 Also, exposure to a high level of lead is linked to ADHD.10 Other rare causes of ADHD are single gene disorders (phenylketonuria, galactosemia), neurofibromatosis, tuberous sclerosis, etc. ADHD is usually associated with comorbid disorders such as: oppositional defiant and conduct disorders, anxiety, depression, autism, mental retardation, sleep disorder, dyslexia and bipolar disorder. ADHD should be differentiated from a long list of other disorders (some of which may be found in association with ADHD) such as: petit mal epilepsy, severe iron deficiency anaemia, hyper- and hypothyroidism, adjustment disorders, child abuse, sleep disorders, drug abuse, lead poisoning, emotional disorders, developmental speech and language disorders, post-traumatic stress disorder, bipolar disorder, and hearing impairment. If not diagnosed and treated early, the consequences of ADHD will be alarming, not only for the person him/herself, but also for the family and the community. These include: school failure, smoking, drug abuse, alcoholism, road traffic accidents, domestic injuries, family problems, juvenile delinquency, occupational difficulties, etc.5,11,12 The treatment of ADHD is multimodal, including special education, psychotherapy and psycho-pharmacotherapy. The prognosis of ADHD depends on many factors including the severity of the condition, early diagnosis and treatment, comorbid conditions (especially mental retardation), and the availability of a supportive environment at school and at home.

Case Report

A 7 year-old Omani girl was referred by a local polyclinic to the Child and Adolescent Psychiatry Clinic at Sultan Qaboos University Hospital (SQUH), Oman. The information giver was the patient’s father. The main complaints were: hyperactivity, aggression and insomnia during the previous year. Also, both parents had noticed that, during the same period, the patient had become over talkative (sometimes making irrelevant remarks), distractible with poor attention and concentration, and had exhibited risk-taking behaviour. Her symptoms had started gradually, but were progressive in nature. Because of her aggressive and risk-taking behavior she had stopped going to school. A few months before the consultation, the patient had
started to have tonic-clonic seizures lasting for about 3 minutes, mostly during the night with uprolling of the eyes, loss of consciousness, frothing in the mouth, and urination. The convulsions had gradually become more frequent (twice a week), occurring both during the day and night. She looked happy, talking and playing with herself most of the time, showing high self-confidence. Although the patient had gained bladder control at an early age, she then became incontinent. Her appetite had also diminished. There was no history of fever, head trauma or child abuse. Regarding her sleep pattern, she was going to sleep very late (around 1–2 A.M.) with initial insomnia, sleep interruptions and early waking (at 5–6 A.M.); she did not sleep during the day. Several months previously, her family had taken her to a local polyclinic (psychiatry outpatient department), and without being investigated she was given the following treatment: haloperidol 1.5 mg, procyclidine 5 mg and phenobarbitone 30 mg all three drugs once a day and carbamazepine 100 mg twice daily. The patient did not improve on that treatment, on the contrary, her symptoms worsened over the time. Her medical and psychiatric histories were uneventful. There was no consanguinity between parents, and no family history of mental disorders. She was the last of 7 siblings (from both parents). The pregnancy and delivery were normal; her birth weight was 2.9 kg. Her development was normal. She was described before her illness as a playful, sociable and intelligent girl. The mental state examination showed a well-dressed, highly hyperactive, impulsive, easily distractible, inattentive, over-familiar child. Her speech was of a high rate and volume with flights of ideas. She maintained eye contact. Her mood looked high with some irritability. She had high self-esteem with evident self-confidence. Her recent memory was disturbed, while her intelligence seemed to be normal. Her weight was 19 kg and height was 113 cm (both at 10th percentile). There were multiple hypomelanotic patches all over the body and a shagreen patch at the sacral area. The physical examination (including neurological) was normal. The computed tomography (CT) and magnetic resonance imaging (MRI) brain scan showed multiple parenchymal calcified foci in both cerebral hemispheres. The largest one was in the right frontal subcortical region and there were multiple subependymal calcified foci noted in both lateral ventricles, which often suggest tuberous sclerosis (TS) [Figures 1, 2 and 3]. The blood investigations were normal. The electroencephalogram (EEG) showed generalised epileptic discharges. She was referred to the neurology section of the Child Health Department for further investigations and for medications to control her seizures. In addition, systemic investigations were done: an echocardiography, a chest X-ray and abdominal ultrasonography, all of which were normal. The fits were controlled with sodium valproate (175 mg twice daily), while the hyperactivity was controlled by methylphenidate (slow release) 20 mg once a day. A diagnosis of tuberous sclerosis, complicated by ADHD and hypomania, was made. A significant change was reported by the parents during follow-up visits in her hyperactivity, inattentiveness and insomnia. She became less talkative, less elated and was seizure-free over follow-up visits.

Discussion

This case represents the commonest neuropsychiatric disorder in child psychiatry, ADHD, which is characterised by disruptive behaviour and disturbed cognitive functions starting in early life. After doing the appropriate clinical assessment and investigations, we found that ADHD was caused by a rare disease, TS. This is a multi-system-genetic disease, resulting in multiple benign tumours affecting different organs, with a prevalence of 1/6,000 newborns. TS is distributed...
equally between the two sexes and is caused by mutations of one or two genes: TS1, ch 9 (produces hamartin) and TS2, ch 16 (produces tuberin). These proteins act as tumour growth suppressors. TS can be transmitted either by autosomal dominance inheritance or by spontaneous mutation. Treatment is directed to control symptoms as there is no cure for TS. The use of adequate doses of valproate controlled the epilepsy in this case, while methylphenidate controlled the hyperactive-impulsive behavior. In addition to the ADHD and TS, this patient showed symptoms and signs of bipolar disorder (mania) as manifested by marked elation, over talkativeness, flight of ideas, high self-confidence and noticeable irritability. Such an association of these conditions is very rare, reported only in two cases in medical literature. Bipolar disorder (BD) in children was previously thought to be an uncommon occurrence, although cases have been diagnosed since the 1970s. It was a matter of debate until few years ago, when psychiatrists start to diagnose and treat such cases with more frequency, possibly due to doctors’ increased awareness of the condition. The majority of the BD cases in children (> 90%) is associated with ADHD, while only a minority of ADHD cases (< 20%) suffer from comorbid BD. Early diagnosis and treatment of BD is of high importance to alleviate the devastating outcome of the disorder, which might end in suicide in many cases. In this case, valproate acted as an anti-epileptic and a mood stabiliser while the symptoms of ADHD were treated by methylphenidate.

This case had been treated at the local health centre by active psychotropic drugs without being fully investigated. It is not surprising that the patient did not improve; on the contrary, her state worsened. We emphasise the importance of appropriate physical examination and proper investigations in medical practice, and stress the necessity of excluding organic causes before commencing any treatment.

Conclusion

This case may be the third one in the world presenting with a rare association of TS, ADHD and BD appearing at an early age. We strongly underline the importance of performing a careful clinical examination and proper investigations, which are of crucial importance for sound diagnosis and treatment.

ACKNOWLEDGMENT

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References

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Incidence of congenital malformations is three to four times more common in infants of diabetic mothers than in the general population. These include neural tube defects, anomalies of the heart, urogenital system, skeleton and alimentary tract, and the caudal regression syndrome (CRS). Caudal regression syndrome is characterised by variable lumbosacrococcygeal or sacrococcygeal agenesis. It is accompanied by symmetrical multiple musculoskeletal anomalies of the pelvis and legs in babies of mothers with diabetes mellitus; however, genetic predisposition and vascular hypoperfusion have been suggested as other causal factors. Agenesis of the corpus callosum and holoprosencephaly has also been described as a component of diabetic embryopathy.

A rare combination of all these three conditions in an infant of a diabetic mother is reported here.

Case Report

A baby boy was born at 38 weeks gestation to a 28 year-old, gravida 6, mother of a non-consanguineous marriage. Her previous five babies were normal. She was diagnosed to have Hodgkin’s lymphoma in 2005 and was in remission at the time of this report. When diagnosed with lymphoma, she was also detected to have diabetes and has been on insulin since that time. The glycaemic control of the mother was poor in the first trimester with a high level of haemoglobin A1C (HbA1C) of 11.6% at 8 weeks of gestation. The control improved subsequently.
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with a drop in HbA1C to 9.5% at 20 weeks and 6.5% at 32 weeks, (the recommended value during pregnancy is <6%). An antenatal scan of the fetus at 24 weeks showed abrupt termination of the lumbar spine with bilateral club feet and bilaterally dilated lateral ventricles with absent septum pellucidum [Figures 1a and 1b]. The baby was born by elective cesarean section for breech presentation at 38 weeks gestation. His Apgar score was 8 at one minute and 9 at 5 minutes. The birth weight was 3610 g (90th percentile for gestational age [GA]); his head circumference 36 (90th percentile for GA). Physical examination of the lower limbs showed muscle wasting below the hips. There were dimples on the lateral aspect of both thighs overlying the greater trochanters and also over the bony prominence in the lower spine. The hips were flexed and adducted with fixed hyperextension of the knees. The femoral bones assumed a V-shaped position [Figures 2a and 2b]. Dribbling of urine was noticed on the second day of birth with a poor urine stream. The anus was patulous.

The baby had transient tachypnea requiring nasal continuous positive airway pressure. The neonatal period was otherwise uneventful. His skeletal survey showed sacral agenesis with iliolumbar articulation (type III) and a narrow pelvis [Figures 3a and 3b]. A magnetic resonance imaging (MRI) scan of the brain showed partial agenesis of the corpus callosum involving the anterior body, genu and rostrum. The T2 weighted image also showed an absence of the septum pellucidum along with partial lobar holoprosencephaly involving the posterior hemispheres [Figures 4a and 4b]. An MRI
scan of the spine showed complete sacral agenesis, a tethered cord, and an intramedullary cyst in the lower part of spinal cord [Figure 5]. His abdominal ultrasound (US) and cardiac echocardiogram were normal. The orthopaedic follow-up showed a progressive enlargement of the intramedullary cyst which required excision at 6 months of age. The renal tract was normal with no infections or vesico-ureteric reflux until the time of this report, but the anus has remained patulous. His weight at 9 months follow-up was 10.1 kg and his head circumference 46 cm. Except for the effect of the lower limb anomaly the developmental milestones have been normal.

Discussion
Prospective and retrospective cohort studies have demonstrated an increased risk of congenital...
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abnormalities with pre-existing diabetes. Experimental studies suggest that hyperglycaemia is the major teratogen in diabetic pregnancies, but other diabetes-related factors may also affect fetal outcomes. The teratogenic insult in diabetic embryopathy occurs between the third and seventh week of gestation at the initiation of organogenesis. Miller et al. found no major anomalies if the HbA1C was less than 6.9%, and significantly lower incidence if the HbA1C was less than 8.5% in the first trimester. Our patient had an HbA1C of 11.6% in the first trimester.

The main differential diagnosis of CRS would be sirenomelia. The relationship between CRS and sirenomelia is still debated with many researchers considering the latter to be a severe form of CRS. The presence of renal and anal agenesis, fused lower limbs and a large single umbilical artery distinguish sirenomelia from CRS.

Maternal diabetes is associated with increased risk of other congenital central nervous system (CNS) malformations in the offspring. Holoprosencephaly (HPE) is a complex human brain malformation resulting from incomplete cleavage of the prosencephalon into right and left hemispheres, occurring between the 18th and the 28th day of gestation. The rostral neuropore closes at 24 days of gestation. Holoprosencephaly occurs due to rostral mesodermal dysfunction. At 74 days of gestation, axons cross through the dorsal region of the commissural plaque and start forming the corpus callosum. At 115 days of gestation, the corpus callosum reaches its adult form. Many phenotypic variants of HPE exist with partial or complete agenesis of the corpus callosum. Our patient had hyperglycaemia in the first trimester and this may explain the presence of both partial lobar HPE and partial agenesis of corpus callosum.

Some researchers have been successful in prenatal diagnosis in the first trimester based on a short crown rump length. The crown rump length was reported to be normal in our patient at 10 weeks of gestation. On the 24 weeks scan, abrupt termination of the lumbar spine was noted.

In CRS, the mental functions are often normal and these children only need neurologic and orthopaedic support for the lower limbs and control of bowel and bladder. Morbidity and mortality is often due to a neurogenic bladder resulting in renal failure. Association of CRS with partial agenesis of the corpus callosum and partial lobar holoprosencephaly, as in our case, may result in additional neurological problems although at age 9 months this child appeared neurologically normal.

The incidence of all forms of diabetes is increasing among the Omani population. In a study in the Dhahira region of north-western Oman, 12.2% of stillbirths were among diabetic mothers. Many Omani multigravida have several normal babies before developing pregestational and gestational diabetes. Because of a previous good obstetric history, they often come late in pregnancy for their first antenatal visit, thus losing out on an opportunity for early diagnosis of hyperglycaemia and anomalies.

Conclusion
Diabetes in pregnancy, whether insulin or non-insulin dependant, can be associated with multiple malformations in the fetus. Recognition of women with, and at risk of, diabetes is important as optimal glycaemic control in the periconceptional period may reduce the risk of embryopathy. In these mothers, early antenatal US may help in identifying this devastating disorder so that appropriate counselling can be offered.

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References


A symptomatic hypercalcaemia is a common metabolic derangement, usually detected incidentally on routine biochemical screening. The most common aetiologies are primary hyperparathyroidism and cancer. Primary hyperparathyroidism is usually mild and asymptomatic. Only a few patients with primary hyperparathyroidism develop severe hypercalcaemia with serum calcium concentrations above 3.5mmol/L and evidence of end-organ involvement, such as bone or kidney. In contrast, a severe hyperparathyroid state is usually present in parathyroid carcinoma. We present a case of severe primary hyperparathyroidism and then discuss in what circumstances it should be treated as parathyroid carcinoma as well as review the evidence for what action clinicians should take when faced with such a dilemma.

**Case Report**

A 44 year-old male with a 4 year history of renal calculi, but no other chronic illness, was admitted to the Urology service at Mubarak Al-Kabeer Teaching Hospital, Jabriya, Kuwait with an impacted urethral stone. He was a naval officer working outdoors, on a normal diet with no symptoms of malabsorption, no neck masses on clinical exam and no cervical lymphadenopathy. He had normal renal and liver functions. He was found to be severely
hypercalcaemic (corrected calcium 3.4 mmol/L) and subsequent investigations revealed severe hyperparathyroidism (intact parathyroid hormone (iPTH) 84 pmol/l (normal range 2.2–7.1 pmol/L) and alkaline phosphatase (ALP) 1200 IU/L (normal range 26–88 IU/L). Hypercalcaemia was controlled with saline diuresis, calcitonin (200 units twice daily subcutaneous) and pamidronate (initially a 60 mg infusion followed by 30 mg 10 days later), but despite these intensive measures, there was only a transient drop in serum calcium down to a nadir of 2.7 mmol/L corrected, after which it slowly began to rise again.

Although, on evaluation, he had vitamin D deficiency: 25-hydroxy (OH) vitamin D was 22 nmol/L (Low < 30 nmol/L; insufficient 30–80 nmol/L; normal > 80 nmol/L), his bone mineral density (BMD) T-scores were normal at anterior-posterior (AP) spine and femoral neck suggesting that this state of severe hyperparathyroidism was not long-standing. Given the previous data and the severity of the hyperparathyroidism plus raised ALP and the presence of radiological evidence of metabolic bone disease, it was suspected that he might have parathyroid carcinoma (PTC) which could have evolved from a state of preceding mild primary hyperparathyroidism (accounting for renal calculi over the preceding 4 years). His normal BMD, in retrospect, was attributed to a possibility of recent PTC transformation. Localisation studies confirmed the presence of a large tumour posterior to the trachea and just above the superior pole of the right thyroid lobe by both sestamibi scanning and a computed tomography (CT) scan of his neck [Figures 1 and 2], but was missed by ultrasound (US) in view of its ectopic location. The CT scan also showed the presence of three large (1cm) lymph nodes in the upper jugular group close to the tumour.

