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Editorial

Vision for the future…

"You can never plan the future by the past" (Edmund Burke 1729-1797)

I have now just completed nine months as the Director of the Joint Health Support Agency. I often get asked how long I have been in the job, as many people imagine, for some bizarre reason, that I have been in the job for longer than I have. Sometimes, I will admit, it does feel like I have been in the job forever. One of the real challenges of this job is to plan for the future. One of the sessions at my next Senior Health Officers Conference, planned for October, will be a look at where the Joint Health Support Agency will be in five years time. The planning for that conference got me thinking about the Australian Military Medicine Association. What are our strategic plans for the next five or ten years? This year AMMA will be having its tenth conference. This will be held on the Gold Coast from the 19 - 21 October, 2001. Where will AMMA be in ten years time? Now is an excellent time for all members of AMMA to reflect on the past decade and to plan for the next one. AMMA is your Association and the direction it takes should and must be dictated by its members. From an editorial point of view, I would like to see *Australian Military Medicine* coming out six times per year and being substantially larger than it is already. The journal is already being catalogued by the National Library of Australia and I would like to see it catalogued as part of MEDLINE in the not too distant future. This is a good time for all members to consider what they would like to see from AMMA and to share some of their visions for the future at the coming AMMA Conference.

This issue of *Australian Military Medicine* is again a diverse and interesting one. We have a number of different themes. Naval medicine is well represented with articles on dangerous marine animals and the impact of sun exposure on Naval personnel at sea. Clinically, articles address key military medical issues of trauma, vaccinology, industrial medicine and infectious disease. We also have the first of the articles from the essay competition, which looks at the future impact of information technology on military health. I also commend you to read Marshall Barr's account of his time in Vietnam as a Civilain Military Force anaesthetist in 1967. This excellent book is due to be released on 07 September 2001 and is reviewed in this issue.

I would like to correct an unfortunate omission from the last Journal. In the review of the RACS Annual Scientific Meeting 2000, we failed to mention the contribution made by Paul Myers, who both convened the meeting and presented an excellent paper on his experience with INTERFET.

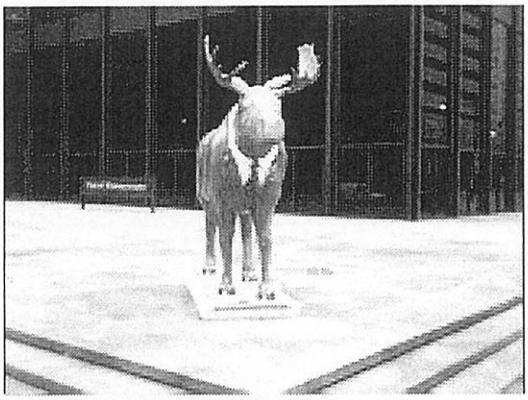

Figure 1: Toronto Moose
(Photograph courtesy of the author)

Burke stated, almost three centuries ago, that 'you cannot plan the future from the past'. As an Association, we need to be relevant for the future. That is not just putting on new coverings like my Moose friend in Figure 1, but planning for the future so we will be a vital and relevant association in 2011.

I look forward to seeing you all on the Gold Coast.

Andy Robertson

President's Message

As I write this, Australia's Defence health personnel involvement in military operations continues apace, with HMAS *Manoora* being despatched to support the planned transfer of refugees from Christmas Island.

This operation highlights yet again the very important rôle of Defence health support to humanitarian operations. In the last decade, we have seen these activities undertaken again and again in all three operational fields, and there is no doubt that ADF health personnel perform this function exceptionally well.

It is also to the credit of Defence planners that we have a health capability that has the flexibility to support such operations on land, sea and in the air, with the final gap being closed with the bringing into service of the two Primary Casualty Reception Facilities (PCRF) in HMA Ships *Manoora* and *Kanimbla*. Already, the PCRFs have been involved in a number of exercises and operations, and during Exercise Tandem Thrust the first "live" operations were undertaken in the orthopaedic care provided to half a dozen paratroopers injured in a jump.

The challenge now is to train and maintain the health personnel capability, both in the Permanent and Reserve Forces, because it is the conjunction and interaction between these two components that is critical to timely and effective health support.

Permanent Defence health personnel are the mainstay of both maintaining the infrastructure and providing the rapid response that is often required. Reserve personnel provide the specialist expertise – both medical and nursing – that cannot be obtained during peacetime military service.

There are moves in Defence Health to provide some integration of aspects of the permanent and reserve service, with permanent medical officers being offered specialist training with a subsequent mix of military and civilian work, coupled to a high level of readiness to deploy. The success of this approach, which mirrors proposed solutions to the problem of attracting medical specialists to remote and rural areas of Australia, will also depend on a high level of cooperation with civilian hospitals.

The practice of military medicine has in many ways been seminal in the development and advancement of medicine and health care, and it is vital that the military health community be strong and vibrant. The Australian Military Medicine Association can play an important rôle in this, with its charter of supporting and promoting military medical research.

I'm sure all our members will agree that one of the pivotal events of the military health year is the Association's Annual Scientific Conference.

It is fair to say that our conferences have, year after year, offered the opportunity to learn of issues that face the military health community and the solutions that have been developed to problems faced.

This year's conference will be no less rewarding. To be held on the Gold Coast – yes, beautiful one day, perfect the next – less than 100m from the beach and in the heart of Surfers' Paradise, I have no doubt that our 10th conference will build on the successes of previous years.

Our keynote speaker is former United States astronaut and Air Force physician, Colonel Jim Bagian. We did have to resist the temptation to call the conference "2001, a space etc ...), but I'm sure that you can guess that Colonel Bagian's address will take us to that last frontier of exploration, and the medical challenges that it poses.

The programme, as it is every year, is packed with a wealth of papers, and there will be special session focussing on posttraumatic stress disorder presented by the ADF Centre for Military Mental Health.

On the afternoon prior to the conference, a workshop will be held at the Australian Malaria Institute, and there will, as always, be every opportunity for catching up with colleagues, and networking with both them and our trade sponsors.

With over 40 golf courses in the vicinity, theme parks etc, and the beach just over the road, there will be no shortage of things to do before and after the conference. If you haven't registered, I urge you to do so now. I look forward to seeing you there.

Russ Schedlich

Original Articles

Ultraviolet Radiation Exposure and Melanoma in Australian Naval Personnel[1]

Scott Kitchener[2]

Abstract

In the tropics of Australia, the Royal Australian Navy operates two permanent bases and conducts a large number of operations. Despite an overall incidence of melanoma not significantly different to that of the general Australian population (Standardised Incident Ratio, SIR = 149, p>0.05), older members of the RAN (SIR = 236, aged >29 years) and those holding duties in engine spaces while at sea (SIR = 412 compared to the remainder of the Navy) have an increased incidence of melanoma after indirect age standardisation, suggesting a risk factor associated with Service.

Introduction

The Royal Australian Navy has two permanent operational bases in the tropics of Australia, at Cairns and Darwin, and conducts many exercises and operations in tropical waters.

Previously, Defence Force personnel serving in tropical latitudes have been found to be significantly over-represented in a skin cancer case group of men at draft age during 1941-451. The latitudinal distribution of skin cancers has been well known for some time2, including both melanotic and non-melanotic skin cancer3. Queensland has the highest rate of skin cancer in the world4,5, probably due to a combined effect of greater exposure and a large population of Caucasian people living in the region6,7.

Outdoor occupations other than in the maritime environment have been associated with an increased risk of developing melanoma such as farmers8,9; however, this is not a consistent association10, especially when controlled for other risks for cancer such as smoking and age11. Links between melanoma and outdoor occupations are not well established12.

Considering the environmental exposure of Naval personnel, the incidence of melanomatous skin cancer for sailors has been evaluated, including closer scrutiny of higher risk groups.

Methods

Rates of melanoma in the Navy were initially ascertained from the ICD9 (172, Melanomatous skin cancers) coded database (MEDREX) employed by the (then) Directorate of Naval Health Services, Canberra. All cases were confirmed by a manual search of Service Medical Documents. Inclusion as a case required histological confirmation of the case by an independent histopathologist. The reported date of a confirmed diagnosis was used for chronological placement of cases. Period of Service has been calculated from the date of enlistment recorded on the Entry Medical Examination contained in Service Medical Documents. Only those personnel enlisted in the Royal Australian Navy as sailors on full time Service during the defined period, from 31 December 1986 to 1 January 1992, were included. All cases initially intended to be included as cases following the confirmation of histopathological diagnosis were retained as cases throughout analysis.

Information regarding the Royal Australian Navy population (numbers of personnel by age and employment categories) during the incident period of years were provided by the Directorate of Personnel - Navy. From these lists, population person-years data were derived. Ordinal data were created based on standard five yearly groupings from the yearly categories provided. This permitted indirect age standardisation[13] and comparison of the Navy rates of melanoma to those recorded by the Australian Institute of Health and Welfare and the Australasian Association of Cancer Regis-

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1 Kitchener S. Ultraviolet radiation exposure and melanoma in Australian Naval personnel. *Aust Miil Med* 2001;10(2): 55-59.

2 Major Scott Kitchener, RAAMC, MBBS MPH FAFPHM FRACMA FACTM, is the Officer Commanding Clinical Field at Australian Army Malaria Institute.

tries as of the general population of Australia. This most recent available data was used under the a priori assumption that rates would not vary significantly in the years immediately following, over which the Navy rates were generated.

Indirect age standardisation was applied as the Navy population is notably skewed towards excluding children and the elderly. This was considered to cause variable bias based on the evidence available regarding the general incidence of melanoma. Age is a significant and enduring risk factor towards melanoma and therefore requires control. The indirect method of standardisation was considered the most appropriate given the incidence of the disease being observed.

From age standardised categories, expected rates of melanoma were found for the Navy group from Australian population rates and compared to observed rates for the Navy using the Poisson distribution[14]. A similar method was used for those age groups greater than 29 years. Superficial analysis of the Navy rates of melanoma revealed an apparent preponderance of cases from the employment categories largely holding duties in the engine spaces when deployed to sea. The group is referred to as "Stokers" and includes personnel from the categories (at that time) of Marine Hull Engineering Sailors, Marine Propulsion Engineering Sailors, and Electrical Propulsion Engineering Sailors. The method of analysis was then further used for the categories of employment based on primary duties in the engine spaces and a consequent low occupational ultraviolet exposure. Standardised incident ratios (SIR) were calculated.

Results

Between the years of 1987 and 1991 inclusive, a total of 62010 person years were recorded. From this period, 14 cases of melanoma were reported and confirmed on histological examination of excision specimens. Based on indirect age standardisation of the Australian rates of melanoma, between nine and ten cases were expected.

From the power generated from the number of person years observed, it is not possible to discern a statistical difference ($p>0.05$) between the incidence of melanoma in the Navy and the general population of Australia. The Standardised Incident Ratio of sailors is 149.1 relative to the Australian population.

Calculation of the power associated with the investigation of the melanoma rate from the Navy with that of the Australian population suggested a low (< 0.10) probability of a β error ($Z\ \beta = 3.19$).

From the age groups of Navy members older than 29 years, a significantly greater number of cases of melanoma were apparent compared to the general population of Australia as ten cases were observed while four (4.23) cases were expected (SIR = 236, 95% confidence intervals = 4.795, 18.390, $p = 0.0233$).

Within the Navy, the population of "Stokers" included 13519 person years of observation. The Stokers experienced a significantly greater number with seven cases of melanoma reported in this period; however, fewer than three cases (2.08) were expected after indirect age standardisation from the Australian population (C.I.95% = 2.814, 14.423, $p=0.011$). This indicates a Standardised Incident Ratio for Stokers of 336.5 compared to the Australian population.

For those Stokers aged greater than 29 years, four cases were recorded while no more than one (0.91) case was expected from indirect age standardisation of the Australian population data, resulting in a SIR of 439 (C.I.95% = 1.090, 10.242, $p=0.028$).

The group of Stokers was compared to the rest of the Navy without age standardisation as it was considered that the distribution of ages would be comparable. No more than two (1.95) cases of melanoma were expected in the group of Stokers based on the rates for the rest of the Navy, whereas seven cases were recorded. Again using Poisson probability, this was found to be a significant difference between the groups (C.I.95% = 2.814, 14.423, $p=0.008$). The (non-standardised) Incident Ratio of Stokers for melanoma on the background of the other serving sailors was 359.

To confirm that the age distribution of Stokers was not significantly different the rest of the Navy with respect to these calculations, a sensitivity analysis was conducted by repeating the procedure with age standardisation on the age profile of the remainder of the Navy. A significant difference remains between the cases expected among the Stokers and that recorded (cases expected = 1.72, observed cases and confidence intervals as above, $p=0.004$). The standardised incident ratio with this procedure is calculated to be 412.

The Navy personnel other than Stokers were found to have a Standardised Incident Ratio (with respect to the Australian population) of 111. This is not of significance. Calculation of power for this comparison was not deemed necessary given the previous results.

Discussion

In recent years, the Royal Australian Navy has maintained an active role in the tropics around Australia with deployments, exercises and two permanent Naval bases in the area. Recognition of the risks confronted from increased solar ultraviolet exposure has

prompted active promotion of sun protection measures.

This investigation has been to assess the rate of melanoma among the members of the Royal Australian Navy. As the population of the Navy is quite obviously skewed in terms of age, standardisation is necessary for valid comment. Despite an increased standardised incident ratio for Naval personnel on crude rates, the difference found between the Navy rates of melanoma and those of the general Australian population, after age standardisation, is not significant.

Is Naval Service associated with increased risk of melanoma?

The power generated from the Navy population sample as a part of the Australian population control indicate that the numbers in the Navy are sufficient to observe a reasonable increase in melanoma rate if it were to be present. From this crude analysis, it is assumed that enlistment in the Royal Australian Navy is not associated with increased risk of melanoma.

Clearly, it is possible that the increased risk observed in the group with greater age (>29 years) is completely related to the well-known risk factor of age; however, the SIR is greater compared to the Australian population. Age is a surrogate measure for duration of service, albeit a rather loose indicator and laden with potential biases. Nevertheless, the greater SIR of sailors older than 29 years indicates that their Naval Service can not be excluded as being associated with this higher risk.

Biases in Navy selection

The Navy is selective in the enlistment of personnel. Enlisting generally healthy individuals may cause a bias towards the null for the overall rates of melanoma for serving personnel. Considering the greater risk associated with more prolonged service after age standardisation of the data, a bias towards the null would tend to mask a greater rate of melanoma associated with Naval Service, some aspect of it, or an occupational group within the population of sailors. Other selection biases may be operating such as ethnicity[15] with selection for those more prone to melanoma. While this is likely to be a bias away from the null, increasing the apparent risk from Naval Service, it is not possible to determine the extent to which it is influence results.

A serious potential confounding bias is the possibility of differential ultraviolet radiation exposure in childhood between the Australian public and those recruited for Navy, or between members of the Stoker group and the remainder of the Navy. This proposes that an apparent modulating effect of adult occupational ultraviolet radiation exposure may indeed be due to an incidental inverse association of childhood ultraviolet radiation exposure 16-18, and adult occupational ultraviolet radiation exposure such that the childhood exposure is the only truly causative association with the outcome of skin cancer and melanoma.

Adequate control of this potential confounding is logistically difficult as an assessment of childhood ultraviolet radiation exposure requires retrospective assessment with the concurrent recall and interpretative biases. The assumption made in this instance is that the groups of comparison have a normally distributed childhood exposure approximating equivalence. This may or may not be a valid assumption. It could be argued that the preponderance of Caucasian Naval personnel reflects an apparent bias in childhood exposure to solar ultraviolet light exposure. Nevertheless, within Navy, there is no apparent selection bias towards being a Stoker related to childhood ultraviolet exposure.

Stokers

"Stokers" are those members serving in categories whose duties at sea are predominantly below decks in the engine spaces, having a low occupational ultraviolet radiation exposure. A notable elevation of risk was found for this group, most distinct when compared to the risk of melanoma for the remainder of the Navy (SIR 412, $p<0.01$).

These research findings are supportive of other research indicating a lack of direct association melanoma risk19 and cumulative ultraviolet radiation exposure as well as a possible protective role from occupational exposure to ultraviolet radiation20. There are several possible confounding associations potentially influencing this relationship, including concurrent exposures to artificial light sources and solvents in the workplace.

While the literature reviewed indicates a possible association of artificial light sources (Arc welders, sun lamps, sterilisers, printing equipment and fluorescent lights), it is at best a weak association21-25. When considered collectively the hypothesis can be discounted26. Further, Stokers are not routinely exposed highly to these sources in the course of their duties.

Duties in engine spaces when deployed to sea are rather ubiquitously associated with occupational exposure to solvents and this exposure could be considered greater than that of Naval members in general. Accounting for solvent exposure is a difficult problem in terms of research design; however, the literature reviewed observing the effect of occupational exposure to solvents in the petroleum and oil in-

dustries27-29 and from industries using PCB30,31 on the rate of melanoma, did not support confounding from this source.

These conventional potential confounding influences have been concluded to be unrelated to the observed association.

Conclusions

This research has not supported an increased risk of melanoma for sailors arising from ultraviolet radiation exposure. Nevertheless, within the Naval population, some cumulative exposure with Service may be increasing risk of melanoma as those sailors over the age of 29 years have an increased risk of melanoma compared to the Australian population. Closer investigation suggests that within the Navy, the risk of melanoma is also greater among those whose primary duties at sea are in engine spaces, protected from natural ultraviolet radiation. In conclusion, occupational ultraviolet radiation exposure does not seem to be related to increased melanoma risk within the Royal Australian Navy; however, some other factor in Service may be related.