He was booked for radical excision (based only on clinical suspicion of PTC) and had this done about 2 weeks after being reviewed by the endocrine team, with central and paratracheal lymph node dissection and right hemithyroidectomy. The three enlarged superior jugular lymph nodes were removed and sent for frozen section that showed no evidence of metastases from the possible parathyroid tumour. This was confirmed by the final pathology report. As expected, he went into hungry bone syndrome post surgery and was managed on parenteral calcium for the first 72 hours. There were no surgical complications and he had complete surgical recovery. He was placed subsequently on alfacalcidol 0.25 mcg twice a day and calcium (Sandoz) 1 gm thrice daily. Histopathology revealed no morphologic features of PTC within the tumour and there was no capsular or vascular invasion. Immumohistochemical studies revealed 5% Ki67 protein positivity and a weakly positive B-cell leukaemia/lymphoma 2 (BCL2). He is doing well.
Severe Hyperparathyroidism versus Parathyroid Carcinoma
A clinical dilemma

Post surgery and is currently normocalcaemic.

Fourteen months after surgery, he had a traumatic fracture of the right neck of his femur. A repeat iPTH was 3.3 pmol/L, calcium 2.6 mmol/L, albumin 32 g/L and BMD revealed normal T-scores. This was thus not attributed to a recurrence of his underlying disease.

Discussion

PTC is often misdiagnosed preoperatively as primary hyperparathyroidism secondary to parathyroid adenoma or hyperplasia. The clinician’s suspicion of malignancy should be aroused in the presence of severe hyperparathyroidism and such suspicion is the most valuable tool in planning surgery thereby optimising the outcome. Although such clinical and laboratory findings may suggest carcinoma, these findings are non-specific and there are no obvious clinical or biochemical markers that can clearly differentiate patients with carcinoma from adenomas.

An important clue is very high serum calcium, although this is not diagnostic. Calcium levels above 3.5 mmol/L are common in contrast to the typical elevation of 0.25 to 0.5 mmol/L above normal seen in benign primary hyperparathyroidism. A majority of patients with subsequently proved PTC have been shown to have a calcium level in excess of 3.8 mmol/L, and indeed 12% of patients present with hypercalcaemic crisis. Alkaline phosphatase is also more commonly elevated in patients with PTC, this finding is thought to result from the higher incidence of bone degradation in this population. Another clue is a severely elevated parathyroid hormone (PTH) levels in patients with subsequently proven PTC. Levels up to 12 times those in normal subjects are the norm in these patients, whereas PTH levels approximately two times normal are the more common presentation in primary hyperparathyroidism. Occasionally, values as high as 75-fold may occur. This is in contrast to benign adenomas where no correlation exists between clinical variables and preoperative biochemical markers of calcium homeostasis and adenoma weight or volume.

The most commonly affected organ systems in patients with primary hyperparathyroidism are the renal and skeletal systems. Benign hyperparathyroidism is reported to cause renal impairment (nephrolithiasis, nephrocalcinosis, impaired glomerular filtration) in fewer than 20% of patients. In contrast, Wynne et al. reported a 56% prevalence of nephrolithiasis and an 84% prevalence of renal insufficiency in PTC. Radiological hyperparathyroid skeletal features such as osteitis fibrosa cystica, subperiosteal erosion and ‘salt and pepper’ skull, are more commonly observed in PTC (39-91%); less than 10% of patients with benign disease have these features. Patients with PTC are also at higher risk for developing complications in other organ systems (severe pancreatitis, peptic ulcer disease and anaemia) than patients with primary hyperparathyroidism.

In addition to severe hyperparathyroidism, careful neck examination may reveal the presence of a palpable firm lump within the neck which has been reported in approximately half of patients with PTC, but in less than 10% of patients with benign primary hyperparathyroidism. Paralysis of the recurrent laryngeal nerve is also a sign of late invasive PTC, but is noted to be rare. At the time of presentation 15-20% of patients with cancer have lymph node metastasis and up to one-third have distant metastasis, usually to lung or bone. Despite the easy access to the tumour in PTC, the use of fine needle aspiration in suspected cases is not recommended for several reasons. First, the diagnosis of PTC can be extremely difficult.

Figure 2: Post-contrast sagittal reformat showing the extent of the lesion (arrow).
cytologically and, further, sampling errors may lead to significant false negative results. Second, by violating the fibrous capsule, there is a risk of seeding of parathyroid tissue. It is noteworthy that one case report of cutaneous seeding of a lesion subsequently proved to be PTC followed a fine needle aspiration which itself showed no cellular atypia.12

While not being specific for malignancy, sestamibi scanning is also an excellent modality to detect the presence of local and distant metastasis.13 US of the neck is the most useful initial method for localisation of parathyroid glands. Distinguishing features of PTC, noted on the US, include a depth-width ratio greater than 1 in 94% of cases in contrast to 5% of patients with adenoma. The US scan may also indicate the lobulated appearance and inhomogeneous echogenicity often associated with PTC.14 Our patient had an ectopic tumour (hence missed on ultrasonography), being in one of the four most common ectopic locations which are: retrotracheal adenoma, mediastinal adenoma, intrathyroid, and carotid sheath adenoma. Finally, bone mineral density scans have been used to detect significant skeletal abnormalities and, when correlated with grossly abnormal laboratory values (calcium, PTH and alkaline phosphatase), have been found helpful in distinguishing patients with PTC from those with adenoma.4

Normalisation of hypercalcaemia prior to surgery is essential for patients with PTC to prevent possible renal failure and cardiac arrest. Adequate rehydration with intravenous normal saline increases renal calcium excretion. The additional use of frusemide or other loop diuretics promotes sodium and calcium diuresis. Bisphosphonates inhibit bone resorption and have become the main line treatment for lowering severe hypercalcaemia. Intravenous pamidronate is commonly used and produces a striking, but transient, fall in serum calcium. Routine blood tests and adequate renal function must be checked prior to surgery. In patients with persistent hypercalcaemia and those with unresectable tumours, medical treatment aimed at reducing calcium levels has been implemented. Also the use of octreotide can inhibit parathyroid hormone secretion from some PTCs. Conservative treatment with saline and loop diuretics is typically not sufficient, and more aggressive medical therapy is required.5 Medications that have been used with some success include pamidronate (bisphosphonates),15 mithramycin,16 calcitonin17 and cinacalcet.18

Surgery is currently the only effective treatment for PTC. The diagnosis of PTC should be suspected in patients with primary hyperparathyroidism if at the time of neck exploration a large white or grey adherent mass is seen (the majority of them weigh in between 2 and 10 gm).8 This is in contradistinction to benign parathyroid neoplasias, which tend to be soft, flatish, and red-brown in colour.9 Frozen section often provides results of little value as microscopic infiltration of tumours can be missed. En bloc resection of the PTC, avoiding capsular rupture with widely adjacent tissue, is the treatment of choice.10 This usually involves a large collar incision with ipsilateral thyroid lobectomy and excision of paratracheal alveolar tissue, lymph nodes and thymic tongue. Sacrifice of the recurrent laryngeal nerve may be required if involved. Although cervical lymph node metastasis occurs in less than 20% of cases, most authors recommend routine dissection of the tracheo-oesophageal groove.10 Surgery offers the patient the best chance of a cure. Unfortunately, the diagnosis of PTC is often made following pathologic review, but if carcinoma is suspected based on laboratory values and intraoperative findings are consistent with PTC, en bloc resection should be completed at the time of initial surgery, before definitive pathologic assessment.5,19 Controversy exists as to whether the patient without obvious tumour extension should be taken back to the operating room for thyroidectomy, isthmusectomy and excision of paratracheal and central neck nodes after the diagnosis of PTC is obtained from the pathology report. If preoperative diagnosis of PTC is suspected, we advocate pre-emptive radical surgery with en bloc resection of the tumour, together with ipsilateral thyroid lobe, paratracheal and central lymph node dissection and adjacent structures (only if involved) avoiding any capsular rupture of the mass. This represents the gold standard of surgical treatment of patients.20

Regular postoperative calcium levels must be monitored after resection as calcium levels may fall rapidly due to the ‘hungry bone syndrome’ where high levels of parathyroid hormone have depleted bone stores of calcium. Intravenous calcium as well as oral calcium and vitamin D may be required for a variable amount of time. After the operation, all patients require careful long-term monitoring.
In the early postoperative period, symptomatic hypocalcaemia may occur secondary to redeposition of calcium into the bones (hungry bone syndrome);\(^\text{21}\) this requires treatment with intravenous calcium and we usually start immediately post surgery with a continuous infusion starting at 0.5 mg/kg/h of elemental calcium. Supplemental calcium and calcitriol must be prescribed to maintain calcium at the lower limit of the normal range.\(^\text{5}\) Once the suppressed parathyroid glands recover and adequate bone deposition has taken place, the requirement for supplemental calcium and calcitriol will drop and eventually these agents can be stopped. Thereafter, serum calcium and PTH levels should be monitored every 3 months.

Although the post-operative diagnosis of PTC relies often on histological examination, the histological criteria for this diagnosis are not definitive. Several authors have suggested that criteria for pathologic diagnosis of PTC should include the presence of a fibrous capsule, fibrous trabeculae, trabecular or rosette-like cellular architecture, presence of mitotic figures and presence of capsular or vascular invasion.\(^\text{22}\) However, other authors have pointed out that mitotic activity can occasionally be seen in adenoma and hyperplastic glands. McKeown et al. have noted that the presence of cellular pleomorphism and atypia per se are not reliable indicators of malignancy, and mitotic activity in parenchymal cells must be distinguished from mitotic activity in endothelial cells.\(^\text{23}\) Others have suggested that spindle cells and coagulation necrosis on standard slides may suggest PTC with a poorer prognosis. However, in the absence of pathognomonic diagnostic criteria, a definitive pathological diagnosis of PTC may not be possible, especially in its less aggressive forms.\(^\text{23}\) Nonetheless, diagnostic accuracy should be improved by recognition of the constellation of macroscopic and microscopic features in combination with multidisciplinary correlation.

With immunohistochemical staining, several cellular proteins have been found to occur more commonly in specimens of PTC than in the parathyroid adenoma.\(^\text{22}\) Ki-67 has been found in about 11%, (range 3-65%) of patients with PTC in contrast to 2% of those with a parathyroid adenoma.\(^\text{22,24}\) The retinoblastoma (Rb) protein has been found to be present in most patients with parathyroid adenoma and to be significantly reduced or entirely absent in various studies in patients with PTC.\(^\text{22}\) Stojadinovic et al. tested several molecular phenotypes and found that 76% of patients with a parathyroid adenoma and no patients with carcinoma had the phenotype “p27(+) bcl-2(+) Ki-67(-) mdm2(+)”.\(^\text{22}\) Although these immunohistochemical markers have shown potential to discriminate between benign and malignant parathyroid disease, probably only vascular invasion that correlates with tumour recurrence and metastases should be considered useful in confirming malignancy.\(^\text{20}\)

Recurrence of tumours can be monitored by calcium and parathyroid hormone levels. Most recurrences occur 2-3 years after the initial operation, but this period is variable and a prolonged disease-free interval of as long as 23 years has been reported in the literature.\(^\text{5,11}\) This emphasises the importance of long-term follow-up of patients who have had a parathyroidectomy for malignant disease. A short disease free interval is associated with poor prognosis. Recurrent disease presents with rising levels of serum calcium and PTH. Rarely, a patient may present with a severe hypercalcaemic crisis. Parathyroid carcinoma metastasises through both lymphatic and haematogenous routes. The regional lymph nodes are common sites of metastatic disease (30%) and distant metastases most frequently involve the lungs and bones, followed by the liver and other visceral organs. Cervical recurrences are frequently palpable in patients.

Modified radical neck dissection has not been reported to improve survival and is associated with higher operative complications.\(^\text{11}\) Therefore modified radical neck dissection may only be indicated in patients with cervical lymph node metastasis, local invasion or with local recurrence.\(^\text{11}\) The lung is the most common site of distant metastasis, followed by the bones and the liver. For localised distant metastasis, multiple, aggressive surgical resection is recommended by most authors as it reduces tumour bulk, thereby reducing the serum calcium and parathyroid hormone levels. When hypercalcaemia is refractory to surgical resection, medical treatment is required. Radiation therapy has been described in the literature with limited data and conflicting results.\(^\text{8}\) Data from treatment groups receiving adjuvant radiation therapy following surgical excision, where margins were positive, have shown evidence of possible improvement in preventing recurrence of disease. Limited data exist regarding
primary treatment with radiation therapy, but there may be a role for adjuvant radiotherapy as it may provide a survival benefit.\textsuperscript{25} Data are also limited for the treatment of PTC with chemotherapy.

### Conclusion

There are no clinical or laboratory data which allow a preoperative diagnosis of parathyroid carcinoma and only occasionally does a definitive histopathologic finding differentiate an adenoma from a carcinoma. We have argued that this sort of presentation should alert the clinician to the presence of a possible parathyroid carcinoma. This should then lead to radical surgery since this is the only effective therapy for parathyroid carcinoma, and it should always be performed if a preoperative suspicion is entertained. Finally, at the time of publication of this report, our patient had been followed for 2 years, and had a normal calcium, iPTh and BMD. He did have a fracture neck of femur that occurred on minimal trauma, but there is no evidence to suggest a recurrence of his disease at this point. It can be argued that this could be a case of primary hyperparathyroidism complicated by vitamin D deficiency, and this is probably true even though there were no features of severe vitamin D deficiency (other than vitamin D levels) including a normal skeletal status. While the Vitamin D deficiency may be aetiologic in the pathogenesis of such a severely hyperparathyroid state, our focus nevertheless is not on why the hyperparathyroidism was so severe. Rather the focus here is that such severe hyperparathyroidism is also seen in parathyroid carcinoma and as such we should have a high index of suspicion for parathyroid carcinoma whenever we are faced with this severity of hyperparathyroidism, as it is the more serious condition and should not be missed. Conversely, parathyroid carcinoma is extremely uncommon and thus, if there is a clear vitamin D deficiency clinically and biochemically with tertiary hyperparathyroidism and hypercalcaemia, the likelihood of carcinoma is extremely low and need not be considered further. –

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Severe Hyperparathyroidism versus Parathyroid Carcinoma: a clinical dilemma


In differentiated thyroid cancer (DTC), metastases occur outside the neck in up to 15% of patients and less than 3% of these are in bone.1,2 Their early detection is made possible by measurement of serum thyroglobulin (Tg) and by whole body scanning (WBS) using I-131. Thyroglobulin is synthesised by all thyroid tissue except anaplastic cancers and, when detected after all non-malignant tissue has been destroyed, indicates the presence of residual DTC. Thyroid stimulating hormone receptors (TSH-R) are present on most but not all DTC metastases. If present, Tg levels usually increase when the patient is hypothyroid, off thyroxine (T4) with elevated endogenous thyroid stimulating hormone (TSH) levels, or after injections of recombinant human TSH (rhTSH) with the patient euthyroid on T4 replacement.3 For those patients without a Tg response to TSH and those who do not take up I-1314, other treatments must be employed as indicated, for example, additional surgery, external radiotherapy, embolisation, etc.5 Treatment guidelines for DTC include total thyroidectomy and removal of any nodal metastases followed by an ablation dose of I-131 4–6 weeks later when TSH levels are elevated.6 This first dose destroys residual normal tissue and may localise any metastatic disease.7 After a further 6 months an I-131 WBS is carried out after withholding T4 or using rhTSH. If the WBS is positive, a further ablation dose is given and the process repeated, when indicated, at 6 monthly intervals until there is no further I-131 uptake. Thyroglobulin measurements are more sensitive than WBS for detecting metastases; however, up to 6% of patients...
may have functioning metastases when serum Tg and Tg antibody levels are unmeasurable.8

In this paper, we present details of a young patient who developed multiple bone metastases and whose treatment, both surgical and isotopic, was delayed by multiple pregnancies, the husband refusing contraception for his wife or for himself. In spite of this, and following surgery and four ablation doses of I-131, the patient has remained in clinical and biochemical remission for more than five years.

Case Report

The patient aged 20, a mother of four children, presented, in 1996, to another hospital in Oman with a large multinodular goitre. Surgery was advised, but delayed until 1999 because of two further pregnancies. After a total thyroidectomy, the histology confirmed a follicular variant of papillary thyroid carcinoma with capsular and vascular invasion [Figures 1 & 2] without lymph node involvement. She was then referred to Sultan Qaboos University Hospital, Oman, for I-131 ablation. Her clinical examination at that time and thyroid function tests were normal with an undetectable Tg level on T4 replacement. She was admitted one month later, having stopped T4, at which time the Tg level was 39 ng/ml. Unfortunately, treatment had to be postponed as she was again pregnant (for the seventh time). Abortion was offered, but refused, and, as a result of the families’ insistence on breast feeding, her first ablation dose was delayed for an additional 2 years until July 2001. The Tg had now risen to 513 ng/ml off T4, and the post I-131 ablation whole body scan (WBS) revealed uptake in the thyroid bed and extensive metastases involving the skull, dorsal and lumbar spine, pelvis, right hip, right humerus, sternum and ribs [Figure 3]. These were not visible on a routine skeletal survey. Additional I-131 ablation doses were planned every 4–6 months and the family was again advised to use contraception until the patient’s treatment was complete. This advice was ignored. The second ablation dose was given 6 months later in January 2002. With the patient off T4, the Tg had now decreased to 164 ng/ml, but the WBS still revealed extensive asymptomatic metastases, but without any uptake in the neck. A further pregnancy (number 8) delayed the third ablation for another two years until November 2004. At this time, however, the Tg was only 2 ng/ml off T4 and the WBS had become negative. She received a fourth ablation dose in March 2006 although the Tg was undetectable off T4.
and the WBS remained negative. Pregnancy number 9 was uneventful and her Tg levels have remained undetectable on T4 for more than 6 years [Figure 4]. Thyroglobulin antibodies were undetectable throughout. Lactation was discontinued 3 months before the first and third ablation doses of I-131. The patient was not lactating before the second and fourth doses. Each time, ablation doses were given after stopping T4 for one month. The TSH levels were >100 on each occasion.

**Discussion**

Patients with DTC have a 10-year survival rate of 80–95%. This drops to 40% when distant metastases are present and to less than 21% when these are in bone. Bone metastases are from mainly follicular or less well differentiated tumours and 80% occur within the axial skeleton, which contains a large number of stored growth factors. Tumour cell products inhibit osteoprotegerin production thus permitting increased interaction of the receptor activator of nuclear factor kappa beta (RANK) and its circulating ligand (RANK-L). This results in excessive bone resorption with release of transforming growth factor beta (TGF-β), platelet derived growth factor (PDGF) and insulin like growth factor (IGF), amongst others, which stimulate further tumour growth. Remission rates for single lesions may be as high as 54%, but this falls to less than 3% with multiple bone metastases and usually occurs in those patients...
under 45 years of age with a small tumour burden and normal appearing skeletal X-rays. This was the case in our patient whose metastases developed 18 months after the delayed thyroid surgery. The I-131 ablation doses were widely spaced due to her intervening pregnancies. Rising outpatient Tg levels and I-131 WBSs confirmed the presence of multiple metastases which were confined to the skeleton, but not visible on routine skeletal surveys.

Our patient’s situation was most unusual as contraception was refused throughout. However, the prevailing view is that pregnancy has no major influence on the prognosis of DTC. Nonetheless, the resultant delays and the effects of her pregnancies undoubtedly encouraged the development of the metastatic disease. In spite of this, her Tg level was undetectable at the time of her fourth admission. Nevertheless, we elected to give another ablation dose in an attempt to destroy any microscopic foci of residual disease or functioning metastases that may be present when Tg and Tg antibody levels are negative. At this point, the WBS was negative and the Tg levels have remained undetectable since then.

**Conclusion**

Inspite of all the delays in this patient’s treatment, it appears that her DTC with multiple bone metastases has been cured.

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Complications involving the abdominal wall, particularly port site hernias, were not expected when laparoscopic procedures were first introduced. With the increasing number of laparoscopic procedures in abdominal surgery, more port site hernias were observed. Port site herniation is a rare, but potentially dangerous complication, following laparoscopic surgery. Visceral herniation into the abdominal trocar entry sites is occasionally mentioned, but seldom reported. Kadar et al. in a large retrospective case review found the incidence of port site hernias after operative laparoscopy to be (0.17%). In another study, the incidence was 0.47%, but none of the cases in the study had small bowel obstruction, secondary to herniation through the trocar entry sites. In another multicentre, prospective, randomised clinical trial by Bhoyrul et al. to study the complications related to laparoscopic port design, with a follow-up period of 6 to 18 months, there were no incisional hernias in any of the patients in the study. In another study done by Nezhat, evaluating the postoperative complication of laparoscopic procedures done on 5,300 patients, only one case needed laparoscopically assisted bowel resection following a strangulated port site hernia. Most of the port site herniations are in the extra umbilical port site. The risk factors for the development of trocar site hernias include: the trocar diameter, the trocar design, preexisting fascial defects, and some operation- and patient-related factors.
The following report describes a case of a trocar site hernia that evolved to a strangulated small bowel after laparoscopic myomectomy. We describe the significance of complete closure of the fascial defect at the trocar site in the prevention of this condition and the risk factors involved, as well as the importance of early diagnosis to avoid serious subsequent events.

Case Report

A 42 year-old lady, who had had a previous laparoscopic cholecystectomy in Chennai, travelled abroad for treatment of her chronic abdominal pain, secondary infertility and second degree vaginal prolapse. She was 158 cm in height and weighed 85 kg. She underwent a hysteroscopy with Fothergill’s operation and laparoscopic myomectomy. Under general anaesthesia the patient was put in the lithotomy position. The hysteroscopy showed a subseptate uterus so septal resection was done. The anterior vaginal wall and posterior vaginal wall reflected off the cervix. The cervix was amputated 5 cm away from the internal os and homeostasis was secured. A Fothergill’s suture was applied to cervix and a neocervix created. Complete homeostasis was then secured and there was no undue bleeding. A 12 mm trocar for the laparoscope was placed in the supraumbilicus area. The pneumoperitoneum was then established with carbon dioxide and the intraperitoneal pressure was maintained at 10 mm Hg. Two more 10 mm trocars were inserted in the right and left iliac fossas. All trocars used were the bladed type. The uterus had two fibroids. One was 2 cm in diameter and deep seated in the anterior uterine wall. It was not indenting the cavity and hence it was not removed. The other fibroid was 2 cm in diameter and situated in the posterior uterine wall. A myomectomy was done, and the specimen was removed through the 12 mm supraumbilical port without extending the skin incision. Complete homeostasis was secured. The fascial defect was closed at the umbilical port site, while the fascia in the right and left iliac fossas port sites was not sutured. The overlying skin was sutured. In the initial post operative period, the patient was asymptomatic and tolerated a normal diet. The patient then returned to Oman seven days after her surgery.

Ten days later she was admitted to sultan Qaboos University Hospital with a history of colicky abdominal pain and bilious vomiting, but had normal bowel habits. On physical examination, her abdomen was soft and there was no tenderness. Her umbilical wound showed some serous discharge. There was a 4 cm x 4 cm tense mobile non-tender fluctuant mass in the left iliac fossa just below the left-sided port site. Aspiration was done for the underlying clinically diagnosed seroma, which revealed 10 ml of sero-sanguinous fluid. An abdominal X-ray was done and was normal so the patient was treated conservatively. On fifteenth post operative day, the patient had an episode of

![Figure 1: Computed tomography (CT) scan shows the dilated small bowel which is protruding into the muscular layer of the abdominal wall (arrow).](image1)

![Figure 2: Computed tomography (CT) scan, coronal view, shows the entrapped small bowel loops in the muscular layer of the abdominal wall (arrow).](image2)
excessive vomiting and severe epigastiric pain, her last bowel movement had been 2 days previously and she had not passed any flatus per rectum for one day. The abdominal X-ray was repeated and showed evidence of small bowel obstruction (dilated small bowel, with multiple air fluid levels). This was followed with an abdominal computed tomography (CT) scan which showed evidence of a left-sided abdominal wall incisional hernia with entrapped bowel loops between the abdominal muscles [Figures 1, 2, and 3]

The patient then was moved to the operating room. Under general anaesthesia and full aseptic condition, a 1 cm infraumbilical incision was made. A 10 mm trocar was introduced using an open technique. Pneumoperitoneum was achieved using carbon dioxide. A 10 mm camera was introduced. Incarcerated small bowel loops were found herniating through the previous left-sided port site. A 5 mm trocar was introduced in right iliac fossa under direct vision; reduction of the herniated bowel loops was attempted laparoscopically, but this was difficult technically. Another attempt was made to release the incarcerated bowel loops through the abdominal wall. A transverse skin incision was made at the previous left-sided port site; subcutaneous and fascial planes were carefully dissected out. A seropurulent collection was found and multiple twisted bowel loops which were stuck to the abdomen wall. Multiple attempts to manipulate and reduce the hernia failed. The procedure was converted to an open laparotomy. A midline incision was made extending from just above the umbilicus to the suprapubic area. The hernia contents were reduced by extending the fascial defect. Multiple distended jejunal loops were found, with a 20 cm area of ischaemic bowel. Resection and stapled primary anastamosis was done. The abdomen was washed with a copious amount of warm saline and an antibiotic based solution. The fascia over the hernia site was closed using a non-absorbable continuous suture. The midline incision was closed with a non-absorbable suture for the fascia and an absorbable subcuticular suture for the skin. No drain was required and the skin over the hernia site was kept open over loose skin sutures which were closed 5 days later after daily dressing. The patient went home on the 6th post operative day with no complications. We saw her in our outpatient clinic a month after her discharge with no further complications.

Discussion

Port-site herniation, which is one of the major complications after laparoscopic procedures, can sometimes develops into serious complications, such as bowel obstruction due to incarceration into the fascial defect at the port site. Boughey et al. have reported four cases of Richter’s hernia that occurred at a port site after laparoscopic surgery. The frequency of incisional hernias was significantly higher for 12 mm than for 10 mm trocars. The frequency of incisional hernias at extraumbilical 10 mm and 12 mm trocar insertion sites was 0.23% and 3.1% respectively suggesting that the wound created by a larger port carries a greater risk of herniation. Incisional hernias were also significantly more common if the fascia was left open, as it the case in our patient. Most surgeons now routinely close the fascia of port sites to prevent this complication. According to previous reports, port site herniation apparently happens more often with the use of...
Indeed, Kolata demonstrated, in a pig experimental model, that the wounds made by the non-bladed trocar were narrower than those created by bladed trocars. Several reports even concluded that port sites created by non-bladed trocars do not require fascial closure. Our current case support this theory as a 10 mm bladed trocar was used here and also suggests that the thick preperitoneum is a potential space that allows the development of bowel herniation. A previous report also described port site herniation, despite the closure of the superficial layer of the fascial defect. Holzinger and Klaiber made an attempt to classify trocar hernias by their onset and related features. They classified trocar hernias into the early-onset type, the late-onset type and the special type. According to this classification our case belongs to the early-onset type that occurred immediately after the operation, with a small-bowel obstruction. The risk factors for the development of trocar site hernias include: 1) the trocar diameter; 2) the trocar design; 3) preexisting fascial defects; 4) enlargement of a port site to remove a specimen; 5) high blood glucose levels; 6) obesity; 7) increase intra-abdominal pressure as in chronic obstructive airway disease; or 8) extensive manipulation of the trocar during relatively prolonged surgical duration, which might enlarge the trocar site and thus induce bowel herniation. The current case had the following risk factors: obesity, the use of a trocar with a large diameter (10 mm), the use of a bladed trocar and the lack of fascial closure. Most surgeons will recommend closure of port sites, especially those measuring 10 mm or more and associated with any of the risk factors described above; unfortunately, this was not done in our case with a 10 mm port site. The prevention of extra-umbilical incisional hernias and dehiscences appears to be more achievable when the closure is performed under laparoscopic vision. Both the aponeurosis and the peritoneal membrane should be treated; however, it is sometimes difficult to completely close the defect, including the peritoneum, especially in obese patients. Shaher reviewed different wound closure techniques by a literature search. In this review, old methods using classical instruments, including the Deschamps needle, are also seen to be useful as well as special wound devices designed for port site closure. Elashry et al. described a prospective randomised study demonstrating that the Carter-Thomason device was faster and resulted in fewer port-closure-related complications among eight different techniques tested. Insertion of a surgical plug into the muscular layer of trocar wounds has also been proposed by Chiu et al. Alternatively, tangential insertion of a trocar through the abdominal wall might be effective in reducing the size of fascial defects. Moreover, recent publications have demonstrated that radially expanding type trocars could be useful to avoid the necessity of closing the fascial defect. From the clinical point of view, we recommend serial radiological examinations of the abdomen as early as possible for any case with suspected bowel obstruction. In our case, intestinal obstruction was missed on an initial normal abdominal X-ray despite the patient been symptomatic, but the repeated X-ray and CT scan showed evidence of small bowel obstruction. Moreover, special attention should be paid to patients with risk factors for port site hernia such as: obesity, the use of large bladed trocars and the lack of fascial defect closure during surgery.

Conclusion

Port-site herniation is a rare, but very dangerous complication, after laparoscopic procedures. Closure of a port site of more than 10mm is highly recommended especially with patients with risk factors such as: obesity, the use of large bladed trocars and the lack of fascial defect closure during surgery. Immediate diagnosis and management of port sites hernias will prevent further complications.

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References


Oculocutaneous albinism and anterior mesodermal dysgenesis of the anterior segment are two distinct disorders with different types of inheritance. Oculocutaneous albinism presents as an autosomal recessive disorder and mesodermal dysgenesis as an autosomal dominant disorder. Although there are several studies reporting an association between the two inherited disorders, in each of these case reports, only one case has been reported as having this association.\(^1,2,3,4,5\) In a study by Izquierdo \textit{et al.},\(^6\) four patients with Hermansky-Pudlak syndrome were described as having Axenfeld anomaly. In our cases, all the three siblings had oculocutaneous albinism with nystagmus, iris transillumination, foveal and optic nerve hypoplasia and poor vision. All of them showed Axenfeld anomaly with prominent Schwalbe’s line and iridocorneal processes.

**Case Reports**

Three of the eight children of a family with a history of consanguinity, [Figure 1] who attended the Low Vision clinic of Sur Hospital, Oman, were diagnosed as having oculocutaneous albinism and were worked up for evaluation of low vision and management.

**CASE ONE**

A boy aged 13 years had been wearing high hypermetropic glasses for the previous three years. On examination, he had a best-corrected visual acuity of 0.2 in each eye. Refraction revealed the following: right eye +9.00 sph/-3.0 at 15 degrees, left eye +9.50/-2.0 at 160 degrees pendular nystagmus, and poliosis. Biomicroscopy revealed an anteriorly displaced irregularly thickened posterior embryotoxon (Schwalbe’s) in both eyes with iris processes extending to the peripheral cornea [Figure 2]. The iris transillumination was positive, intraocular pressure was 14 mm Hg in both eyes and the fundus showed gross choroidal...
hypopigmentation, small hypoplastic discs and absent foveal reflex suggestive of foveal hypoplasia [Figure 3]. His systemic history was unremarkable with regard to any evidence of bleeding diathesis or recurrent infections or respiratory problems.

CASE TWO
A boy aged 9 years presented, also with a history of wearing high hypermetropic glasses. His systemic history revealed that he had an extra digit, which was excised. On examination, he had a visual acuity of 0.1 in the right eye and 0.05 in the left one. Refraction showed: right eye +8.00/-3.00 @ 10 degrees, left eye +8.00sph/-3.00 at 165 degrees. Intraocular pressure (IOP) 15mm Hg right eye, 14mm Hg left eye. The rest of the anterior and posterior segments were remarkably similar to his brother’s eyes. Blood investigations were negative for sickling. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were 17.2 secs and 33.0 secs respectively and international normalised ratio (INR) was 1.38.