References

1. Brown J, Kopf AW, Rigel DS, Friedman RJ. Malignant melanoma in World War II veterans. Int J Derm 1984; 23(10): 661-663.
2. Lancaster HO. Some geographical aspects of the mortality from melanoma in Europeans. MJA 1956; (1):1082-1087.
3. Schreiber MM. Exposure to sunlight: effects on the skin., Comprehensive Therapy 1986; 12: 38-42.
4. Green A, Beardmore G, Hart V, Leslie D, Marks R, Staines D. Skin cancer in a Queensland population. J Amer Acad Derm 1988; 19(6): 1045-1052.
5. MacLennan R, Green AC, Macleod GR , Martin NG. Increasing incidence of cutaneous melanoma in Queensland, Australia. J Nat Cancer Inst 1992; 84(18): 1427-32.
6. Green A, Siskind V. Geographical distribution of cutaneous melanoma in Queensland. MJA 1983;(1): 407-410.
7. Armstrong BK, Kricker A. How much melanoma is caused by sun exposure? Melanoma Res 1993; 3(6): 395-401.
8. Reif J, Pearce N, Fraser J. Cancer risks in New Zealand farmers. Int J Epidem 1989; 18(4): 768-774.
9. Garbe C. The German melanoma register and environmental risk factors implied. J Cancer Res Clinical Oncol 1991; 117 (Supp 2): 66.
10. Brownson RC, Reif JS, Chang JC, Davis JR. Cancer risks among Missouri farmers. Cancer 1989; 64(11): 2381-2386.
11. Fincham SM, Hansen J, Berkel J. Patterns and risks of cancer in farmers in Alberta. Cancer 1992; 69(5): 1276-1285.
12. Elwood JM, Koh HK. Etiology, epidemiology, risk factors, and public health issues of melanoma. Curr Opinion Oncology 1994; 6(2): 179-87.
13. Lilianfield AM, Lilianfield DE. Foundations of epidemiology (2nd ed.). New York: Oxford University Press; 1980.
14. Gardner MJ, Douglas GA. Statistics with confidence. London: British Medical Journal; 1989.
15. Khlat MA, Vail A, Parkin M, Green A. Mortality from melanoma in migrants to Australia: variation by age at arrival and duration of stay. Amer J Epidem 1992; 135(10): 1103-13.
16. Marks R. Epidemiology of non-melanoma skin cancer and solar keratoses in Australia: a tale of self-immolation in Elysian fields. Australasian J Derm 1997; 38(Supp 1): S26-9.
17. Marks R. Skin cancer -- childhood protection affords lifetime protection. MJA 1987; 147(10): 475-6.
18. Moise AF, Buttner PG, Harrison SL. Sun exposure at school. Photochem Photobiol 1999; 70(2): 269-74.
19. Green AD, Whiteman D, Frost C, Battistutta D. Sun exposure, skin cancers and related skin conditions. J Epidem 1999; 9(6 Supp): S7-13.
20. Garland FC, White MR, Garland CF, Shaw E, Gorham ED. Occupational sunlight exposure and melanoma in the US Navy. Arch Environ Health 1990; 45(5): 261-267.
21. Dircks R, Goldsmith P, McCosker N. Skin Cancer in the workplace J Occ Health Safety - Australia and New Zealand 1987; 3(1): 53-60.
22. Lynge E. Occupational mortality and cancer analysis. Public Health Rev 1990, 18(2): 99-116.
23. Lynge E, Thygesen L. Use of surveillance systems for occupational cancer: data from the Danish National System. Int J Epidem 1988; 17(3): 493-500.
24. McLaughlin JK, Malker HSR, Blot WJ, Ericsson JLE, Gemne G, Fraumeni JF. Malignant melanoma in the printing industry. Amer J Indust Med 1988; 13(2): 301-304.
25. Swerdlow AJ, English JSC, Mackie RM, O'Doherty CJ, Hunter JAA, Clark J, Hole DJ. Fluorescent lights, ultraviolet lamps and risk of cutaneous melanoma. BMJ 1988; 297(6649): 647-650.
26. Anonymous. Fluorescent lighting and malignant melanoma. Health Physics 1990; 58(1): 111-112.
27. Christie D, Robinson K, Gordon I, Bisby J. A prospective study in the Australian petroleum industry. II. Incidence of cancer. Brit J Indust Med 1991; 48(8): 511-514.
28. Marsh GM, Enterline PE, McCraw D. Mortality patterns among petroleum refinery and chemical plant workers. Amer J Indust Med 1991; 19(1): 29-42.
29. Ingram AJ. Review of chemical and UV light-induced melanomas in experimental animals in relation to human melanoma incidence. J Toxicol 1991; 12(1): 39-43.
30. Sinks T, Steele G, Smith AB, Watkins K, Shults RA. Mortality among workers exposed to polychlorinated biphenyls. Amer J Epidem 1992; 136(4): 389-398.
31. Mazzuckelli LF, Schulte, PA Notification of workers about an excess of malignant melanoma: a case study, Amer J Indust Med 1993; 23(1): 85-91.

Genetic Vaccination: Can Plasmid DNA deliver its expectations?[1]

Malcolm R. Alderton, Peter J. Gray and David F. Proll[2]

Vaccines are effective at protecting not only individuals, but also communities. In the last fifty years, global immunisation programs have developed such strong "herd immunity" that some diseases, eg smallpox and polio, have been effectively eliminated.

Currently, in terms of commercially available vaccines, the traditional methods of vaccine development are still leading the attack against infectious agents. These vaccines are produced from dead or an attenuated (non-pathogenic) form of the pathogen, which induces immunity in an individual and protects against clinical disease. The first of these - attenuated vaccines - cause a mild infection using a strain or serotype of the pathogen that has reduced pathogenicity.

Examples of this type of vaccine include the original smallpox vaccine pioneered by Jenner, and those currently used to protect against polio (Sabin), tuberculosis (BCG), typhoid, measles, mumps, yellow fever and rubella[1]. However, live attenuated vaccines carry the risk, albeit very low, that the live attenuated preparations may revert to pathogenic forms. To circumvent the risks associated with live attenuated vaccines, killed microbes, toxoids and recombinant subunit preparations have been developed to protect against diseases such as the plague, Q fever, hepatitis A and B, tetanus and diphtheria. These vaccines are safer than live attenuated vaccines, but do not stimulate the same level of immunity.

Agent	Disease	Vaccine
Bacteria		
Bacillus anthracis	Anthrax	Yes
Brucella *spp.*	Brucellosis	No
Vibrio cholerae	Cholera	Yes
Burkholderia mallei	Glanders	No
Burkholderia pseudomallei	Melioidosis	No
Yersinia pestis	Plague	Yes
Francisella tularensis	Tularemia	Yes, but investigational
Rickettsia		
Coxiella burnetii	Q fever	Yes, Australia only
Rickettsia prowazekii	Typhus	No
Viruses		
Variola virus	Smallpox	Yes
Venezuelan equine encephalitis (VEE) virus	VEE	Yes
Ebola virus	Viral hemorrhagic fever	No
Marburg virus	Viral hemorrhagic fever	No
Argentine hemorrhagic fever virus	Viral hemorrhagic fever	Yes, but investigational
Congo-Crimean hemorrhagic fever virus	Viral hemorrhagic fever	No
Rift valley fever virus	Viral hemorrhagic fever	Yes, but investigational
Hantavirus	Viral hemorrhagic fever	No
Yellow fever virus	Viral hemorrhagic fever	Yes
Dengue fever virus	Viral hemorrhagic fever	No
Toxins		
Botulinum toxin	Botulism	Yes
Ricin	Ricin poisoning	No
Staphylococcal entertoxin B (SEB)	SEB intoxication	No

Table 1. Availability of vaccines to potential biological warfare agents[41]

[1] Alderton MR, Gray PJ, Proll DF. Genetic vaccination: Can plasmid DNA deliver its expectations. *Aust Mil Med* 2001;10(2): 59-67.

The authors are research scientists in the Combatant Protection and Nutrition Branch, Aeronautical and Maritime Research Laboratory, Defence Science & Technology Organisation, Melbourne, Vic., Australia.

Because of a lack of interest by commercial vaccine producers in the diseases caused by potential biological warfare (BW) agents (Table 1), the vaccines currently available are first-generation vaccines. These often require a course of vaccinations with regular boosters and are therefore not ideal for military applications. The ideal vaccine for military use should possess the following characteristics[2]:

i) induce rapid and complete protection,
ii) require only one oral immunization to reduced logistic burden and cost,
iii) safe with no debilitating side effects,
iv) provide life-long immunity without the requirement of boosters vaccinations,
v) stable at high temperatures thereby eliminating the need of refrigeration and increasing the shelf-life of the vaccine, and
vi) low production costs.

New Methods in Vaccine Development

Although there have been successes with traditional vaccination, current vaccines target only a tiny fraction of infectious diseases. Table 1 lists possible biological warfare agents and highlights the fact that of the 23 organisms/toxins listed, only 11 currently have vaccines available. Furthermore, the increasing vulnerability of human populations to new and re-emerging infections, and the dramatic rise in antibiotic resistant microorganisms, has indicated the urgent need for new vaccine research. Vaccines are an effective way of preventing disease but traditional vaccine strategies, based on either an attenuated or inactivated microorganism, have provided limited or no protection against some pathogens. For example, tens of millions of dollars have been spent over the last 30 years to develop a traditional vaccine to prevent malaria, without success. However, advances in biotechnology and genetic engineering techniques have enabled new approaches to vaccine development - such as DNA vaccines.

DNA Vaccines

It has been a decade since the discovery that the injection of naked DNA into muscle cells, resulted in long-term gene expression in transfected cells[3]. Subsequently it was shown that if the plasmid encoded an antigenic protein, it was possible to elicit an immune response[4]. From this spawned a new era in vaccine development, and hence the technology of DNA (or genetic, nucleic acid) vaccination. The application and design of novel DNA vaccines grew rapidly. From the beginnings in 1990-1992, it was only three years later that the first human trials with a DNA vaccine began[5-9]. Despite this, to date not a single DNA vaccine has been licensed for human use. It may be asked, therefore, if there is a future for this technology. The mechanisms underlying DNA vaccination are discussed below, outlining the current developments and future prospects and its application to the development of vaccines for military application.

DNA vaccines are considered to be the technology that will address the efficacy problems of the current vaccines, and are often referred to as the third generation of vaccines. The methodology was an offshoot of gene therapy, a technology developed to deliver genes coding for proteins that could replace a defective enzyme or tag a cancer cell for destruction. In the search for an appropriate vehicle that would deliver the DNA to cells in a way that would promote uptake and expression of the DNA, it was discovered that injection of DNA plasmids in saline stimulated expression of foreign proteins in mice. Unfortunately, the amounts of protein produced by the tissue receiving the plasmids was not enough to correct an enzyme defect or provoke destruction of a tumour, but the levels were high enough to stimulate an immune response3,4.