CASE THREE
A girl aged 6 years, sister of the two other siblings mentioned above, presented without a history of wearing glasses with other ocular findings very similar to her those of her brothers. Her uncorrected visual acuity was counting fingers 3m in both eyes. Refraction showed: right eye +8.00sph/-1.00 at 10 degrees, left eye +7.00sph/-2.00 at 160 degrees.

Discussion
Albinism refers to a group of hereditary disorders that involve an abnormality of melanin synthesis or distribution. The term albinism comes from the Latin word albus, which means white, and, in 1908, Garrod first scientifically described it. Clinically, albinism presents as a pigmentation abnormality of the skin, the hair, and/or the eyes. Albinism can be divided into two broad categories, as follows: oculocutaneous albinism and ocular albinism. Oculocutaneous albinism involves both the skin and the eyes, whereas ocular albinism mainly affects the eyes with minimal to no skin involvement.

The primary morbidity of both oculocutaneous albinism and ocular albinism is eye related. Signs and symptoms include photophobia, refractive errors, monocular vision, strabismus, pendular nystagmus, iris transillumination defects, foveal hypoplasia, and abnormal decussation of the optic nerve fibres. These ocular manifestations are almost always present in both forms of albinism; however, the degree of their presentation can vary depending on the type of albinism and the racial background of the patient.

Oculocutaneous albinism mostly presents in an autosomal recessive form and is mainly of two types, namely tyrosine negative and tyrosine positive albinism. Mesodermal dysgenesis is an autosomal dominant disorder characterised by iridogonio dysgenesis with iris hypopiasia and may be associated with glaucoma and systemic features.

Of the various types of mesodermal dysgenesis, the Axenfield anomaly is the least severe and presents as an anteriorly displaced Schwalbe’s line and iridocorneal processes with or without glaucoma. Only a few studies in the literature have shown the association of albinism and iridocorneal dysgenesis. Lubin et al. published a case of a tyrosine negative albino having mesodermal dysgenesis of the Axenfield type and thought that the association could be coincidental. Another study by Hayakawa et al. showed an association of ocular albinism with an Axenfeld type of mesodermal dysgenesis in one Japanese patient and postulated that there could be a common defective factor leading to these two disorders.

In our report, the occurrence of this association in three siblings in an identical fashion shows that the association is more than coincidental. It has been speculated that mesodermal deficiency is a developmental anomaly that is related to lack of pigmentation in the tissues thus connecting the two diseases. It has been postulated that a developmental arrest, in the third trimester of gestation, of tissues derived from the neural crest cells accounts for the
ocular and most of the nonocular abnormalities in this group. Even the melanocytes are of neural crest origin thus supporting their occurrence in a single individual. Our cases also conform to other reports of the common type of mesodermal dysgenesis associated with albinism, which is the Axenfeld anomaly. It is important to be aware of this particular ocular association of anterior mesodermal dysgenesis with albinism. This is because it could be one of the causes of ocular morbidity and loss of vision in albinism, apart from other inherent factors namely: foveal hypoplasia, nystagmus, optic nerve hypoplasia, and increased number of crossed fibres in the optic tract leading to defective cortical projection and squinting.

Conclusion
Several case reports have been published hitherto on the association of oculocutaneous albinism and ocular albinism with anterior mesodermal dysgenesis. Our case report of three siblings with a similar association not only supports this but also goes a step further in proving that the association is more than coincidental and could be caused by a common defective factor. A further insight into the genetics of both the disorders may throw light on the possible genetic linkage between them.

References
Asymptomatic Permanent Left Bundle Branch Block (LBBB) complicating Diagnostic Left Heart Catheterisation

Hafidh Al-Hadi*, Mansour Sallam

In general, diagnostic cardiac catheterisation is recommended whenever it is clinically important to define the presence or severity of a suspected cardiac lesion that cannot be adequately evaluated by other non-invasive techniques. Most of the indications for cardiac catheterisations can be collectively classified into management of patients under the following categories: valvular heart disease, chronic heart failure, acute myocardial infarction (AMI), percutaneous coronary intervention (PCI), and coronary artery bypass surgery (CABG). Cardiac catheterisation is a relatively safe procedure, but it has a well defined risk of morbidity and mortality. In an analysis of 59,792 patients who underwent cardiac catheterisation and coronary angiography, the following were recognised complications (percentage of risk in brackets): mortality (0.11%), myocardial infarction (0.05%), cerebrovascular accidents (0.07%), arrhythmias (0.38%), vascular accidents (0.07%), arrhythmias (0.38%), vascular accidents (0.07%), arrhythmias (0.38%), vascular...
In general, diagnostic cardiac catheterisation is recommended whenever it is clinically important to define the presence or severity of a suspected cardiac lesion that cannot be adequately evaluated by other non-invasive techniques. Most of the indications for cardiac catheterisations can be collectively classified into management of patients under the following categories: valvular heart disease;1 chronic heart failure;2 acute myocardial infarction (AMI);3 percutaneous coronary intervention (PCI),4 and coronary artery bypass surgery (CABG).5 Cardiac catheterisation is a relatively safe procedure, but has a well defined risk of morbidity and mortality. In an analysis of 59,792 patients who underwent cardiac catheterisation and coronary angiography, the following were recognised complications (percentage of risk in brackets): mortality (0.11%), myocardial infarction (0.05%), cerebrovascular accidents (0.07%), arrhythmias (0.38%), vascular complications (0.43%), contrast reactions (0.37%), haemodynamic complications (0.26%), perforation of heart chambers (0.03%), other complications, including renal failure, heart failure and vasovagal reactions (0.26%).6 The overall risks of cardiac catheterisation are less than 2%. Arrhythmias most commonly encountered during cardiac catheterisations include frequent ventricular ectopic beats, short runs of ventricular or supraventricular tachycardia, bradycardia, heart block, asystole, atrial fibrillation and, rarely, ventricular fibrillation with sudden cardiac death. These arrhythmic

Figure 1: The initial ECG taken one day prior to the cardiac catheterisation procedure.

Figure 2: The ECG of the patient taken immediately after left heart catheterisation procedure. It shows a typical left bundle branch block pattern that was not present on the initial ECG [Figure 1].
Asymptomatic Permanent Left Bundle Branch Block (LBBB) complicating Diagnostic Left Heart Catheterisation

Complications are more common with right heart catheterisation, patients with left main stem (LMS) coronary artery disease (CAD), patients with low ejection fraction (EF) < 30%, and patients with high New York Heart Association (NYHA) class IV. This report describes the case and reviews the literature on the incidence, significance and the implication of this complication during cardiac catheterisation procedures.

Case Report

A 67 year-old man, on regular treatment for hypertension (HTN) for the previous six years, presented at Sultan Qaboos University Hospital, Oman. He had had a history of shortness of breath (SOB) on exertion for the previous few years, but this had recently worsened. The echocardiogram showed a mitral valve prolapse (MVP) with severe mitral regurgitation. He was referred for work-up for mitral valve surgery. He was on the following medications: aspirin 81 mg once a day, ranitidine 150 mg twice a day, bisoprolol 2.5 mg once a day, and simvastatin 20 mg at night.

The patient had an appearance of good health. Heart auscultation revealed a normal first sound, a faint second sound and a pansystolic murmur at the apical region radiating to the axilla. The lungs were clear and the rest of the examination was unremarkable. Initial investigations, including total blood count, urea and electrolytes, coagulation profile, lipids, electrocardiogram (ECG), routine chest X-ray, hepatitis B screening and human immunodeficiency virus (HIV) screening were all normal. Figure 1 shows the baseline ECG of this patient on admission. It shows a normal sinus rhythm, left atrial abnormalities, Rsr' pattern in frontal leads, and a QT interval that was at the upper limit of normal.

The left heart catheterisation procedure was explained and consent was obtained. The procedure was done through the right femoral artery using the Seldinger technique. Coronary angiography was done using 6F, JL4 and JR4 diagnostic catheters. This required multiple small injections of contrast (5–8ml) by hand at high speed and acquisition of coronary images in different projections.

An aortogram was done using a pigtail catheter. Thirty-five millilitres of contrast were injected at a rate of 15 ml per second using a power injector. Left ventriculography was done after crossing the aortic valve using a J-shaped guide wire followed by the pigtail catheter. Twenty-five millilitres were injected at 10 ml per second using a power injector. These investigations revealed the following results: the coronary angiography showed two vessels with CAD disease; the first diagonal revealing 75% long stenosis proximally and 75% stenosis distally. The posterior descending artery had 75% stenosis proximally. The rest of the vessels were normal. Ventriculography showed good left ventricular (LV) systolic function, severe mitral regurgitation (MR) grade IV, mildly dilated LV and grossly dilated left atrium. There was no significant aortic pressure gradient across the aortic valve. The aortogram showed no aortic root dilatation and mild grade I aortic regurgitation. Overall the patient had severe MR and two vessels with CAD disease.

Towards the end of the procedure, it was noticed incidentally on the monitored ECG that the sinus rhythm had changed to an LBBB pattern. The patient heart rate was 75 beats per minutes and was completely asymptomatic and haemodynamically stable, and the catheterisation procedure had no
complications. After sheath removal, the patient was moved back to the ward. The patient had no chest pain or SOB. His vital signs were all normal. The physical examination was also entirely normal. A repeat ECG showed a widening of the QRS complex typical for an LBBB pattern [Figure 2]. A chest X-ray was similar to the previous one with a normal appearance of pulmonary vasculature, no pleural effusion, and no signs of lung oedema or consolidation.

An urgent bed-side echocardiogram revealed:
1) LV: upper limit of normal internal dimensions, no regional wall motion abnormality, excellent systolic function, and a normal relaxation pattern, and an intact septum; 2) mitral valve: thickened, fibrosed and calcified with a significant prolapse of the posterior leaflet with severe MR; 3) aortic valve: mild aortic stenosis (AS) with trivial aortic regurgitation (AR); 4) tricuspid valve: normal with trivial tricuspid regurgitation (TR) with estimated pulmonary artery pressure of 20 mm Hg; 5) thickened pericardium with no effusion; 6) no intra-cardiac masses or thrombi noted. Serum cardiac troponin I (CTnI) was 0.03 µg/L four hours after the procedure and, when repeated next day, was again 0.03 µg/L (normal ≤ 0.03 µg/L). As the patient was asymptomatic and clinically and haemodynamically stable, the investigations did not reveal any specific cause for this new LBBB (normal troponins and echocardiographic findings); he was therefore treated conservatively. He was allowed to proceed with surgery during the index admission. A CABG (one vein graft) with mitral valve replacement (MVR) (tissue bioprosthetic valve) was carried out successfully 8 days after the cardiac catheterisation. The postoperative course was only complicated by transient atrial fibrillation (that eventually reverted to sinus rhythm after a short course of amiodarone and an on-demand pacemaker), and abdominal pain (a computed tomography (CT) scan of the abdomen showed no major pathologies). The patient was discharged home in a stable condition 12 days after surgery. The pre-discharge ECG still showed a LBBB.

Discussion
The appearance of transient LBBB in the setting of cardiac catheterisation (and specifically during left ventriculography) is a well known, although very uncommon complication. In the pivotal article of Bourassa M and Noble J, in which 5.250 coronary arteriographies were reviewed, the incidence of LBBB was 0.17%. However, LBBB in all the above cases subsided either spontaneously or responded rapidly to appropriate drug therapy. An iatrogenic left bundle branch block is a rare complication of left ventricular catheterisation and coronary arteriography because unlike the branches of the right bundle, which pass superficially within the thin-walled right ventricle, the left bundle is a fan-like structure that radiates from the left interventricular septum through the thicker-walled left ventricle. This structure results in relatively greater protection of the left bundles from focal mechanical injury. In contrast to catheters frequently used in the right ventricle, left heart catheters such as “pigtails” are usually spatially located in the left ventricle so that the interventricular septum is spared mechanical contact.

We have reviewed the available literature, but did not find anything on this topic. A permanent LBBB complication as a result of diagnostic cardiac catheterisation has, to the best of our knowledge, not been reported before. Our case was admitted for a routine procedure. The patient was not classified into high risk category for the development of arrhythmias. These categories include patients with left main stem (LMS) lesions, heart failure and recent acute coronary syndrome (ACS) events. He had no renal or liver dysfunction, and the basic electrolytes (potassium, calcium, and magnesium) were normal. None of the medications he received were known to be associated with the development of this complication.

The guide wire used was J wire, which means it has a J-shaped soft curve at the terminal end. This protects against left ventricular wall trauma or puncture. This type of guide wire rarely causes trauma to the aorta or LV wall [Figure 3A]. Other guide wires for example straight-tip guide wires which are sometimes used (but not in this case) to cross heavily calcified stenotic aortic valves, may sometimes cause LV wall trauma or perforation or LMS dissection if they are manipulated aggressively. Performing a left ventriculogram or an aortogram requires the injection of a large volume of contrast solution using a powered injector at high speed into the LV and aorta respectively through a pigtail catheter that has a hole at one end and many small side holes to allow the contrast to leak out [Figure
The end of the catheter is placed near (but not in contact with) the apex and away from the free wall. This is very important to avoid the powered injection jet being injected directly into the wall of the LV. Inadvertent injection of contrast solution into the free wall of the LV under high pressure may lead to free wall rupture or perforation with subsequent cardiac tamponade or free septal wall rupture with free left to right shunt. The presence of many side holes in the pigtail catheter is a very important safeguard to reduce the force of the jet by allowing the contrast to leak side ways if the end hole were inadvertently placed in direct contact with the wall.

This LBBB complication appeared during heart catheterisation suggesting a direct contribution of the latter to its development. The exact cause(s) of the LBBB in this case is not known, but could be due to one of the following several possible mechanisms: 1) during coronary angiography or aortography, it is possible that a small amount of foreign body material (air, thrombus, coronary plaque, cholesterol or calcium) may have embolised distally and blocked the blood supply to the left bundle branch or some of its fibres; 2) it is possible that manipulation of either the guide wire or the pig-tail might have produced a minimal, localised, septal contusion (without any troponin elevation or pathologic findings in the echo study) leading to LBBB onset; 3) the powered injection of contrast medium into the left ventricle may have caused trauma to the septum or left ventricle and the left bundle branch or one of its distal branches. The overall findings suggests that the trauma to the heart (if any) may have been non-mechanical (as per the echocardiogram) and most probably was very slight, because there was no subsequent significant cTnI rise in the serum.

LBBB is rare in normal individuals and is most commonly seen in patients with CAD; however, as many as 12% of patients with LBBB have no demonstrable heart disease. Even among patients without overt heart diseases, LBBB is associated with a higher than normal risks of cardiovascular events and all cause mortality. It is associated with high grade atrioventricular (AV) block and sudden cardiac death. The abnormal ventricular activation pattern of LBBB induces an abnormal systolic function with reduced ejection fraction and stoke volumes and abnormal diastolic function. It carries a more serious prognosis than right bundle branch block, but neither form requires specific treatment.

**Conclusion**

This case report describes the development of a de novo permanent LBBB after a left heart catheterisation procedure. We have reviewed the literature and, to the best of our knowledge, this has not been described before. We have offered several possible hypotheses to explain the association between left heart catheterisation and the development of LBBB. It is difficult to predict the long-term prognosis of such a complication in this patient. In general, LBBB, whatever the cause, has a poor prognosis and carries significant morbidity and mortality risks. It remains to be seen whether these risks also apply to the specific case described in this report.

**ACKNOWLEDGMENTS**

We would like to thank the patient and all the nursing staff in the Catheterisation Laboratory and in Ward Two Purple of Sultan Qaboos University Hospital, Oman, who were involved in the management of this case.

**References**


Ever since the beginning of aviation in 1904, rapid strides have been made in the development of aircraft performance. This has imposed severe stress on the human operator whose physiologic has remained unchanged. Development of life support systems such as sophisticated oxygen systems, escape systems, flying clothing and cockpit layout and instrumentation have helped man to cope with the increasing stress. And yet there are occasions when, under a given set of circumstances, various factors interact to produce an untoward incident called an accident. In military aviation, an aircraft accident is defined as: "An occurrence, not directly caused by enemy action, involving one or more aircraft, which happens during the operation of any one of these aircraft, and which results in injury to one or persons, or damage to aircraft or property."

A variety of reasons such as technical failure and inclement weather conditions may have a role to play, but it is has been generally accepted that in as many as 70–80% of aircraft accidents, various levels of human operator error are likely to be a contributory cause. An analysis of fatal aircraft accidents in the Indian Air Force indicated that 68% were caused by "pilot error."
A flow chart has been constructed to outline various reasons which may induce pilot error [Figure 1]. The final outcome may be precipitated because of pilot incapacitation or an error of judgment and possibly caused by a combination of circumstances. This case report attempts to highlight human frailty which may have led to fatal outcomes in two accidents involving Indian Air Force aircraft and aircrew. These incidents have been chosen as they had occurred in the early 1970s, and hence do not compromise military intelligence. Where ever possible, an attempt has been made to use the findings at autopsy to explain the possible reasons for a fatal outcome to the pilot involved.

**Case Report One**

The pilot of a Sukhoi 7 B supersonic fighter bomber (Flying Officer V) was seen to eject from the aircraft at low level. The army rescue patrol found the pilot dead. No obvious injury was noticed. The flying clothing of the pilot, including the oxygen mask and the protective helmet were apparently intact, as was the parachute to which he was still attached. The ejection seat was recovered from some distance from the site where he was found. The body was evacuated to a forward dressing station where it was examined by an Army medical officer (MO). He noted that there was a large contusion on the forehead, and an extensive pulpy swelling which he described as a possible haematoma on the back of the head. He disposed of the body as per operational orders, but had the ejection seat and the flying clothing sent to the pilot’s airbase. There the items were examined by the flight surgeon. He noticed that the protective helmet had a dent in the front area which would have been covering the forehead. The area of impact had some debris which could be matched with the front, lower margin of the aircraft cockpit canopy. The back of the helmet was also dented. This dent was impacted with the leather debris from the head rest of the ejection seat. The findings indicated that the forehead of the pilot was struck by the rear end of the canopy, which in turn had smashed the back of the head in to the head rest of the ejection seat. When this possibility was correlated to the findings of an abrasion and pulpy swelling noted by the MO in the field, it was concluded that the probable cause of death was severe head injury.

**Discussion**

The Sukhoi 7B fighter aircraft was equipped with an ejection seat which could be used in three positions: low, medium and high. Pilots with high sitting heights (sitting height is the vertical distance between the base of the spine while sitting erect on a hard surface, and the top of the head) were advised to use either the medium or the low position depending on their “eye datum” line which was marked in the cockpit.

If a pilot had to eject from the aeroplane, the canopy of the aircraft would slide backwards over the pilot’s head and leave the aircraft at its rear end. If the pilot sat in a position which was too high for him, there was the strong possibility that the leading lower border of the canopy would strike his forehead as it slid over him.

The pilot, Flying Officer V, had a high sitting height and had been advised to fly in the low seat position. The possibility of his head being fouled by...
the canopy while ejecting had been demonstrated to him; however, he had chosen to use the high seat position because he found the bomb sight and the front gun sight easier to operate in the high position.

Given this information, the possible sequence of events may be reconstructed. The pilot was flying as per his practice in the “high” position which was inappropriate for him. When he initiated ejection (once initiated, the ejection sequence, which occurs in less than a second, can not be arrested) the canopy which weighed approximately 60kg, was jettisoned by the explosive charge, developing extremely high kinetic energy. It slid backwards along the cockpit, and as it was about to leave the aircraft from the rear of the cockpit its leading edge struck a hammer blow on the forehead of the pilot. This accounted for the dent seen on the frontal region of the helmet which had taken the shape of the lower ridge of the canopy. The impact jolted the pilot’s head backward striking the head rest of the ejection seat so denting the back of the helmet covering the occipital region. Both the impacts, which probably occurred in about 200-300msecs, were enough to produce a fatal head injury as noted by the army doctor in the battle zone.

Conclusion

The correlation of head injury of the pilot to the various marks on his helmet was strong enough evidence to prove that he had fouled the canopy fatally as he tried to eject from the aircraft. As per the classical definition, this incident may not be classified as an accident as it happened indirectly as a result of enemy action during operations. Nevertheless, such an event was inevitable when the pilot chose to fly in a position which would compromise his flight safety. If he had chosen the prescribed seat position, he would probably have made an uneventful escape from his aircraft. It was thus the attitudinal error of the pilot which led to this uncalled for incident. No other failure on the part of the pilot was responsible for the event. It is for this reason that it has been classified as an accident.

Case Report Two

Two Sukhoi 7B fighter aircraft were detailed to undertake a low level high speed navigation sortie (flight). The aim of the mission was to familiarise the newly posted flight commander of the squadron, who had a considerable amount of recent flying experience on Hawker Hunter fighter aircraft, with the Sukhoi aircraft. The flight was led by No 1. pilot who, though junior in rank to his flight commander, was experienced on the Sukhoi and had been flying in the area for about two years. The flight commander was No. 2 in the formation. The sortie progressed as planned until the last part of the exercise. In this, the aircraft were to simulate a dummy attack on an imagined target. Both aircraft, with No. 1 in the lead, were to ‘pull up’ rapidly from their flight altitude of about 100 meters above ground level to about 2 km, dive towards the imagined target, and then pull gradually out of the dive and resume the low level course. In flying terminology, this is known as a loop followed by a dummy dive. Accordingly, the section leader (No. 1) initiated the manoeuvre into which both the aircraft entered. A few seconds later No. 2 crashed fatally into the ground.

Discussion

Both pilots had been declared medically fit to fly by the Squadron Flight Surgeon during the routine pre-flight medical examination. The sequence of events as per an eye witness account of the lead pilot was as follows. The aircraft were airborne at around 0800 hours on a warm April day, and set course for the designated flying area as per the pre-flight briefing. Towards the end of the mission, No. 1 “pulled up” to go into ground attack mode as shown in Figure 2. He completed his manoeuvre and when he was on the descent he saw his No. 2 also reach the top of the loop. However, after that the lead pilot noticed that the No. 2 aircraft seemed to be out of control and started to “fall out of the sky”. He called the pilot, but got no response. Within 15-20 seconds, he saw the aircraft hit the ground on its belly and burst into flames. The pilot had made no attempt to eject. No. 1 also stated that just before the aircraft finally hit the ground, he may have heard some sort of a grunt on his radio transmitter. He reported the accident to the air traffic control and returned to base.

The rescue team found the crashed aircraft had landed on its belly and was almost completely burnt. The cockpit had been destroyed. The pilot
had also almost burnt to ashes, and only a few of his remains could be identified. His flying clothing was burnt, and the helmet had melted. The aircraft had not exploded. There was no evidence to indicate aircraft malfunction and this was corroborated later by a technical investigation. Body parts/tissue were not available for a postmortem examination.

During a loop manoeuvre, the pilot experiences effects of +Gz (positive acceleration) which drives the blood column towards the lower part of the body thus reducing perfusion to the brain. Autonomic reflex activity is brought in to play to restore the brain circulation. This reaction takes between 5-7 seconds to be established in a normal individual.\(^4\) The reflex response may found to be wanting in a number of circumstances such as heat stress, hypoxia, medication with centrally acting drugs, use of antihypertensives, and consumption of alcohol.\(^5\) The response may also be affected adversely by the magnitude and the rate of application of the +Gz force. The contribution of circadian rhythm effects contributing to the pilot’s incapacitation is ruled out as the flight was launched in the morning as per the routine operations schedule. The pilot had not been flying late into the preceding night. Hence he had not altered his routine circadian rhythm. There was no history to suggest that he had indulged in any other activity that may have altered their night-day physiologic cycle. In fact, it has been suggested that cardiovascular reflex activity may be functioning at its peak during the morning hours.\(^6\) Hence the scheduling of the flight in the morning should have enhanced his performance.

In the manoeuvre undertaken [Figure 2], the magnitude of the stress is usually about +5Gz, and is considered within tolerable limits for a trained fighter pilot. The rate of application may vary, but pilots usually control it to less than 1 Gz/sec in a planned manoeuvre as undertaken in this case. The manoeuvre was successful until No. 2 had almost reached the peak of the loop, a point at which the maximal +Gz stress is felt. For unexplained reasons, it may be presumed that the pilot then suffered a gravity-induced loss of consciousness (G-LOC) which incapacitated him.

The aircraft in question was not equipped with an in-flight data recorder (the so-called black box). Hence it was not possible to establish whether the pilot had inadvertently applied a +Gz force in excess of the usual tolerable limits.

From the available documents, it appears that he had not been grounded at any time in his career, nor was he taking any medications; however, consumption of unprescribed medications, such as

\[\text{Figure 2: The construction of the flight profile which may have led to the fatal crash because of possible pilot incapacitation due to a gravity-induced loss of consciousness (G-LOC). Note the figure is not mathematically accurate.}\]
antihistamines, or tranquillisers, cannot be ruled out. Such medications are known to affect tolerance to +Gz stress. He was reported to have put on the anti-G suit before getting into the cockpit. It may be argued that for unknown reasons, he did not connect the suit to the aircraft system, and hence did not get the protection against the Gz force which the G-suit offers. This in turn may have led to the G LoC.

April mornings in the north of India are often quite warm. The ambient temperature at the time of the sortie was around 27°C–28°C. During high speed low level flight, aerodynamic friction is known to increase the cockpit temperature by about 8–10°C. Therefore at the time of the manoeuvre, the cockpit temperature may have been around 36–38°C, and would have been so for about 20–25 minutes before the episode. Whole body heating causes vasodilatation with sweating as a heat dissipating mechanism. It is possible that No. 2 reacted to the increase in cockpit temperature with these mechanisms, and the mild dehydration and peripheral vasodilatation aggravated the adverse effects of +Gz stress and induced the G LoC.

There are two phases of G LoC: 1) the stage of complete incapacitation which lasts for about 12–16 seconds. This is followed by a period of mental confusion and partial incapacitation during which consciousness is partly regained, but the pilot is incapable of performing useful tasks. This phase may last or another 12–15 seconds. Therefore, after suffering a G LoC, a pilot is not in control of the aircraft for as long as 25–30 seconds. In the case under discussion, No. 1 had estimated that 15–20 seconds had elapsed from the time he noticed that No. 2 was not in control to the time he crashed. The possible grunt he heard before impact may have been the sounds made in the cockpit by the partially conscious No. 2. Given the time frame of recovery from G LoC, this may have happened before any perceivable recovery had occurred. It may be presumed then that, at time of impact, No. 2 had just about regained partial consciousness and he died because of the crash impact and the post crash fire. If the episode had occurred at a much higher altitude, the pilot might have been able to regain control of his aircraft.

In-flight spatial disorientation (SD) has been associated with partial or total pilot incapacitation resulting in an accident. In the case under discussion, the weather at the time of flight was clear, devoid of clouds, or poor visibility which are often the contributing factors to SD. The manoeuvre performed by the pilot was not one which would have caused stimulation of more than one set of semicircular canals or the otoliths to generate conflicting vestibular sensations which might have progressed to SD. The pilot was fit to fly on the day of the accident, and there was no reason to suspect the presence of vestibular pathology. This rules out the occurrence of in-flight disorientation as a cause of the fatal accident.

**Conclusion**

On the basis of circumstantial evidence, it is postulated that the accident occurred because the pilot had become incapacitated during the flight. There is a strong likelihood that this happened because his physiological mechanisms failed to sustain brain perfusion when he went in to a loop manoeuvre.

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A stylet is an essential airway adjunct, frequently used to facilitate endotracheal intubation. There have been several case reports of the shearing of the tip of a stylet.1-4. We report a case of broken piece of metallic stylet which remained initially unnoticed in an endotracheal tube.

Case Report

A 58 years old patient, who underwent surgery for a fracture to the neck of the femur. Tracheal intubation was performed with the aid of a stylet; however, 15 minutes later, it was brought to the notice of the attending anesthesiologist that a broken piece of stylet had been left inside the lumen of the endotracheal tube. Prior to this, there was no evidence of a foreign body in the endotracheal tube or tracheobronchial tree. The broken piece of stylet was successfully retrieved with the help of a Kocher’s forceps.

**Keywords:** Broken stylet; Endotracheal tube obstruction; Foreign body; Case report; Oman.

**Abstract:** We report a 58 years old patient, who underwent surgery for a fracture to the neck of the femur. Tracheal intubation was performed with the aid of a stylet; however, 15 minutes later, it was brought to the notice of the attending anesthesiologist that a broken piece of stylet had been left inside the lumen of the endotracheal tube. Prior to this, there was no evidence of a foreign body in the endotracheal tube or tracheobronchial tree. The broken piece of stylet was successfully retrieved with the help of a Kocher’s forceps.

7.5 mg orally one hour prior to anaesthesia. Following induction of the anaesthesia and adequate neuromuscular relaxation, laryngoscopy and intubation were attempted by a senior anaesthetist. The first attempt was unsuccessful as the larynx was noted to be very anterior. The second attempt at tracheal intubation aided by a sheathed metallic stylet was successful. The trachea was intubated with an endotracheal tube size 8.0 mm. Immediately after intubation the chest was auscultated. Air entry was noted to be equal bilaterally and there were no adventitious sounds. Peak airway pressure and oxygen saturation were well maintained between 18-20 cm H₂O and 97–99% respectively.

About 15 minutes later, while patient was being painted and draped, the anaesthesia staff nurse brought to the notice of the attending anaesthetist that part of stylet was missing. Immediately...
laryngoscopy was done and something could be visualised above the vocal cord inside the lumen of the endotracheal tube. The surgeon was informed of the incident and requested not to proceed further, till the diagnosis of broken stylet could be confirmed and remediable measures taken.

The radiographer was asked to perform a C-arm (X-ray image intensifier) screening of the head and neck region. During screening a radio opaque shadow could be visualised around the glottic region. Immediately after confirmation of the foreign body, a Kocher’s forceps was introduced in the oropharynx and the endotracheal tube was firmly grasped just above the vocal cord. The endotracheal tube was now gently pulled out along with the broken stylet in-situ. The sheared portion of the stylet measured 13.2 cm [Figure 1].

The trachea was now re-intubated with the help of a new sheathed metallic stylet. After confirmation of correct the placement of endotracheal tube, the surgeon was allowed to proceed. The surgery lasted for about 90 minutes and the intra-operative period remained uneventful.

After completion of surgery, the residual neuromuscular blockade was reversed and the endotracheal tube removed. The postoperative period was uneventful.

Discussion

There are occasional reports in the literature regarding broken stylets, especially unsheathed metallic stylets. Despite this fact, this type of stylet is still being used in third world countries, may be because of cost constraints or ignorance. In many places anaesthetists have abandoned the use of stylet and are pre-shaping the endotracheal tube by immersing it in ice cold water.5 In the present case, we used a sheathed metallic stylet, but our anaesthesia staff nurse did not notice that its sheath had been damaged.

The shearing off of a tip can occur in both metallic and plastic covered stylets, especially when removal of the stylet from an endotracheal tube is difficult.6 However, in our case, we did not encounter any difficulty in removing the stylet. These patients usually show some chest signs or a change in ventilatory parameters which mimics a partial endotracheal tube obstruction, or increasing resistance to flow, or bronchospasm. Surprisingly, our case remained asymptomatic. This could have been because the broken stylet may not have occupied enough of the internal diameter of the endotracheal tube to produce respiratory signs or increased airway resistance. Had it not been for the vigilance of the anaesthesia staff nurse, the event could have gone unnoticed until it progressed into the trachea with signs and symptoms of a foreign

Figure 1: The broken stylet with sheath measuring 13.2 cm.
body in the tracheobronchial tree or, rarely, until tracheal extubation.