In its simplest form, a DNA vaccine consists of the DNA sequence encoding the potential antigen under the control of a eukaryotic promoter to drive gene expression in the host cell. However, they generally consist of a bacterial plasmid engineered for gene expression in eukaryotic cells. Thus they contain a eukaryotic promoter and a transcription termination/polyadenylation signal sequence to aid in mRNA stability. In association with this, they also have a bacterial origin of replication and an antibiotic selectable marker to enable growth and manipulation in bacterial cells (Figure 1).

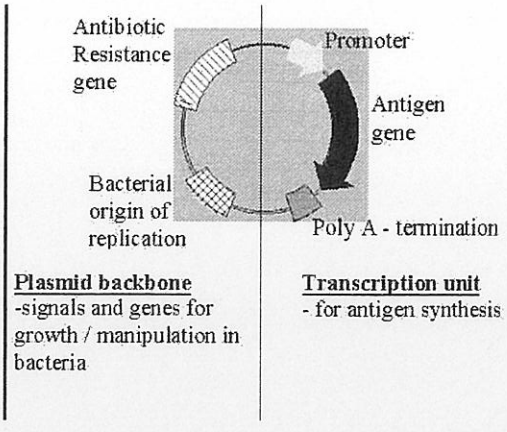

Figure 1: Schematic representation of a DNA vaccine. Plasmid DNA used for vaccination is composed of two domains. A transcription unit composed of a promoter to drive mRNA synthesis and a polyadenylation / termination signal to correctly process the transcribed mRNA. These two regions flank the sequence coding for the antigen to be synthesised. The second domain enables the plasmid to be genetically manipulated in bacterial

cells during the production and growth of the plasmid DNA vaccine.

The antigen-encoding DNA molecule has been delivered into the host by a wide variety of methods and routes. These include: (i) into the skin via the epidermal gene gun, intradermal or subcutaneous injection, (ii) into the nasal and gastrointestinal mucosa via intranasal and oral delivery, (iii) into the bloodstream by intravenous injection, and (iv) into the genitourinary tract by intravaginal injection or instillation10. Following inoculation of the plasmid DNA into the host, transcription/translation occurs to produce a mature protein (Figure 2). The protein is then exposed to the host's immune cells resulting in an immune response.

A variety of immune responses have been characterised following vaccination with DNA molecules. Generally, the response by DNA immunisation is characterised as a T helper cell type 1 (Th1) response, rather than a T helper type 2 (Th2) response11. Th1 are inflammatory cells that are associated with the cell-mediated response, whereas, Th2 are associated with antibody production.

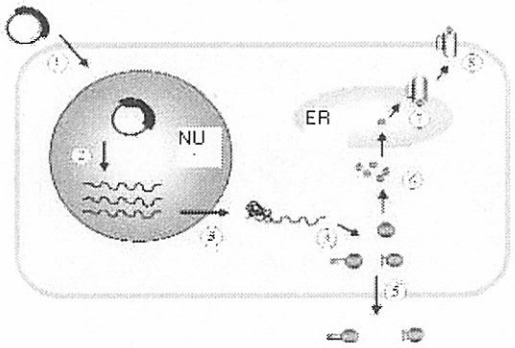

Figure 2: Schematic representation for the production of antigens from DNA vaccines within a host cell. Following the introduction of the plasmid DNA into the cell (1), mRNA is produced in the nucleus (NU), through transcription from the gene encoding the antigen (2). Export of the mRNA molecules from the nucleus into the cytoplasm (3) allows interaction with the cells translational apparatus to produce mature proteins (4). The antigens that are engineered to contain secretion signals, or signals to target them to immune cells, are secreted from the cell (5) and interact or travel to immune cells for processing. Alternatively, the antigens that do not contain secretion signals are proteolytically degraded into smaller peptides (6) and transported to the endoplasmic reticulum (ER). Within this cellular organelle the peptides become associated with the Major Histocompatibility Complex (MHC) (7) and transported to the outer cell membrane where the MHC associated antigen is exposed on the outer cell surface for interaction with immune cells.

However, this characterisation is not all or nothing choice between Th1 and Th2 immunity but rather a dominant response profile that depends on a series of factors, including the antigen, the dose, the route and method of delivery, whether the antigen is secreted, and if adjuvants or immunostimulators are used12-15. On the other hand, traditional vaccines mostly, and sometimes exclusively, generate a humoral response. As a result DNA vaccines are particularly well suited to deal with viral diseases against which traditional vaccines have failed, or have not been produced.

Advantages of DNA Vaccines

DNA vaccines have several advantages over traditional vaccines. Studies have shown them to be well tolerated, and stimulatory of a full spectrum of immune responses, including cytotoxic T lymphocytes (CTL), a response generally not induced by protein based vaccines. The induction of CTL, by virtue of the in vivo antigen synthesis and MHC class I molecule presentation, provides the efficacy of a live attenuated vaccine without the risk of infection. They also generate exceptionally long-lasting immune responses[16-18], thus possibly reducing the need for booster immunisations.

There is also the possibility of producing multivalent vaccines against several pathogens by cloning genes encoding for different antigens into a single vector, or by mixing different plasmids together. The ease of cloning allows new vaccines to be created quickly, for example in response to new or changing strains of pathogens.

Furthermore the new generation vaccines will be more cost-effective, since they can all be produced using similar techniques. The simplicity of producing DNA vaccines is one of the most attractive aspects of the process; the only steps required being the construction and purification of the plasmid. The robustness of DNA eliminates the need for cold storage, so cost of storage and transport will also be reduced. These characteristics make DNA vaccinology very attractive to the military, which desire greater disease protection for combat personnel, with fewer immunisations, and at less cost.

DNA Vaccine Safety Issues

Although the immunogenicity of DNA vaccines is well established, there are still some concerns regarding their safety, including the integration of DNA plasmids into the host chromosome, the production of antibodies to DNA and the generation of neonatal antigen tolerance[19]. Integration of vaccine DNA into the chromosome is perceived as a problem because of the possible activation of oncogenes or the disruption of normal gene function and regulation. Clearly, these events could have serious consequences for the host, but in studies to date the integration of plasmid DNA into the host chromosome has not been re-

ported. Shroff and colleagues[20] were unable to detect plasmid integration in several preclinical studies using an assay that can detect one integration event in 1 x 106 cells. Davis and McCluskie[15] argue the likelihood of integration of the DNA vaccine plasmid into the host chromosome is very low, since, (i) most injected DNA is rapidly degraded in the extracellular space, (ii) the plasmid DNA vectors are designed to remain episomal, (iii) most non-integrated DNA would soon be lost during subsequent cell division, and (iv) integration is not possible in mature muscle fibres, as they are permanently post mitotic.

The production of anti-DNA antibodies is also of concern, especially to individuals with autoimmune diseases, eg systemic lupus erythematosus (SLE). Although double-stranded DNA can induce low levels of antibodies21, the fear that this will initiate unwanted autoimmune reactions has not materialised. In addition, Mor et al.21 also suggested that neonatal immunisation with a DNA vaccine plasmid generated immune tolerance but all subsequent studies using newborn animal hosts have not substantiated this claim. Although significantly more work is required on the safety of DNA vaccines, the work to date suggests most of the concerns are likely to prove unfounded.

Human Clinical Trials

Despite the wealth of accumulated data on the vaccination of animals with DNA and the subsequent characterisation of the immune response, until recently their effectiveness in humans was unknown. Due in part to the safety concerns discussed above, the rapid advancement of the technology for application to human disease had stalled somewhat. However, with investigations now addressing these concerns, human trials have slowly begun - albeit with caution and scepticism.

One of the first human trials of DNA vaccination was against the malarial parasite *Plasmodium falciparum* [22]. These phase I clinical trials established the safety, tolerability and immunogenicity of DNA vaccines encoding malarial antigens. They also established their capacity to induce antigen specific CD8+T cell-dependant CTL and INF-γ responses in humans by three different routes of administration. However, antibodies were not produced despite the fact that the vaccines used had previously been shown to induce antibody responses in a range of animals including primates[7-9].

Similar phase I clinical trials have also evaluated HIV and Hepatitis B DNA vaccines[23,24]. Not only were a number of safety issues monitored, but also the ability of the DNA vaccines to induce an immune response measured. A range of parameters was examined, including: the amount and isotype of antibody produced against the encoded proteins, the production of cytokines, the activation and proliferation of peripheral blood mononuclear cells and for antigen specific cytotoxic activity[23-25]. Although both B and T cell immune response has been reported following the phase I trials, the magnitude of the elicited responses were modest.

Although the results obtained from these preliminary trials were somewhat mixed they did provide evidence that the concept of DNA vaccination works in humans, and generated some invaluable data in relation to the dose and route of administration suitable for humans. The results also demonstrated that the observed responses were suboptimal for effective vaccines and needed to be significantly improved to yield increased immune responses. This has now paved the way for future trials to address these problems.

Future Prospects and Developments

Despite the early optimism for the potential of DNA vaccines, much of the work to date has found that the immune responses induced through injection of DNA are insufficient to provide immunity against subsequent challenge by the infectious agent. Thus, more recently much effort has focused on means to increase and direct more specifically the immune response by modifying the plasmids and/or their mode of delivery.

Co-delivery of cytokines

Cytokines and co-stimulatory cell surface molecules play a crucial role in directing and determining the magnitude of an immune response. Consequently, numerous workers have used plasmid DNA encoding various cytokines and co-stimulatory molecules to enhance or direct the immune response generated following DNA vaccination[10]. These included the cytokines: Interleukins 1, 2, 4, 5, 6, 7, 8, 10, 12, 15 and18, Granulocyte-macrophage colony stimulating factor (GM-CSF), Tumour necrosis factor (TNF) and Interferon-γ. Generally these have resulted in increased antibody responses while some have also increased T-cell responses.