Conclusion

In conclusion, it is strongly recommended that a routine, regular check of equipment be performed to avoid such mishaps. If the removal of the stylet proves difficult, the attending anaesthetist should immediately examine the stylet to note if any portion of it has been damaged, broken or shorn off into the endotracheal tube or tracheobronchial tree.

References

A Combined Surgical and Prosthetic Approach for the Successful Management of a Mutilated Eye Socket

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THE RECONSTRUCTION OF AN EYE SOCKET

The reconstruction of an eye socket presents a series of complex problems. The interdependence of the elements of the orbit is such that change in one element will automatically affect the function and structure of each of the other elements, and thus the integrity of the whole. Therefore the surgical approach should provide a soft tissue bed for movements and aesthetics in order for the prosthesis to have a natural appearance.

This case report describes the timely intervention of a prosthodontist resulting in a prosthesis which prevented contraction and prolapse of the contents of the eye ball and ensured its satisfactory appearance.

Case Report

A male patient aged 35 years was referred to the Department of Prosthodontics and Implantology, Government Dental College and Research Institute, Bangalore, India, with a missing right eye. The patient had had a major road traffic accident one year previously, following which he had undergone emergency surgical treatment at a local hospital.

The initial treatment was the enucleation of the right eye as it was badly ruptured with no visual potential. The tears in the upper and lower eyelid of the right eye were also repaired. The initial management of the injury was unsatisfactory as the socket was left with disrupted tissues and suture.

A year later, the examination of the patient revealed a right anophthalmic socket with severe loss
of contour, depressed and with scarred tissues. The contour of the upper eyelid was lost as the medial end of the eye lid was sutured near the supraorbital rim. As it had remained like this for about a year, this had resulted in the formation of a notch at the medial end of the socket. The lower eye lid was shrunken with medial fornix contracture leading to a shortening of the lower fornix. A fibrous band running from the medial margin of lower lid to the bulbar conjunctiva was also seen. There was a nasoethmoidal fracture on the right side which resulted in the distance of the nasion from right medial canthus having increased to almost double that of the left eye (traumatic telecanthus) [Figure 1].

Cosmetic rehabilitation surgery was performed. In the upper eyelid, the notch was removed by releasing the lateral portion that was adherent to the supraorbital rim. The edges were freshened and the medial end was reapproximated to the medial canthus. In the lower lid, the fibrous band was released and fornix reconstruction stitches were placed from the inferior fornix to the skin over the intraorbital rim.

The healed socket was found suitable to support the prosthesis [Figure 2] so then the prosthetic rehabilitation procedure could begin. According to Allen and Webster’s “modified impression method”, an impression was made using a stock ocular tray along with syringe filled with irreversible hydrocolloid. In the first appointment, an iris button was selected according to the size of iris of other eye. The selected iris button was preliminarily painted under natural light, to match the basic colour and tint of the other eye. The impression was poured with irreversible hydrocolloid into a small tumbler. On setting, it was cut to remove the impression, leaving the mould space behind. The mould space was filled with a combination of molten inlay wax and carving wax in order to have sufficient rigidity for carving and handling. The poured wax was then removed and smoothened carefully for a trial to verify its fit and support of the soft tissue for bulge in the depressed socket. After the contour and retention were assured, the movements of the wax template in the socket were matched with that of the other eye. Therefore, an aluminium button (to simulate the movement of the iris) with an outward projection or stent was secured to the centre of the external surface of the wax template in order to help to assess the movement easily. The patient was instructed to gaze in different directions and then the movement of the aluminium button was matched with the other iris. Following this, the wax template and attached aluminium button were invested. After dewaxing, the aluminium button was replaced with a pre-painted iris button in the mold space. Acrylization was completed with white acrylic. The processed eye shell was removed, trimmed and tried on the patient. At this stage, the support, fit and movements were checked. Later, final scleral painting was carried out. To give the effect of blood vessels small red fibers were incorporated [Figure 3]. During the painting, patient was asked to remain calm to keep the sympathetic reflexes down in order to avoid redness and watering of the other eye. Subsequently the shell was trimmed about 1-2 mm on the external surface and then packed with transparent acrylic to give a natural appearance. Later it was removed, trimmed, finished and polished. Finally, it was tried on the patient and was suitable.
found to support the surrounding natural tissue with acceptable aesthetics [Figure 4].

Due to persisting traumatic telecanthus, the distance from the medial end of the prosthesis to the nasion appeared to be more than the distance from the medial canthus of other eye to the nasion. To mask this asymmetry, it was decided that the patient should wear spectacles of same power for both the eyes. This camouflage provided an enhanced natural appearance [Figure 5].

**Discussion**

In a long standing case like this where suture has been present for around a year, the soft tissue anatomy changes considerably. The postoperative changes as described by Iverson and Vistness result in superior sulcus depression, pseudoptosis of the upper eyelid and ptosis of the lower eyelid.\(^3\) This further leads to a backward shift of the entire muscle cone and a downward and forward shift of the orbital fat.

Frequently, patients report to the prosthodontist after surgery is over when little can be done to improve the anatomy of the existing socket. A socket that is not treated bearing the requirements of the prosthodontist in mind may result in an ill-fitting prosthesis. On the other hand, if the prosthesis is not well designed it eventually alters the size, shape and surface of the conjunctival sac. Thus the maxillofacial prosthodontist plays an important role in the surgery and subsequent fabrication of an aesthetically acceptable ocular prosthesis in order to restore facial symmetry and a normal appearance for an anophthalmic patient.\(^4\)

The fabrication of an ocular prosthesis is arguably the most difficult of the three single-site facial prostheses, including the nasal and auricular prosthesis. The difficulty arises because the ocular prosthesis must correctly match the other eye in size and contour, and should be positioned exactly in a 3-dimensional space to simulate the correct gaze and interlid opening.\(^5\) The movement of the prosthesis in harmony with other eye is the most realistic aspect of an ocular prosthesis. Close adaptation to the tissue beds uses the full potential of the prosthesis to produce movement.\(^6\) Thus it is critical to ensure that the soft tissue of the eye socket is handled to support the prosthesis fabricated by prosthodontist.

**Conclusion**

This case report shows how a carefully constructed ocular prosthesis can markedly improve the facial appearance of an anophthalmic patient.
References


Smashed to Pieces
A patient’s view of a road traffic accident

Helen Freeman

On May 18th 2009, I left work and set off to collect my children from school in Muscat, Oman’s capital city. Seat belt securely fastened, I was alone in my new car, a Tucson Hyundai. The next thing I knew was floating in and out of consciousness three days later in a Hospital Intensive Care Unit, gradually realising I had been the victim of a serious road traffic accident.

Apparently, one car had overtaken another on the main Sultan Qaboos Highway causing the driver to lose control, collide with a central lamp post and fly over the very low divide, hitting me on the other side of the highway. My car then hit a fourth car. The driver of a car behind, on a visit to me in the ICU, later described the car that hit me as, “Flying over like a rocket or a bolt of light.” He saw smoke rising from my car engine. Fearing an explosion, he decided to move me before the ambulance arrived and with...
the help of two other men, lifted me out of the back of my car. He found my phone and called someone who knew my husband’s number. An ambulance quickly arrived and took the man from the car that hit me to a nearby hospital; he died nine days later, apparently just a week before his planned wedding day. A second ambulance arrived fifteen minutes later and took me to the same hospital and then to one with orthopaedic expertise.

My family arrived in A&E, where, according to my records, I was “fully conscious and oriented,” although to this day I remember nothing. The staff took X-rays, began stabilizing me and wheeled me into the ICU. Swollen, bruised and broken, I had 17 fractures (to my skull, thorax, pelvis, upper and lower limbs), a collapsed lung and severe polytrauma.

The first days passed in a complete blur. Then I became vaguely aware of visitors popping in, nurses turning me every few hours, which was agony, tubes sticking out of my body and non-stop noise in the ward. A team of general ICU surgeons came daily to treat my chest injuries and prepare me for surgery. The CT scans were a huge ordeal, making me feel like I was falling completely out of control. Being shifted off the bed onto a stretcher and into the scanner caused enormous pain, so I prayed hard for help to be able to cope. The medicine I received brought on hallucinations: embarrassing and frustrating experiences. I was vaguely aware of other patients, some needing frantic attention, some not making it. I didn’t eat or drink much, which obviously would have helped my recovery.

My first operation took place 10 days after being admitted to hospital. I just remember that I wanted to get on with it and become more comfortable. I had retrograde nailing of the right femur fracture, which had broken into three pieces, a partial patellectomy and fixation of five pieces with cerclage wires. The team of orthopaedic surgeons also plated my left radius and ulna, taking 8 hours. Five days later, the second operation, lasting nearly 6 hours, consisted of plating of my left femur with bone grafting. This had been badly smashed into over 50 pieces and was a difficult repair job. I remember being wheeled into the theatre, feeling like a slab of meat being laid onto a cold table with doctors and their knives gathering round ready to carve me up. Both operations went well, although the second lung collapsed around this time. A scaphoid cast was applied to my right wrist, so I now had plaster on all four limbs. A hole was drilled through my right heel bone and a pin fitted from which 4 kgs of weight were suspended as a way of treating the acetabular fracture in my pelvis with skeletal traction. Although doctors told me this was standard procedure, it seemed like medieval torture and remained severely uncomfortable until it was eventually removed. My nasal bone, base of skull, clavicle, and ribs healed without intervention.

Three weeks after the accident and a week after my second operation, I was discharged from the ICU to the women’s orthopaedic ward. Still on a lot of medication I was plagued by hallucinations, vomiting and diarrhoea. There was no one to one patient to nurse ratio in this ward and most patients had an attendant, often a sister or mother, staying with them. I therefore struggled to get the attention I needed. Family and friends came to look after me and could see that my condition was bad. I felt their concern and worry, which in turn upset me. My hair, which had been washed on a daily basis in the ICU,
became badly knotted. A nurse gave me what ranks as my worst ever hair cut! At the time, I hardly noticed. After three days, the senior doctor was called up from ICU to see me. She immediately decided to rush me back into ICU suspecting septicaemia, lung and urine infections. This time the ICU doctors thought I would not make it. They put me in an isolation room and onto a ventilator and other vital organ monitors, with round the clock nursing care. Three days passed without my knowing it, and then I spent the rest of that week slowly recovering. I really hated having nasal tubes and needles stuck into various parts of my body. It was such a relief to have them removed. The ICU nurses and doctors showed great compassion, efficiency and kindness and we really appreciated their care. Personal touches comforted me: one doctor came bearing coffee and sat with me.

Moved back to the women’s ward, this time in a better condition, I started to eat again and interact with others. Many people visited - wafts of incense, chatting, laughing and sharing fruit, the flimsy curtains separating beds allowing little privacy. I found sleeping difficult due to chanting, neighbours snoring, cell phones, crying, TV blaring, nurses talking and early morning bed baths.

I began to realise my condition more and felt aghast at the sight of my swollen knees. I was able to cry about the enormity of my situation for the first time. Gradually nurses removed tubes, bandages and stitches and physiotherapists introduced gentle exercises for my totally atrophied muscles. It took four physiotherapists to lift me into a wheelchair and after half an hour of wheeling around the corridors with a friend in attendance, I would be exhausted. I also used a passive exercise machine for my very stiff left leg, but with only one in the hospital, it was not often available. I found this rather surprising in an orthopaedic hospital and a country where so many people suffer as a result of road traffic accidents. One mother commented: “In some countries they have guns and bombs, here we have car crashes.”

My husband managed to get me a private room in the hospital, but there I had no physiotherapist visits and 5 days later was shifted back to the women’s ward in floods of tears with a multi-drug resistant hospital infection feeling this was a huge step backwards. I just wanted to go home. My small windowless isolation room confined me like a leper for a further nine days. On 4 July, 48 days after admission, I returned home in an ambulance as I couldn’t yet manage a wheelchair. I remember seeing the tops of buildings go past and feeling sorry that I wasn’t driving, then quickly realising that I could have left hospital in a coffin. That turned my griping into gratitude.

A health carer we had employed in hospital helped me for the next two months on the long journey of recuperation. I also had regular and intensive high quality home-based physiotherapy, which really helped me gain perspective and make progress. My unstable condition, as well as recommendations about the quality of ICU care and orthopaedic surgery in Oman, had encouraged us to remain rather than seek the treatment abroad offered by my employers. Visitors during the summer cheered me up and helped my recovery.

Throughout this whole process, I needed 11 units of blood. During one operation the surgeons requested 4 units, but only 3 were available. This prompted a friend and my husband to instigate a blood donation drive. People donated 100 units of blood and others were turned away, as staff in the mobile unit couldn’t cope. I felt happy to hear of such a positive response to my horrible accident.

Since July, 2 months after my accident, I have progressed from the wheelchair to standing and walking, initially in the swimming pool and then with a Zimmer frame, crutches and a walking stick. Now, 7 months later, I walk without aid. We, as a family, have celebrated every small step as a great achievement: bed sores healing, extracting a stray stitch from a scar and my first shower. Relief flooded in as I became able to do things myself.

One day my left arm became hot, red and swollen. We rushed to hospital dreading being readmitted. The X-rays indicated a loose screw in the ulna fixation. The doctor allayed our fears saying that I had probably just bumped my arm. My consultant surgeon wondered whether I would need manipulation under anaesthetic or open quadricepsplasty of my left knee, but decided to see how much aggressive physiotherapy could improve knee and hip movement first. Exercise is crucial and I spend time on a bike, in the pool and with steps and weights. The limited movement in my stiff left knee is likely permanent and I may later require a total hip replacement.

I thank all the doctors, nurses, physiotherapist, orthopaedic osteopath, chiropractor, my employers, friends, all those who prayed for my recovery and especially my family for their amazing support.
A ten-year girl presented at Sultan Qaboos University Hospital with poor school performance and generalised tonic clonic seizures in the previous three months. Her birth history and antenatal history were normal. She also had poor school performance. Her other siblings were normal. Her general physical examination and neurological examination was unremarkable. There were no neurocutaneous lesions. An assessment revealed an IQ of 57, which is very low. The routine blood work up was normal. An electroencephalogram showed left temporal region seizure discharges with generalisation. A magnetic resonance imaging scan of the brain revealed complete band heterotopias in both hemispheres (double cortex) [Figures 1 and 2].

Neuronal migration disorders (NMD), are seen in children with psychomotor developmental delay, epilepsy and mental retardation. Physical examination is usually normal in these children.
except neurocutaneous disorders. Minor forms of NMD are picked up only when imaging is done. The normal human brain goes through three major phases of morphogenesis which are neuronal production, neuronal migration and differentiation. This mechanism is complex and chemical signals and guides control this. Neuronal production and migration starts at six weeks of gestation and proceeds until twenty-six weeks. After this phase, differentiation and maturation continue until the age of 15 years. Heterotopias are one of the NMDs, where in ectopic grey matter cells get arrested in inappropriate sites in the brain. The cells may be arrested between the leptomeninges and periventricular region. The cells arrested in the subependymal region are called subependymal nodular heterotopias. The cells arrested below the proper cortex and separated from the cortex by a thin band of white matter, are called subcortical band heterotopias (SBH). When this band is circumferential beneath the cortex, it is called a double cortex as was seen in our child. This condition is very rare with only about 120 cases reported in the world medical literature. The syndrome is usually associated with mutations in the doublecortin (DCX) (Xq22.3-q23) gene, and much less frequently in the LIS1 (17p13.3) gene. The majority of patients with SBH are sporadic, most patients are females and few patients with familial X-linked inheritance have been seen. Heterotopias may be isolated or part of a syndrome. The exact incidence of heterotopias in the general population is unknown; however, heterotopias formed 11.6% of cases of NMD in our series. Only one of them had SBH, forming about one percent of NMD.

ACKNOWLEDGMENT
This case was presented on 12th November 2008 in the SQU Clinical-Pathological Conference Series (SCRAPS) as: “Are two brains better than one?”


To the Editor

We write in response to the above mentioned article which appeared in the August 2009 issue of SQUMJ. Radiation regulations in most countries permit treatment of thyrotoxicosis using radioactive iodine (I-131) as an outpatient procedure. Hospitals provide instructions to the patients receiving these treatments about the precautions to be observed in their homes in terms of avoiding local radioactive contaminations and also protect other inmates restricting the radiation exposures ‘as low as reasonably achievable’. Therefore it is of interest to quantify the radiation exposures incurred from these patients to spouse, children and attendants. Early works addressed different related issues in this regard.

From this objective, we appreciated the work of Al-Maskery and Bererhi reported in your August 2009 issue. The following are the highlights of their work. Their study involved 22 thyrotoxic patients treated on an out-patient basis. Thermo-luminescent dosimeters (TLD) monitoring was carried out on 86 inmates in their homes (29 children and 57 adults). The quantity of I-131 radioactivity administered was 610 ± 79 MBq in the range of 520–862 MBq. Measured mean radiation levels around these patients immediately post-administrations was 23.4 ± 6.3 µSv/h in the range of 13–42 µSv/h. The cumulative radiation doses by other inmates in the homes of these thyrotoxic treated patients during 10 days are shown in two categories. Spouses (n = 11) received a mean radiation dose of 105 ± 152 µSv in the range of 7-425 µSv. Other relatives or attendants received a mean radiation dose of 206 ± 440 µSv in the range of 0–2921 µSv.

In Oman, our hospital is another centre where radioactive I-131 treatments for thyrotoxicosis and carcinoma thyroid are offered. From the data of measured exposure rates around these patients, we have obtained the following results. The mean activities administered were 4.19 GBq (in the range of 2.04–9.3 GBq) and 574.7 MBq (in the range of 479–627 MBq) for thyroid cancer and hyperthyroidism treatments respectively. Mean exposure rates immediately after administration of the I-131 therapy doses were 88 µSv/h (n = 69 in the range of 34–184 µSv/h) for thyroid cancer patients, and 14.9 µSv/h (n = 49 in the range of 4.5–34 µSv/h) for thyrotoxic patients. Our study revealed that the radioactive body burden for post-operative thyroid carcinoma had a tri-exponential clearance pattern with T½eff values 14.4h, 22.0h and 41.3h. The body burden of the treated patients for hyperthyroidism cleared with an effective half life T½eff = 111.4h. Figure 1 shows the clearance pattern of I-131 with time elapsed post administration in these thyrotoxic patients. With our data accrued from the Omani patients, taking the effective half life (T½eff) of clearance in the patients with hyperthyroidism viz. T½eff = 111.4h, we tried to explain the results of cumulative radiation exposure.
exposures received by the inmates observed in the recent study as below:

Method of estimation of radiation level around the patients (for administered I-131 activity 610 MBq):

Dose rate constant for I-131, at 1metre, $\Gamma$ in mSv/m²/MBq.hr (Ref. 6) = $7.467 \times 10^{-5}$ mSv/h = $0.07467 \mu$Sv/h.

Total emitted dose at 1m from the patient administered with 610 MBq of I-131 = (Activity administered in MBq) x (1.44 times $T_{1/2}$ in hours x (Exposure rate in $\mu$Sv/h) = 610 MBq x (1.44 x 111.4 hours) x ($0.07467 \mu$Sv/h/MBq) $\mu$Sv = 7307 $\mu$Sv

Therefore, if we assume that in 10 days the administered activity of I-131(610MBq) has fully emitted all its emissions, this emitted radiation 7307 $\mu$Sv at 1m should be taken to represent the cumulated dose received by the individuals moving around the patient in the house. This can be safely assumed because 10 days (240 h) elapsed time duration is nearing 2.5 $T_{1/2}$ eliminating 83% of administered activity.

CALCULATED RADIATION DOSES BY INMATES AT HOME

As the patient has already received instructions, as indicated in Table 1 of the referred work, there will not be permanent presence of other people near the patient. We have to assume some model to explain the local situations around treated patients in their homes. For this, if we take 2 m as reference distance, we can calculate cumulated radiation doses with approximate 'use factors' $\frac{1}{4}$ (6 hours/Day), $\frac{1}{12}$ (2 hours/Day), $\frac{1}{24}$ (1 hour/day).

In these 3 circumstances, the cumulated radiation doses at 2m will be:

(Emitted dose 7307 $\mu$Sv at 1m) x (Inverse square factor $\frac{1}{4}$) x (Use factor $\frac{1}{4}$) = 457 $\mu$Sv

(Emitted dose 7307 $\mu$Sv at 1m) x (Inverse square factor $\frac{1}{12}$) x (Use factor $\frac{1}{12}$) = 152 $\mu$Sv

(Emitted dose 7307 $\mu$Sv at 1m) x (Inverse square factor $\frac{1}{24}$) x (Use factor $\frac{1}{24}$) = 76 $\mu$Sv

DOSE ESTIMATES

In the above circumstances, the estimates of radiation dose in the reported study for spouses (105 ± 152 $\mu$Sv in the range of 7 to 425$\mu$Sv) and other relatives or attendants received a mean radiation dose of 206 ± 440 $\mu$Sv in the range of 0 to 2921 $\mu$Sv seems to be realistic. True situations could be approximated within 2 m movement distances in the house, and a representation of 'use factor', as it is conventionally taken to represent approximate situations encountered in health physics calculations, could be assumed. The uncertainties in this communication are: a) the effective half life estimated is based on the mean exposure rates measured on consecutive days in the patients; b) the measured exposure rates are based on beta, gamma survey meters which have inaccuracies in terms of estimated $\mu$Sv/h, and c) there are difficulties in reproducing true circumstances encountered by the inmates spending time with the patients in their homes.

This communication gives a theoretical account to explain the radiation dose estimates by TL detectors, which could be applicable to the similar earlier report also. Pant et al. reported higher doses to the family members from thyrotoxic patients, viz. 0.4 to 2.4 mSv (mean 1.1 mSv) and 0 to 1.9 mSv (mean 0.6 mSv). This report is from India, where the living conditions in homes are different from those encountered in

Figure 1: Clearance of I-131 in thyrotoxic patients (n = 49)
Oman, as individual patients may be moving in closer proximity to other people at home because of higher population density in cities like Delhi. This type of approximation of 1 m emitted dose around patients is the first of its kind and had not been reported earlier in the literature. More insight has to be given to this hypothesis, for health physics applications with the use of ingested radioisotopes in humans.

To conclude, in this study we simplify the calculation of radiation exposure to patient’s family members with a theoretical modelling, by using a fixed factor called ‘emitted dose at 1m’ around the patient. This data is based on the effective half life of clearance estimated from patients from Royal Hospital. By showing agreement with the estimated exposure by TLD in the referred study, it is opined that I-131 thyrotoxicosis patients can be treated as outpatients with proper instructions provided to them.

References


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Author’s Response

I am writing to respond to Dr. Ramamoorthy Ravichandran and Amal Al-Saadi’s letter of 7th January 2010 regarding our article, Radiation exposure level in family members of Omani patients with thyrotoxicosis treated with radioiodine as outpatients.1

The authors used a radioiodine-131 (I-131) kinetic model (submitted for publication to the Indian J Nuclear Medicine journal) and input data on thyrotoxic patients from our clinical studies to estimate the radiation dose received by relatives at home. They found that the kinetic model gave results that were very similar to our clinic trials. We appreciate the effort of the authors to run the model on our data. Kinetic models of radioiodine are well established and are extensively used to estimate radiation exposures.

When we started radioiodine therapy 20 years ago in Sultan Qaboos University, we knew that kinetic models could be used instead of clinical trials because the models had been and continue to be successfully used in other countries. However, the kinetic models were applied on patients from very different cultures.
Because the social and cultural traditions in Oman were so different, we did not know how patients might react to this new radioactive treatment and so we started by using rather stringent regulations whereby patients remained in hospital until the radiation level at one meter from the patient dropped to 2µSv/h. This policy was derived from the UK guidance notes, which allow an internal body activity limit of 30MBq of I-131 for contact with children. Progressively, we cautiously began to reduce these stringent regulations after making sure that the instructions were generally well followed. We performed two clinical studies to better understand patient and relatives response to radiation safety instructions and we are now convinced, especially after this most recent study, that we should treat thyrotoxic patients as outpatients because the radiation dose received by patient relatives is within radiation safety regulations.

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References
Snakes have always been creatures of myth, intriguing but fascinating, and long associated with good as well as with evil, representing life and death, creation and destruction. However, in modern times with the advent of scientific know-how, one aspect of these captivating creatures has given birth to a research discipline, christened "snake venom research", specifically pertaining to venomous snakes. Now, “What is snake venom?”

Snake venoms are complex mixtures of pharmacologically active polypeptides and proteins, and are therefore veritable gold mines for various drug leads. A case in point is Captopril, the first venom-based drug, discovered in 1975 from Bothrops jaracusa (the Brazilian arrowhead viper venom) by Nobel Prize winner Sir John Vane and later commercialised by the pharmaceutical giant Squibb. Captopril is an angiotensin-converting enzyme inhibitor and therefore a potent anti-hypertensive agent.

At present in the Sultanate of Oman, there are 9 species of poisonous snakes (see Figures 1 and 2 for images of two of the venomous species), but little is known about the venom biochemistry of these enthralling serpents. One of the long term scientific interests of the lead authors of this communication has been to study the biochemistry of venoms in order to identify novel pharmacologically active molecules. In this endeavour, a team has been formed in the Department of Biochemistry in the College of Medicine and Health Sciences at Sultan Qaboos University. This group, designated the Venom Research Group, consists of Drs. Yajnavalka Banerjee, Professor Riad Bayoumi, Yahya Al-Tamimi and Naseer Al-Nazwani. Mr Seyad Farook of the University Small Animal House, who is in charge of the University herpetarium, is also an ardent member of this team. The team aims to obtain insight into the venoms of these 9 species of serpents through diverse proteomic and transcriptomic tools, which will hopefully lead to the identification of drug leads targeting some common
human diseases. Additional goals of the Group include mapping the geographical distribution of these species as well as studying the evolution of these snakes. Researchers from the Ministry of Defense, under the supervision of Dr Yahya Al-Rashdi, will also participate in this project. Scientists from Saudi Arabia and Ministry of Health in Oman have also expressed their keenness to contribute towards this endeavour. In line with the enthusiasm expressed by researchers and clinicians, and in order to establish a more holistic group of researchers a workshop was organised on the 31st of March 2010 under the theme of “Initiatives into Snake Venom Research”, which aimed at informing the scientific community and the general public about the immediate and long term goals of this project. In summary, we sincerely believe that the above project provides the revelation that “Deadly snake venom does have the potential to save life”.

References


To the Editor

Unable to return to Afghanistan initially after 9/11, I worked for five months in Yemen and found myself constantly drawing parallels between the two countries. Recently, during a visit to Oman I found myself constantly remarking on the stark contrasts with both Yemen and Afghanistan. Not surprisingly, the direction my reflections took was influenced in large part by my recent master’s thesis research which focused on the role of epistemology in surgical training in Afghanistan. The casual observer might latch on to the most obvious difference in relation to the two countries’ ministries of health, namely availability of finances. Alshishtawy’s article in this issue highlights a difference more important than quantity of finances; namely, quality. By that I mean the quality of decision making in relation to finances. For the foreseeable future, Afghanistan’s government is dependent on donor funding because clearly it will be a long time before taxes can fund health care. Even if there were technocrats in the Afghan Ministry of Health (MOH) who saw the need to allow cost recovery in the public system, the parliament seems set against allowing such pragmatism. When I recently asked a senior technocrat in the MOH in Kabul what form plans are taking for financing of health care 10 years from now he was not aware of anyone addressing this question. Clearly, it is not just the absence of conflict or the size of GDP that make Oman’s health care such a remarkable success, but rather such elements as systematic analysis, practical planning and effective leadership in implementing plans.

The analytical framework used for my master’s research I derived from the foundational document which led to the establishment of the modern research university. Von Humboldt’s classic 1810 paper listed four conditions for developing the modern research university which I believe apply to the development of any knowledge derived profession: 1. Providing the Organizational Context; 2. Collaborative arousing of passion; 3. Challenging closure (“…science and scholarship do not consist of closed bodies of permanently settled truths”); 4. Seeking feedback. The condition that I have found most obviously lacking in Afghanistan was the one so visible for its successful application in Oman; namely the first condition, that “…the state must supply the organizational framework and the resources necessary for the practice of science and scholarship…” The remarkable success of the past few decades in developing Oman’s education and health infrastructure is outstanding. It goes without saying that Afghanistan’s chronic continuing civil conflict accounts for a large part of the difference between the two countries’ health care systems. However, a number of questions arose during my visit which I believe have broader relevance to the culture of training for the health professions.

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Who gets into Medical School?

This question parallels an issue we have in Afghanistan. Both countries base selection of medical school candidates solely on examination performance. Hearing of a large majority of female medical students in Sohar, Oman leads me to wonder what effect this will have on health care delivery if many of them go on to work only part time in order to have a family. Some have openly admitted no interest in practising medicine. In the Afghan system one’s post-secondary career path is assigned on the basis of ranking in the nationwide “concours” examination unless one asks to be switched to a lower ranked faculty. With top-scoring candidates assigned to medicine and lowest scoring to nursing it is no surprise that Afghan doctors often end up leaving the profession when they can be better paid as English-Dari translators for foreign organisations and that nursing as a profession shows clear signs of being undervalued. In both countries there appears to be a significant element of socially motivated career choice at the expense of decision-making based on suitability of personal aptitudes and enjoyments. Perhaps in both contexts a significant part of the blame is to be laid on the society at large and how it has developed; not just on the higher education system alone. Any rapidly changing society is likely to have elements of disequilibrium between traditional ideas about health and the epistemology that constitutes the foundation of professional expertise. In Afghanistan, I see almost weekly a case of severe morbidity from treatment at the hands of traditional bone-setters and yet I have also seen doctors who have taken their own family members to traditional healers. Clearly society’s relationship to both the traditional and modern medicine communities is a strong determinant of health care delivery. Selection of candidates for the profession and selection of the professional to treat a given patient are key determinants of this relationship.

What to think versus how to think

One of the observations that stands out in Oman by way of contrast with Afghanistan is the large majority of expatriate doctors in Oman. A recent study showed the figure to be 75%. For most of my time in Afghanistan, I have to my knowledge been the only non-Afghan working in the national hospital system. The few foreign doctors have been for the most part in non-governmental organisation (NGO) programme management. This difference of course reflects the capacity of Oman to pay generous salaries to attract foreign personnel. In turn, this raises the question of indigenisation of medical expertise. Clearly, progress is being made in this regard in Oman. Is it then appropriate to raise the concerns that have been raised more generally about graduate education in the region? The general focus of these concerns can be characterised by an emphasis on content or skill-set transmission to the trainee without adequate attention to the capacity for critical thinking. In a world increasingly ‘opportunity-flat’ because of the internet, the capacity to negotiate the torrent of information for what is actually relevant and true requires more than ever before in history the capacity of critical thinking.

The NGO for which I work in Afghanistan has been focusing lately on strengths: Richard Koch’s 80/20 Principle. This approach is very useful as far as maximising a given individual’s contribution when there are other players to choose from. However, when one is the only option to meet a particular urgent need, as is often the case in health care, then one should also incorporate a focus on analysing one’s weaknesses. This principle of focusing on weaknesses should be even truer of whole systems. In the professional realm, it is this tension between focusing on strengths (often oriented toward keeping everyone happy) and focusing on weaknesses (to cut out inefficiency and error) that informs much of the cultural divide between ‘East’ and ‘West’. Victor Davis Hanson has highlighted this difference perhaps more effectively than anyone else by looking at the history of the military profession. In his book Carnage & Culture he looks at nine military campaigns over the last 2,500 years and concludes that ‘the West’ has dominated militarily because it has built on the foundations of 1) freedom of individual expression (and maybe also rights) and 2) the centrality of rational enquiry/reflective analysis. This difference led to the inability of the hero on horseback with superior individual power to overcome the disciplined coordinated systematic defences of a phalanx of Greek infantry, for example at the Battle of Marathon in 490 BCE. Perhaps the cultural parallels of lessons
drawn from the military profession are more clearly highlighted in the battle of Midway in 1942 in which overconfidence, focus on blaming rather than analysing bad outcomes, suppression of questioning from junior officers, following traditional tactics, resistance to initiative, honour motivated planning (the best pilots earned the right to go kamikaze, leaving behind a less experienced pool of trainers) played a role in producing failure analogous to the dynamics in the operating room that I am familiar with as a surgeon. Recently there has been interest in applying the lessons from aviation in the operating room environment. These have also highlighted the central role of reflective analysis of how we function as a community or as a system rather than just asking what piece of equipment or individual skill-set is lacking. This systems approach is becoming increasingly accepted as the preferred approach to preventing medical error. However, it can also be the prime force for improving the use of limited human resources – whether limited by quantity or quality.