Delivery mechanisms

Clearly, there is a wide variety of ways of administering DNA vaccines and each may have advantages specific to the vaccine in question. There is, however, a problem of DNA degradation in the vaccine recipient. The extent of the DNA degradation by extracellular deoxyribonucleases may vary for the different routes of administration, but approaches to

protect the DNA vaccine and assist efficient entry into host cells are imperative in DNA vaccine design[26,27].

Sizemore et al.[28] used a highly attenuated Shigella spp to deliver and express DNA vaccines in mucosal surfaces. The bacterium, which enters the mucosa via M cells, evades phagosome formation in phagocytic cells by entering the cytosol. This improves vaccine efficacy by initiating a strong CTL response as well as a humoral response. Other microorganisms that generate strong cell-mediated responses and could be used in a similar way to deliver antigens encoded by DNA vaccines include attenuated *Salmonella typhimurium*, *Listeria monocytogenes*, Leishmania major and *Mycobacterium tuberculosis*.

Gregoriadis et al.[29] identified uptake and expression of DNA vaccines by antigen-presenting cells (APC), in particular dendritic cells, which is preferable to uptake and expression by muscle cells. In 1990, he also demonstrated liposome's were avidly taken up by APC, and later revealed liposome coated DNA vaccines were also preferentially targeted by APC. The liposomes also protect the DNA vaccines from deoxyribonuclease degradation. Moreover, a number of liposome-based drug formulations, including a hepatitis A vaccine, have been licensed in the USA and Europe, making future licensing of liposome coated DNA vaccines more likely.

Cochleates are rigid, calcium-induced structures consisting of spiral bilayers of anionic phospholipids[30], a unique structure that differs from liposomes. It is believed that following fusion of the cochleate with the cell membrane the contents (i.e. the DNA vaccine) are released into the cytosol. DNA vaccines delivered encapsulated in cochleates have been shown to promote strong long-lasting humoral, mucosal and cell-mediated responses[31-33].

Another potential delivery method for DNA vaccines is the use of biodegradable microparticles. DNA contained within microparticles, composed of polylactide-co-glycoside, can be given systemically or to mucosal surfaces. The ability of microparticle encapsulated DNA vaccines to induce mucosal and systemic immune responses has been demonstrated[31-33]. Thus by protecting the DNA vaccine from extracellular elements a more enhanced immune response can be generated, which is probably due to increased antigen production.

Targeting antigen molecules

Incorporating signalling sequences within the vaccine antigen that directs it to the cytosol or endosome in antigen-presenting cells, eg macrophages and dendritic cells, ensures the antigen is associated with MHC Class I and Class II molecules, respectively. Antigens associated with MHC Class I molecules initiate a cell-mediated immune response, whereas, antigens associated with MHC Class II molecules initiate a humoral response[34,35]. The ability to direct antigens to the most appropriate cell and/or cellular compartment would greatly benefit vaccine production, by generating the most appropriate immune response for the particular disease.

Addressins are surface molecules expressed by several different cells including subpopulations of lymphocytes and are responsible for directing these cells to the appropriate lymphoid tissue. They interact with specific receptors on cells located in these tissues, eg thymus, spleen, lymph node, Peyer's patch and bone[36]. Fusing vaccine antigens to these homing molecules may provide a way of transporting the antigens to sites where the pathogen will be first encountered. Experiments performed by Boyle et al.[37], using DNA vaccines encoding antigen-ligand fusions targeting the antigen to lymphoid organs, showed a significant increase in both the humoral and the cellular immune response.

Expression Library Immunisation

Despite the progress in the development of DNA vaccines, one of the greatest hurdles that still remain, is the identification of suitable antigens that will provide protection against disease. An approach to circumvent this may be through the use of Expression Library Immunisation (ELI). The ELI approach was first described by Barry et al[38] who applied the technique to protect mice against *Mycoplasma pulmonis*. A similar approach has also been used to protect mice against other parasites, including malaria (personal observations)[39] and Leishmania[40]. In this approach the entire genome (in small fragments) is cloned into a eukaryotic expression vector similar to those used in DNA vaccination, and then the entire library (or fractions thereof) is used to vaccinate the subjects. Using a mathematical model, sufficiently large enough numbers of plasmids are generated to ensure the probability that every gene contained in the organisms genome is represented in the library. For example the mouse infecting malaria parasite, *Plasmodium chabaudi*, which possess a genome of approximately 25-30Mb, requires approximately 70,000 plasmids (each containing a median size of 1.5kb of P. chabaudi DNA) in order for the entire genome to be represented. However, not all genes encode "protective antigens" therefore a significant reduction in the number of plasmids may still provide protective immunity. This is highlighted using the

example above where protection against a lethal challenge of malaria was observed when mice are vaccinated with a subset of the entire library containing as little as 3,000 plasmids (personal observations)[39]. Further sequential partitioning of these subsets could lead to the identification of individual protective antigens - a technique that may have generic applicability to the discovery of vaccine antigens.

ELI has enormous potential for military application. It is feasible that the concept could be applied to the battlefield. A potential vaccine, which could provide suitable protection following the onset of disease, could be produced as follows. A soldier falls ills and the causative organism is isolated (2 days). The organism is grown and genomic DNA purified and used to construct an expression library (2-3 days). The library is expanded to produce sufficient amounts of DNA to vaccinate other soldiers (2 days). Hence, within less than ten days from the onset of illness a vaccine could be produced. The reason for the rapid speed at which this type of vaccine can be produced lies in the fact that because (at least in mathematical theory - determined by the number of individual DNA plasmids) every protein encoded by the target organism is contained within the library. Thus eliminating the need to identify and characterise specific protective antigens. The US recently announced a large project, to be headed by Stephen L Hoffman of the Navel Medical Research Centre, to investigate further the application of ELI technology to military applications.

Conclusions

The development of DNA vaccine technology has been rapid, with the progression from a laboratory phenomenon to clinical trials occurring at breakneck speeds. The DNA vaccine vacuum fueled a desire to harness the tools of molecular biology to construct antigen-encoding plasmids capable of inducing protective immune responses to pathogens for which there were no conventional vaccines. However, many questions regarding the basic science of DNA vaccine technology remain unanswered - and this will ultimately determine the success or failure of the application to find a place in our immunological arsenal against disease.

References:

1. MIMS. MIMS Annual 1998. Sydney: Griffin Press; 1998.
2. Cleland JL. Single-administration vaccines: Controlled-release technology to mimic repeated immunizations. Trends Biotechnology 1999;17(1):25-9.
3. Wolff JA, Malone RW, Williams P, Chong W, Acsadi G, Jani A, Felgner PL. Direct gene transfer into mouse muscle in vivo. Science 1990;247:1465-8.
4. Tang D, De Vit M, Johnston SA. Genetic immunization is a simple method for eliciting an immune response. Nature 1992;356:152-4.
5. Martin T, Parker SE, Hedstrom R, Le T, Hoffman SL, Norman J, Hobart P, Lew D. Plasmid DNA malaria vaccine: The potential for genomic integration after intramuscular injection. Hum Gene Ther 1999;10(5):759-68.
6. Parker SE, Borellini F, Wenk ML, Hobart P, Hoffman SL, Hedstrom R, Le T, Norman JA. Plasmid DNA malaria vaccine: Tissue distribution and safety studies in mice and rabbits. Hum Gene Ther 1999;10(5):741-58.
7. Hedstrom RC, Doolan DL, Wang R, Kumar A, Sacci JB Jr., Gardner MJ, Aguiar JC, Charoenvit Y, Sedegah M, Tine JA, Margalith M, Hobart P, Hoffman SL. In vitro expression and in vivo immunogenicity of Plasmodium Falciparum pre-erythrocytic stage DNA vaccines. Int J Mol Med 1998;2(1):29-38.
8. Gramzinski RA, Obaldia N III, Jones TR, Rossan RN, Collins WE, Garrett DO, Lal AA, Hoffman SL. Susceptibility of Panamanian Aotus Lemurinus Lemurinus to sporozoite- induced Plasmodium Falciparum (Santa Lucia) infection. Am J Trop Med Hyg 1999;61(1):19-25.
9. Wang R, Doolan DL, Le TP, Hedstrom RC, Coonan KM, Charoenvit Y, Jones TR, Hobart P, Margalith M, Ng J, Weiss WR, Sedegah M, de Taisne C, Norman JA, Hoffman SL. Induction of antigen-specific Cytotoxic T Lymphocytes in humans by a Malaria DNA vaccine. Science 1998;282(5388):476-80.
10. Gurunathan S, Klinman DM, Seder RA. DNA vaccines: Immunology, application, and optimization. Annual Rev Immunol. 2000;18:927-74.
11. Shroff KE, Marcucci LA, de Bruin SJ, Winter LA, Tiberio L, Pachuk C, Synder LA, Satishchandran C, Ciccarelli RB, Higgins TJ. Induction of HSV-GD2 specific CD4(+) cells in peyer's patches and mucosal antibody responses in mice following DNA immunisation by both parenteral and mucosal administration. Vaccine 1999;18(3-4):222-30.
12. Barry MA, Johnston SA. Biological features of genetic immunization. Vaccine 1997;15:788.
13. Feltquate DM, Heaney S, Webster RG, Robinson HL. Different Th cell types and antibody isotypes generated by saline and Gene Gun DNA immunization. J Immunology 1997;158.
14. Torres CA, Iwasaki A, Barber BH, Robinson HL. Differential dependence of target site tissue for Gene Gun and intramuscular DNA immunizations. J Immunology 1997;158:4529.
15. Davis HL, McCluskie MJ. DNA vaccines for viral diseases. Microbes Infect 1999;1:7-21.
16. Yankaukas MA, Morrow JE, Parker SE, Abai A, Rhodes GH, Dwarki VJ, Gromkowski SH. Long-term Anti-Nucleoprotein cellular and humoral immunity is induced by intramuscular injection of Plasmid DNA containing NP Gene. Cellular Biology 1993;12:7712-7.

17. Davis HL, Michel M-L, Whalen RG. DNA-based immunization induces continuous secretion of Hepatitis B surface antigen and high levels of circulating antibody. Human Molecular Genetics 1993;2:1847-51.
18. Lozes E, Huygen K., Content K, Dennis O, Montgomery DL, Yawman AM, Vandenbussche P, Van Vooren JP, Drowart A, Ulmer JB, Lui MA. Immunogenicity and efficacy of a Tuberculosis DNA Vaccine encoding the components of the secreted Antigen 85 Complex. Vaccine 1997;15:830-4.
19. Smith HA, Klinman DM. The regulation of DNA vaccines. Curr Opin Biotechnol 2001;12(3):299-303.
20. Shroff KE, Smith LR, Baine Y, Higgins TJ. Potential for Plasmid DNAs as vaccines for the new millennium. Pharmaceut Science Technology Today 1999;2(5):205-12.
21. Mor G, Yamshchikov G, Sedegah M, Takeno M, Wang R, Houghten RA, Hoffman S, Klinman DM. Induction of neonatal tolerance by plasmid DNA vaccination of mice. J Clin Investigations 1996;98:2700-5.
22. Doolan DL, Hoffman SL. DNA-based vaccines against malaria: Status and promise of the multi-stage Malaria DNA Vaccine operation. Int J Parasitol 2001;31(8):753-62.
23. MacGregor RR, Boyer JD, Ugen KE, Lacy KE, Gluckman SJ, Bagarazzi ML, Chattergoon MA, Baine Y, Higgins TJ, Ciccarelli RB, Coney LR, Ginsberg RS, Weiner DB. First human trial of a DNA-Based vaccine for treatment of Human Immunodeficiency Virus Type 1 infection: Safety and host response. J Infect Dis 1998;178(1):92-100.
24. Tacket CO, Roy MJ, Widera G, Swain WF, Broome S, Edelman R. Phase 1 safety and immune response studies of a DNA Vaccine encoding Hepatitis B Surface Antigen delivered by a gene delivery device. Vaccine 1999;17(22):2826-9.
25. Calarota S, Bratt G, Nordlund S, Hinkula J, Leandersson AC, Sandstrom E, Wahren B. Cellular cytotoxic response induced by DNA Vaccination in HIV-1- infected patients. Lancet 1998;351(9112):1320-5.
26. Manickan E, Karem KL, Rouse BT. DNA Vaccines - A modern gimmick or a boon to Vaccinology. Critical Rev Immunology 1997;17(2):139-54.
27. Gregoriadis G. Genetic Vaccines: Strategies for optimisation. Pharmaceut Research 1998;15(5):661-70.
28. Sizemore DR, Branstrom A, Sadoff J. Attenuated Shigella as a DNA delivery vehicle for DNA-mediated immunogenicity. Science 1995;270:299-302.
29. Gregoriadis G, Saffie R, DeSouza JB. Liposome-mediated DNA vaccination. FEBS Letters 1997;402:107.
30. Papahadjopoulos D, Vail WJ, Jacobson K, Poste G. Cochleate lipid cylinders: Formation by fusion of unilamellar vesicles. Biochimica Biophysica Acta 1975;394:483-91.
31. Gould-Fogerite S, Mannino RJ. Mucosal and systemic immunization using Cochleate and Liposome Vaccines. J Liposome Research 1996;6:357-79.
32. Mannino RJ, Gould-Fogerite S. Lipid matrix-based vaccines for mucosal and systemic immunization. Pharm Biotechnol 1995;6:363-87.
33. Gould-Fogerite S, Kheiri MT, Zang F, Wang Z, Scolpino AJ, Feketeova E, Canki M, Mannino RJ. Targeting immune response induction with Cochleate and Liposome-based vaccines (Review). Adv Drug Delivery Rev 1998;32(3):273-87.
34. Isobe H, Moran T, Li S, Young A, Nathenson S, Palese P, Bona C. Presentation of a Major Histocompatibility Complex Class I Molecule of Nucleo-Protein Peptide expressed in two different genes of an Influenza Virus Transfectant. J Experiment Med 1995;181:203-13.
35. Schutze-Redelmeier MP, Gournier H, Garcia-Pons F, Moussa M, Joliot A, Volovitch M, Prochiantz A, Lemmonier FA. Introduction of endogenous antigens into the MHC Class I processing and presentation pathway by Drosophila Antennapedia Homeodomain primes Cytotoxic T Cells in vivo. J Immunology 1996;157:650-5.
36. Kraal G, Mebius RE. High endothelial venules: Lymphocyte traffic control and controlled traffic. Advances Immunology 1997;65:347-95.
37. Boyle JS, Brady JL, Lew AM. Enhanced responses to a DNA vaccine encoding a fusion antigen that is directed to sites of immune induction. Nature 1998;392(6674):408-11.
38. Barry MA, Lai WC, Johnston SA. Protection against Mycoplasma infection using Expression-Library Immunization. Nature 1995;377(6550):632-5.
39. Smooker PM, Setiady YY, Rainczuk A, Spithill TW. Expression Library Immunization protects mice against a challenge with virulent rodent malaria. Vaccine 2000;18(23):2533-40.
40. Piedrafita D, Xu D, Hunter D, Harrison RA, Liew FY. Protective immune responses induced by vaccination with an expression genomic library of Leishmania Major. J Immunol 1999;163(3):1467-72.
41. Geissler E. Biological and Toxin Weapons Today. Oxford: Oxford University Press; 1986.

A View from the Front

Variola Virus - Destruction Imminent[1]

Jan Thomas[2]

Most medical personnel will not have seen smallpox, the disease resulting from infection by the variola virus. Hopefully, they never will. The last case of naturally acquired smallpox occurred in 1977, in Somalia, and global eradication was declared in 1980. From 1981 to 1986, the World Health Organisation (WHO) undertook a program to implement post-eradication policies.

One of the actions taken was to implement measures to assure the biosafety and security of the remaining variola virus stocks. This entailed consolidating all known samples in two WHO collaborating centres, one in the Russian Federation and the other in the United States of America. The WHO Committee on Orthopoxvirus Infections then recommended that the remaining stocks of live variola virus be destroyed in the future.

An Ad Hoc Committee was appointed to review this recommendation and assess progress and activities of the post-eradication program. There has been continuous debate in the scientific community about the ethical, scientific and social issues associated with destruction of the remaining known virus stocks in Novosibirsk and Atlanta.

In 1996, the World Health General Assembly adopted a resolution to destroy, in June 1999, the remaining stocks of variola virus, including all whitepox viruses, viral genomic DNA, clinical specimens and other material containing infectious variola virus. When the question of destruction was considered in 1999, a decision was made not to destroy the virus so that further international research into antiviral agents and improved vaccines could be conducted. This would also allow high priority investigations of the genetic structure and pathogenesis of smallpox to take place. All the work is carried out under the very careful control of the WHO.

In 2002, the question of destruction will be revisited. There is still deep concern among many members of the scientific community about the prudence of destroying a virus which causes a disease for which we have no cure, particularly as the global population is now more susceptible to smallpox.

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Review Article

Aortic Trauma[1]

Sulman Ahmed[2]

Abstract

Aortic trauma is often poorly recognised in a trauma setting, and represents a significant cause of lethal injury. Most casualties will die at the scene[1]. This article attempts to define the mechanisms and clinical features of aortic trauma. An understanding of aortic trauma may allow early recognition of such an injury in a trauma patient, and therefore prompt immediate transfer to a level 4 or 5 facility with cardiothoracic support.

Introduction

Aortic trauma is often associated with severe blunt trauma. Vesalius made the first reference of aortic trauma in 1557[2]; however, it has been in the last 50 years that further advancements in diagnosis and management of this condition have occurred. Around 85% of such victims will die at the scene of injury[3]. It has a high mortality rate. This may be a result of the aortic injury itself but also may encompass other concomitant injuries the casualty may have sustained. Smith et al found aortic trauma to be the second most common cause of death behind head injury in a study of 387 blunt trauma deaths[4]. Such trauma, once recognised, is time consuming and takes up precious health resources. This is most challenging in a military setting with limited health personnel. Trauma of this scale implies a significant risk of loss of life resulting in a priority one status. Evacuation to a level 4 or 5 facility would be justified.

Aetiology

Traumatic aortic rupture is caused primarily by motor vehicle/pedestrian collisions[4]. Other important causes include falls from great heights, airplane accidents and landslide burials. All of these examples are classified as blunt aortic trauma and need to be recognised, especially in a military setting.

Penetrating aortic injuries result in a puncture or laceration of the aorta. It is usually caused by projectiles (e.g. high velocity round) or knives. The consequence of such an injury depends on the site and severity of the injury and immediate surgical treatment is indicated.

Traumatic aortic rupture is rapidly lethal. 85-90% of casualties will die prior to a resuscitation facility. Most will succumb to rapid haemorrhage culminating in hypovolaemic shock and death. The natural history of an untreated aortic injury in those who will survive the next 24 hours is unknown.

The site of rupture can be categorised as[2]:

- Aortic isthmus (90%).
- Right brachiocephalic artery origin (5%).
- Left Subclavian origin (3%).
- Descending thoracic aorta (2%).