Whose learning comes first – The Profession’s or the Professional’s?

As a surgeon doing primarily upper extremity surgery in Afghanistan’s main orthopaedic hospital I am constantly faced with examples illustrating a failure of the above two principles of reflective analysis and individual expression. I have no doubt that the single largest source of loss of hand function in Afghanistan is not the injury per se but iatrogenic joint and tendon stiffness that could have been prevented with a little bit of knowledge and modest effort – but certainly not requiring expensive or complex technology. Repeated attempts to introduce change in this regard have been without significant effect, despite the absence of any clearly identifiable resistance. Without doubt a large part of the reason for this inertia is the simple absence of a systematic habit of looking for new ideas and then evaluating them before incorporating them into working practice. In other words, when reflective analysis and freedom of expression are suppressed the threshold for change becomes too high and impedes progress. It often happened that an individual would be convinced of the benefit of some new development, but there was little mechanism for dissemination of the new idea throughout the department unless it was instigated from the top of the hierarchy. By contrast Dr C.Thomas’ description of how new ideas become adopted in the Khoula Hospital plastic surgery department seemed to approach the ideal in terms of openness to exchange of ideas. Despite the large difference between the two countries in how their medical communities function, it is safe to say that for each country the road to success is paved with the same stones. These include critical self-assessment and openness to new ideas. Two of the best measures of reflective analysis in a medical community are well conducted departmental morbidity and mortality rounds. In this day and age a good measure of the presence of the other foundational principle, individual expression, could be openness to new ideas. In a hierarchical honour/shame society a good measure of this openness might be the promotion of young members of the department on the basis of merit rather than connectedness. Nowadays it probably also correlates closely with how much the department relies on Medline searches for the answers to clinically relevant questions. Development of both of these aspects of the profession is sorely needed in Afghanistan. How much they could be further developed in Oman I cannot say, but the question is worth addressing in relation to the profession throughout the country and not just in the academic centres.

An answer to the Geography Challenge?

This leads me to conclude with the one parallel challenge that both countries share. Each faces the challenge of delivering health care to sparsely populated mountainous and arid regions that have been traditionally rather isolated from the outside world. Many of our patients in Afghanistan take four or more days of travel to reach Kabul and when they do they tend to find it an inimical environment where they quickly go into debt to pay for their family member’s care. Although the trip from Nizwa to Muscat has shrunk in a generation from a week long camel trip to a one and a half hour motorway trip, there still seems to be sufficient paucity of specialist medical care outside of the main urban centres to pose a relative barrier to care. I sense this may
be the case notwithstanding the truly remarkable achievement of, for example, virtually all cleft lip patients being registered within a week or two of birth for surgery at three months. I say this in part because in my own country of Canada, with a much longer history of developed health care, there are still challenges in providing specialty services at a distance from the large urban centres. Two solutions seem to offer the most help in meeting this challenge: 1) an internet based program for onsite professional development using PubMed literature searching to promote an evidence-based approach to practice combined with video conferencing to provide specialist input on difficult cases 2) targeted provision of resources and training to handle the most common conditions amenable to a non-specialist type of surgical "generalist". Thus competencies such as bowel resection, hernia repair, C-section, care of modest burn injury and common fractures could be combined with improvement in the early management of trauma and prevention of complications such as joint stiffness and compartment syndrome – all combined in a surgical generalist role for small towns. It could be tailored to the specific professional resources in a given town and evolve with the health care system while improving access for the rural population. These two keys constitute my dream for Afghanistan, and I feel that some aspects of this approach would have relevance to any country with a geographically challenging distribution of its population such as Canada, Australia and at this stage in its development of its medical profession, Oman.

Kudos to Oman's great progress to date! May Omanis soon comprise the majority of their own health care team.

References

Pharmacology textbooks are often dull because of detailed presentation of volumes of information in a drab manner, making the subject even more volatile and distant for a neophyte! This textbook, however, deviates from the routine old-fashioned textbook of pharmacology, moving into the new spectrum of more ‘sellable pharmacology’ and is presented in a palatable style. The book describes recent advances in basic pharmacology and relates them to their application in practical therapeutics. It emphasises drug discovery, translational research, and evidence-based medicine. The style of narration and the format of the book are user friendly. The complete contents of the book are available online allowing free access to diagrams and other resource material.

The book is presented in an integrated, disease-oriented manner which makes it an attractive and innovative book to enhance learning about diseases and therapeutics, rather than stand alone drugs. This approach is in line with the learning needs of today’s medical students, clinical pharmacists and other medical and nursing professionals.

The book is divided into two parts: Principles and Practice. The first part has four sections comprising of twenty-one chapters dealing with the Pharmacotherapeutic Continuum, Molecular Pharmacology, Systems Pharmacology and Clinical Pharmacology. The second part is divided into sixteen main sections on therapeutics, and these sections are further subdivided into seventy-three chapters dealing with different diseases. Chapters in this section include pathophysiology, epidemiology, therapeutics, clinical pharmacology and therapeutics, and emerging drug targets. The book also includes an interesting, though brief chapter on Sex Differences in Pharmacology.

The main strength of the book lies in the chapters dealing with the continuum of knowledge including basic concepts of drugs gradually presented with an increasing layer of complexity and integration.
With therapy. The pathophysiology and rationale of drug use are clearly explained so that the reader is prepared for a lifetime of prescribing and practice. Another striking feature of the book is the strategy of bulky text broken down by use of detailed diagrams. Hence, each chapter in the book is well illustrated with high quality coloured diagrams, comprehensive flowcharts, extensive summary tables and treatment algorithms. These make the book more attractive to the reader.

Although most chapters are exhaustively referenced, one of the limitations of the book lies in the use of older references. This is particularly evident in areas of therapeutics that are rapidly changing. An example is the section on Therapy of Infectious Diseases wherein the chapters on treatment of community acquired pneumonia and tuberculosis refer to American Thoracic Society guidelines from 2003, and the chapter on bacterial meningitis refers to Infectious Diseases Society of America guidelines from 2004. In addition, Chapter 12 on the Pharmacobiology of Infection gives more weight to antiviral and antifungal drugs compared to antibacterial agents. This could give a novice reader of pharmacology the impression that the former are more commonly used drugs.

Overall this book is a useful addition to the rapidly emerging armamentarium of ‘new look’ pharmacology and therapeutics textbooks. I would definitely use both the text and the online versions and recommend them to others.

REVIEWER

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The title of the book is interesting and concise giving the reader ability to forecast the contents, and this is exactly what a good title should do. The contents and targeted groups are very clearly described, and this definitely makes it easy to select or deselect it depending on your needs. Imagine being in a bookshop looking for a book in pediatrics; titles such as this make it easy to locate the right book and make a decision.

The structure of the book is reader-friendly with clear objectives for each chapter and summary boxes enabling the reader to navigate very easily and have quick access to the needed information. The figures and diagrams are clear, optimal and appropriate to the contents. They are very illustrative and many of them could be used when counselling or giving explanations to parents.

The authors have adopted a symptomatic, rather than disease oriented approach in writing the book chapters (breathing difficulty, convulsions, vomiting, diarrhea, feeding problems, fever etc.). Definitely, this approach is easily linked to real life as babies will present with symptoms that could be due to a disease affecting any of the body’s systems.

The book also contains chapters on prenatal screening, neonatal resuscitation, some of the common neonatal problems and low birth weight. The chapters give the reader a general view of the process of birth and the basic life-saving measures that may be necessary at birth in a simplified practical way.

The book also includes chapters on the normal processes of the first year, such as growth, feeding and weaning. Such information is of major importance for non-specialists working in primary health facilities, as the information will have a positive impact on the mother’s practice if given to her at the appropriate time during well baby visits or vaccination appointments. The authors’ emphasis in each chapter on communication with parents and counselling aspects is a very important issue not covered in many other books.

Although the book is very good in general there
are two omissions which, if rectified, would add greatly to the usefulness of the book. First, I think the authors should add a chapter on accidental injuries with illustrations, examples of common injuries and dangerous places as well as basic first aid information and tips to parents on safety measures. Second, it would be useful to add a chapter on “review at 12 months”.

REVIEWER
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The Paediatric Handbook evolved from the 1960s as a management guide intended for in-house use by medical officers at the Royal Children’s Hospital in Melbourne, a leading clinical and training centre for paediatric medicine in Australia. This new eighth edition is the fruit of the tireless efforts and contributions of its staff team. It was developed from evidence-based practice and longstanding clinical experience as a succinct and relevant guide to those who care medically for children from infancy through adolescence. This new edition has been updated from the last (2003) edition and is available both in print and PDA version online.

The current edition contains new and revised chapters aligned with the hospital clinical practice guidelines. It comprises a table of contents with a list of contributors, editorial committee, forward, preface and health problems divided into seven parts followed by appendices and finally the index. The different Parts are: Emergencies, with up-to-date guidelines and algorithms regarding resuscitation; Procedures and Pain Management; Fluids and Nutrition; Child Public Health; Development; Psychosocial Problems and, lastly, important paediatric conditions in Medicine and Surgery. Each of the Parts has from 2 to 20 chapters. There are four appendices: Growth Charts; Pharmacopoeia; Antimicrobial guidelines and Formulae. A Resuscitation Guide and Australian immunization schedule are also included on the front and back pages for easy reference.

New topics for this edition include sleep problems, continence, slow weight gain (failure to thrive), obesity, continuous SC insulin infusion pumps, cystic fibrosis and illicit drug poisoning. Chapters on renal conditions, pain management, management of stroke, immigrant health and the immunisation schedule have been extensively revised. Each chapter provides useful web links to assist the reader with further references. The illustrations, diagnostic and management algorithms greatly enhance the accessibility of the information. The Handbook would be further enhanced by including a chapter on history taking and physical examination in children. In addition, a darker font would minimise strain on the eyes and make for easier and more rapid reading.
The Paediatric Handbook, with its concise descriptions, is a useful source of quick revision for medical students and paediatric residents. Practising general physicians and busy nurses will also find it a ready reference tool for clinical management and fast decisions making at the point of care. Being comprehensive, it is easy to use, thus providing a practical guide to the diagnosis and management of common and serious health problems in children. It also complements and extends information in the clinical practice guidelines. The book will have a wide appeal as a comprehensive and clear guide to managing common and serious disorders of childhood. To conclude, this is an excellent handbook which serves the needs of all health professionals involved in the day-to-day care of paediatric patients. It emphasises the community-based approach to the practical management of children's problems and paediatric pharmacopoeia as well as covering the current significant advances in paediatric practice.

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13-15 April 2010: Dubai World Dermatology & Laser Conference & Exhibition, Dubai International Convention & Exhibition Centre, Dubai, UAE.
Email: easloffice@easloffice.eu Website: www.aeedc.com

Email: easloffice@easloffice.eu Website: www.easl.eu/liver-congress

15-18 April 2010: International Conference on Advances in Diabetes & Insulin Therapy, Dubrovnik, Croatia.
Email: info@adit2010.org Website: www.adit2010.org

Website: www.kfsrhc.edu.sa

4-6 May 2010: 4th International Conference of Biomarkers in Chronic Diseases, Diabetes, Obesity & Cardiovascular Diseases. King Saud University, Riyadh, Saudi Arabia.
Website: www.ksu.edu.sa

Website: www.ebcog2010.be

5-8 May 2010: 2010 World Congress on Osteoporosis. Florence, Italy.
Email: info@osteofound.org Website: www.iofwco-ecceo10.org

12-16 May 2010: 7th Metabolic Syndrome, Type 2 Diabetes & Atherosclerosis Congress. Marrakech, Morocco.
Website: www.msidacongress.com/congress_2010/index.html

13-15 May 2010: 31st Annual Advances in Infectious Diseases: New Directions for Primary Care. San Francisco, USA.
Email: info@ocme.ucsf.edu Website: www.cme.ucsf.edu

12-14 May 2010: 3rd World Congress on Controversies to Consensus in Diabetes, Obesity & Hypertension. Prague, Czech Republic.
Email: info@comtecmcd.com Website: www.comtecmcd.com/codhy/2010/

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2-4 June 2010: Dementia: A Comprehensive Update. Boston, USA.
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7-9 June 2010: British Cardiovascular Society Annual Conference & Exhibition. Manchester, United Kingdom.
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10-12 June 2010: International Conference on Adult Hearing Screening. Cernobbio, Italy.
Email: als2010@polimi.it Website: www.als2010.polimi.it

10-12 June 2010: 6th Research Congress of The European Association for Palliative Care. Glasgow, United Kingdom.
Email: heather@compleatconference.co.uk Website: www.eapcnet.org/research2010/index.html
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13-16 June 2010: Mammograms to MRI: Breast Imaging & Interventions 2010. Kiawah Island, South Carolina, USA.  
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Email: office@cars-int.org  Website: www.cars-int.org

Website: www.emwc.net

Email: nnezi@canc-group.com  Website: www.idof2010.com

11-13 November 2010: 2nd Future Trends in Implantology. Florence, Italy.  
Email: fti@ftidental.com

Email: eso@eso.net  Website: www.eso.net

Email: rkatzir@paragon-conventions.com Website: www.fixedcombination.com/2010
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راجيف خانديكار، ياسمين جعفر |
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المجلة الطبية لجامعة السلطان قابوس مجلة وطنية وعالمية محكمة للأبحاث الطبية البايولوجية

المجلة الطبية لجامعة السلطان قابوس ينشر المجلة البحوث الأصلية مطبوعة والالكترونية، حيث تعد المجلة منتدى لتبادل ونشر المعارف الطبية والبحوث بين العاملين في مجال الطب، وتعزز الوعي في التطورات الطبية.

محرر المجلة: الدكتور نيكولاس وودهاوس

المجلة الطبية لجامعة السلطان قابوس تصدر ثلاث مرات في السنة وتوزع مجانا لكل الكليات والمعاهد الطبية في عمان ودول الخليج ومنطقة الشرق الأوسط.

المجلة ليست مسئولة عن الآراء المنشورة فيها والتي تمثل رأي كاتبيها.

المجلة الطبية لجامعة السلطان قابوس مجاهدة في تشجيع وتحفيز البحث الطبي والنشر العلمي في عمان ومنظمة الخليج، وجذب المشاركين من المناطق الأخرى.

تُطبع المجلة في جامعة السلطان قابوس بالتعاون مع كلية الطب والعلوم الصحية.

المجلة محققة في جامعة السلطان قابوس بالتعاون مع كلية الطب والعلوم الصحية، جامعة السلطان قابوس.

المجلة الطبية لجامعة السلطان قابوس مسجلة بالفهرس الطبي لمنظمة الصحة العالمية.

المجلة الطبية لجامعة السلطان قابوس، النسخة العربية، تحت أكثر من 1000 اسمية من أعضاء مجلس التحرير من موظفي جامعة السلطان قابوس، وتضم 1400 اسمية من المستشارين العالميين.

هيئة الإشراف على إصدار أفلام الطب جامعة السلطان قابوس

任命 إلى الدوام النهاري للحصول على المعلومات المتعلقة بتقديم البحث.

المجلة الطبية لجامعة السلطان قابوس مجلة وطنية وعالمية محكمة للأبحاث الطبية البايولوجية

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