Mechanism of Injury

There are 3 possible stresses that can be applied to the aorta[5,6]:

1. A horizontal deceleration with or without chest compression (e.g. MVA). The deceleration difference between the mobile aortic arch and the relatively immobile descending aorta exposes the aortic isthmus to tension. This leads to rupture opposite the site of fixation.
2. Marked chest compression (e.g. landslide burial). This creates a bending stress when the heart exerts traction on the aortic arch, resulting in hyperflexion of the blood filled aortic arch against the hilar structures of the left lung.
3. Crushing injuries involving flexing of the spine.

These mechanisms produce stresses in the form of shearing, bending, and torsion respectively. Most tears are linear and may involve partial or complete transection of the aorta. Death is instantaneous if all the layers

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of the aorta, mediastinal tissues and parietal pleura are breached. Sudden uncontrolled blood loss thus ensues. However, a false aneurysm may occur if the mediastinal tissues remains intact producing a tamponade effect which reduces the amount of blood loss.

The reason why 10% of patients are alive that reach a resuscitation facility is because they have developed a false aneurysm.

Diagnosis

Aortic trauma is difficult to diagnose. A high index of suspicion is required; and this can be difficult when multiple injuries are present which can confound the resuscitation team's minds. However, a history of a motor vehicle accident involving high speed with an acceleration/deceleration component should alert to the possibility of such an injury.

Diagram 1: Points of Impact in typical decelerating injury

Symptoms may be non-existent or subtle. Retrosternal or interscapular pain maybe secondary to stretching of the aortic adventitia. Other symptoms include cough, stridor, haemoptysis, and dyspnoea[6]. Examination of the patient may reveal acute onset of upper extremity hyperextension and a harsh systolic murmur over the praecordium. At this point, the collection of signs and symptoms may not herald a diagnosis of aortic trauma. If possible, a supine chest x-ray should be done as part of the trauma series.

Features suggestive of aortic trauma on a chest x-ray include:

- Increase in the width of the mediastinum.
- Loss of sharpness of the aortic outline.
- Depression of the left main bronchus.
- Deviation of the trachea to the right.
- Obliteration of the aortopulmonary window.
- Left pleural effusion; fractures of the first rib, thoracic spine, sternum, clavicle; and a deviated naso-gastric tube.

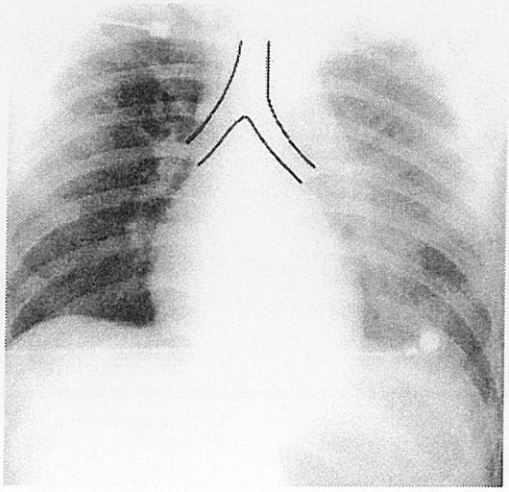

Figure 1 - Chest x-ray

Given the many features that may be evident on the chest x-ray, the three most sensitive findings are mediastinal widening >8 cm; mediastinal widening by a mediastinum to chest ratio >0.25; and opacificaton of the aortopulmonary window[7]. According to Woodring et al., the negative predictive value of a normal chest x-ray ranges between 75-94%[8]. Also, it is possible for a blunt aortic injury to be sustained in the presence of a normal chest x-ray[9]. However, many authors stress that no individual radiographic sign is sufficiently sensitive, specific, or predictive as a diagnostic finding[10].

Management

As with all trauma scenarios, the principles of resuscitation should be adhered to. Airway, breathing and circulation should be given utmost priority in stabilising the patient. Once the patient is stable, a thorough secondary survey is required to elucidate the extent of injuries present and to formulate possible diagnoses. If aortic trauma is thought to be present, the casualty should be classified as priority one and evacuated by aeromedical evacuation to a level 4/5 facility with cardiothoracic support. Such a facility may not be readily accessible due to distance or logistical reasons. If possible, the blood pressure should be kept below 120 mmHg systolic so as to decrease the shearing effect of the pulse on the aortic tissues. Controlled blood pressure via the use of beta-blockers is important when treatment is delayed or non-operative management is contemplated[6]. Prompt surgical repair of the aortic injury is the definitive step in the management of such patients. Therefore, aortic trauma not able to be managed expediently carries a poor

prognosis. If multiple casualties are present, consideration must be given to those patients who carry a more positive prognosis versus those with a poor prognosis. These ethical considerations may arise in military settings, where resources are limited.

Conclusion

Aortic trauma represents one extreme of injuries that can be sustained in a military scenario. It can not be further emphasised that prompt resuscitation of the casualty is the best management at a level 1 or 2 facility. Recognition of complex injuries, such as aortic trauma, is not only important, but necessitates the immediate evacuation to a higher level facility. However, such injuries carry a poor prognosis.

References

1. Parmley LF, Mattingly TW, Manion TW et al. Non penetrating traumatic injury of the aorta. Circulation 1958; 17:1086.
2. Dosios TJ, Salemis N, Angouras D, Nonas E. Blunt and penetrating trauma of the thoracic aorta and aortic arch branches: An autopsy study. J Trauma - Injury Infect Critical Care 2000; 49(4): 696-703.
3. Fabian TC, Richardson JD, Croce MA, et al. Prospective study of blunt aortic injury: Multicenter trial of the American Association for the Surgery of Trauma. J Trauma 1997; 42:374-380.
4. Smith RS, Chang FC. Traumatic rupture of the aorta: Still a lethal injury. Amer J Surg 1986; (152); 660.
5. Rosenberg JM, Bredenberg CE, Marvasti MA, Bucknam C, Conti C, Parker FB Jr. Blunt injuries to the aortic arch vessels. Annal Thor Surg 1989;48(4):508-513.
6. Kirsh MM, Behrendt DM, Orringer MB, et al. The treatment of acute traumatic rupture of the aorta: A 10 year experience. Annal Surg 1976;184(3): 308-316.
7. Cook AD, Klein JS, Rogers FB, Osler TM, Shackford SR. Chest radiographs of limited utility in the diagnosis of blunt traumatic aortic laceration. J Trauma - Injury Infect Critical Care 2001; 50(5):843-847.
8. Woodring JH, Fried AM, Hatfield DR, Stevens RK, Todd EP. Fractures of first and second ribs: Predictive value for arterial and bronchial injury. Amer J Roentogenol 1982; 138:211-215.
9. Nagy K, Fabian T, Rodman G, Fulda G, Rodriguez A, Mirvis S. Guidelines for the diagnosis and management of blunt aortic injury: An EAST Practice Management Guidelines Work Group. J Trauma - Injury Infect Critical Care 2000; 48(6):1128-1143.
10. Marsh D, Sturm J. Traumatic aortic rupture: Indications for angiography. Annal Thor Surg 1976; 21: 337-340.

CONTACT POISONS: A BRIEF TOUCH[1]

Andrew Robertson[2]

'Murder by poisoning is a crime of devilish wickedness and inhumanity which no language can adequately describe. '

John Glaister (1954)[1]

Introduction

Gail Bell, in her book 'The Poison Principle', tries to establish why people use poison[2]. She looks back over the centuries, from Cleopatra and Socrates to more modern poisoners like Crippen, and speculates that, with advanced analytical technology, the heyday of poisons is over[2]. But is it?

Contact poisons are those chemicals and toxins which are absorbed in sufficient quantities by direct skin contact to produce toxic effects, including death, in an individual. The popular media, literature and film commonly portray the use of contact poisons to murder various individuals. This perception has been reinforced by some relatively recent criminal trials. In May 1991, members of the Minnesota Patriots Council procured a ricin kit from an anarchist source. The kit included instructions on how to mix the ricin with dimethyl sulfoxide (DMSO) to produce a poison, which would be absorbed across the skin when the victim contacted it[3].

In the subsequent trial, the FBI expressed doubts about the ability of DMSO to carry ricin across the skin into the bloodstream because of the toxin's high molecular weight[4]. In April 1997, Thomas Leahy was arrested in Wisconsin for possession of ricin. According to the Assistant U.S. Attorney, police also discovered three spray bottles containing a mixture of nicotine and DMSO[5].

While the majority of these cases are of academic (or in some cases, literary) interest, military physicians should be aware that there are contact poisons which may produce morbidity if not mortality. These poisons are of far more concern from an industrial health viewpoint than they are as an intentional poison. The recent F-111 Seal-Reseal Board of Inquiry dealt with a number of chemicals, some of which could be absorbed through the skin. This paper will look at various chemical agents, of military, industrial or agricultural interest, which fall into the category of contact poisons.

Percutaneous Toxicity

The skin is an important portal of entry for many chemical substances. The two most important factors affecting absorption are the concentration of the applied chemical and the surface area of contact. Percutaneous toxicity is enhanced by delivering the largest concentration of agent over the greatest area. Percutaneous uptake will also usually increase if the skin has been damaged by the chemical. Other important factors are the solvent used to deliver a chemical, the site of application (e.g. scalp is 4 times more porous than the hand), the condition of the skin (e.g. DMSO dissolves lipids), the frequency of application,[6] age, race and the general hydration of the skin[7]. Areas of greater hydration have greater absorption.

Discussion

Nerve agents, particularly VX, soman (GD) and GF, remain the quintessential contact poisons. Fortunately, they are generally difficult to either manufacture or procure. Other chemicals, whilst not having the extreme toxicity of the nerve agents, are more available industrially or agriculturally and are toxic enough to cause death, generally within a week. Both the organophosphate (TEPP, Parathion) and organochlorine pesticides (Chlordane, Endrin) are sufficiently toxic to cause death and have been implicated in a number of industrial and accidental deaths.[8-14] Other agents which pose a danger as contact poisons include organic solvents (carbon tetrachloride), explosive-related chemicals (nitroglycerin, ethylene glycol dinitrate), industrial dyes and related chemicals (aniline, benzidine, toluidine), and assorted other chemicals (carbon disulfide, ethylene chlorohydrin, dimethyl sulfate, glycolonitrile, nicotine).[8-14] Nicotine and aniline, particularly, have been responsible for a number of accidental contact poisonings[12]. Many of these agents have a noticeable odour which may, fortunately, discourage prolonged contact. Most are, however, commonly used in

[1] Robertson AG. Contact poisons: A brief touch. *Aust Miil Med* 2001;10(2): 71-73.

[2] CAPT Andy Robertson is the Director of JHSA and the current editor of *Aust Mil Med.*

industry or commercially. Generally, the various toxins, plant poisons, toxic gases and poisonous metals are very poorly absorbed transdermally and pose a greater risk as ingestional or inhalational poisons.

DMSO

One interesting area of current research in the pharmaceutical industry is the development of drug delivery systems, which enhance the percutaneous absorption of various drugs[7]. These agents include Dimethyl Sulfoxide (DMSO), Azone (Laurocapram), Propylene glycol and N-methylpyrrolidone. Solvents such as DMSO can facilitate the penetration of toxicants through the skin by increasing the permeability of the barrier layer of the skin[15], principally by disrupting the lipid layers. A number of these solvents are commercially available. While this is may be effective in improving the absorption of relatively simple organic molecules, like carbon tetrachloride, the percutaneous absorption of complex molecules like toxins utilising such solvents is expected to be very limited. Leahy's alleged mixture of DMSO and nicotine, however, could be a very effective contact poison.

Conclusion

Although contact poisons remain a favourite of crime fiction writers, they should not be dismissed as a mere literary device. Many military, industrial and agricultural chemicals pose a contact risk. Medical officers should be aware of the possible morbidity from such agents and should consider taking a detailed industrial/commercial exposure history, particularly where there are non-specific health complaints in an industrial setting. Rapid identification and management may prevent long term damage and possible death.

References

1. Glaister J. The power of poison. London: Christopher Johnson;1954.
2. Bell G. The poison principle. Sydney: Picador;2001.
3. Tucker JB. Toxic Terror: Assessing terrorist use of chemical and biological weapons. Cambridge: MIT Press; 2000.
4. Transcript of United States of America v Douglas Allen Baker and LeRoy Charles Wheeler, Feb 23 1995, p. 162.
5. Carus S. Bioterrorism and biocrimes: The illicit use of biological agents in the 20th Century. Washington: National Defence University; 1999.
6. Ballantyne B, Marrs T, Turner P (Eds). General and applied toxicology. Basingstoke: Macmillan Press; 1995.
7. Tarcher AB. Principles and practice of environmental medicine. New York: plenum Medical Book Company: 1992.
8. Dreisbach RH. Handbook of poisoning (8th Ed.). Los Altos: Lange Medical Publications; 1974.
9. International Labour Office. Encyclopaedia of health and safety. Geneva: ILO; 1983.
10. Klassen CD, Amdur MO, Doull J (Eds.). Casarett and Doull's Toxicology. New York: Macmillan Publishing Company; 1986.
11. Hallenbeck WH, Cunningham-Burns KM. Pesticides and human health. New York: Springer-Verlag, 1985.
12. Stevens SD, Klarner A. Deadly doses. Cincinnati: Writers Digest; 1990.
13. National Library of Medicine. TOXNET. Washington: NLM; 2001.
14. Trevethick RA. Environmental and industrial health hazards. London: William Heineman; 1985.
15. Amdur MO, Doull J, Klaasen CD. (eds). Casarett and Doull's Toxicology. 4th ed. New York, NY: Pergamon Press, 1991.

Essay Article

THE FUTURE ROLE OF INFORMATION TECHNOLOGY IN MILITARY HEALTH[1]

Darrell Duncan[2]

On technology: The press, the machine, the railway, the telegraph are premises whose thousand-year conclusion no one has yet dared to draw.

Friedrich Nietzsche (1844-1900), German philosopher.[1]

On information: Information is the oxygen of the modern age. It seeps through the walls topped by barbed wire; it wafts across the electrified borders.

Ronald Reagan (b. 1911), U.S. Republican politician and president.[2]

Introduction

Through the centuries, different advances in social organization, usually associated with advances in technology, have produced profound changes in civilization. In the prehistoric era, the end of the Stone Age was marked by the move from socially isolated hunters and gatherers to communities reliant on agriculture and domestic animals. The Middle Ages continued for many years through the renaissance until the introduction of modern industrial processes and systems in the industrial revolution gave way to the industrially based society of the last two hundred years.

The term information age has been used to describe the phase we have entered where information technology has diminished geographical frontiers and rendered time, space and physical constraints less restrictive.[3] Whether the changes to society bought about by these advances constitute a revolution remains to be seen. Toffler and Toffler[4] argue that, as we leave the industrial age, the cultural and value changes, in conjunction with economic upheaval wrought by technological breakthroughs, will produce a lasting revolution. Negroponte[5] points out that the key difference between the industrial age and the information age is in the difference between atoms and bits. Our information is currently delivered to us in the physical form of paper and books and trade is measured as atoms although the real value is the information, not the form.

History of Information Technology

Information technology arguably had its genesis when information was first written down and stored in some manner by the Sumerians circa 3000 BC.[6] There was no significant progress until the 17th Century, when Oughtred developed the slide rule based on logarithmic tables developed by Napier and Gunter, and late in that century Leibniz developed his wheel that could perform mathematical calculations. Leibniz also advocated the use of the binary counting system in mechanical calculating devices.

The 19th Century saw the use of punched cards to provide instructions to various devices, including the Jacquard Loom, Charles Babbage's Analytical Machine and Herman Hollreith's (who went on to found IBM) tabulating device that was used by the United States Government to tally the results of the 1890 census.

To make the required quantum leap to allow these fledgling devices to become more than just the ideas of keen inventors, scientists and mathematicians, a new way of switching current was required. The mechanical switching devices used up to the early 1900s had clear physical limitations on potential speed. The breakthrough was made in the late 1930s with the development of vacuum tubes that led to significant increases in speed. John Anatasoff's ABC Computer and the ENIAC all purpose computer finished in 1945 were the initial first generation computers. As an example of increased performance, ENIAC could calculate the trajectory of a missile in 30 seconds, a task

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1 Duncan D. The future role of information technology in military health. *Aust Miil Med* 2001;10(2): 74-81.

2 Lieutenant Colonel Darrell Duncan, RAAMC was the SMO of 1 Brigade and is now deployed to East Timor. This is a submission by LTCOL Duncan in the AMMA 2001 Essay Competition.

which took a skilled person with a desk calculator over 20 hours.

This period also saw the first significant use of computing power to aid the military. The German mechanical coding machine ENIGMA was able to create codes that were difficult to break using the normal means available at the time. The British developed COLOSSUS, a device that contained 1,800 vacuum tubes, used binary arithmetic and was capable of reading input at the rate of 5,000 characters (5K) per second.

Transistors provided the next significant improvement in computing power and by 1957 the second generation of computers based on transistors and running assembler languages were gaining acceptance in large organisations. They were used to solve problems that involved large volumes of data. In the field of health care, there was some progress to office automation but no clinical use of the emerging technology. There was some recognition of the potential for computer assisted decision making in medicine; however, the cost and size of computers at this time prevented wide spread use.[7]

The development of integrated circuits in the 1960's followed by integrated microchips allowed hardware to advance at a rapid rate. This was in accordance with 'Moore's Law' which states 'every 18 months, processing power doubles while cost remains constant.'[8]

Advances in operating systems and software matched the development of hardware and, with miniaturisation made possible by chip technology, the third and fourth generation computers appeared. The use of computers in everyday business and home life mirrored both the cost and the increasing user friendliness of the machines, in particular office automation systems. The increasing use of personal computers in their own right did not result in significant social change. Key developments to launch the information age were made through research and development primarily funded through the United States military in the hardware and software needed to allow computers to communicate with each other over distance. This led to the development of networking protocols and standards that have allowed the vast network known as the Internet to develop.

Information Technology in the Military

The need to use information technology in warfare is well recognized. As Buckley, Francke and Milton[9] noted in 1998, 'the US Army has long recognized that technology enables new warfighting concepts and offers opportunities to develop new capabilities.' The possibilities for the use of more timely, accurate and detailed information is leading to the so called revolution in military affairs and has coined the phrase 'net centric warfare'[10]. The United States Army has a program to study warfare in 2010 and beyond that aims to foresee what this explosion of information possibilities will do for the military.[11]

The need to project the future concerning military-technological capabilities is indeed not new. Echevarria[12] discusses the similarities that can be demonstrated between military technology salesmen from the start of the 20th Century to those at the end of that century. He points out that a key aspect is the need to sift through the diverse range of primary, supporting and enabling technologies to determine what to test and evaluate in detail (and by implication invest in).

Information Technology in Health Care

The management of clinical information in health care is still primarily in the form of atoms rather than bits. The recorded data of health care is contained in the medical record. This is still largely paper based and includes the clinician's recording of symptoms and signs, physiological parameters and the results of investigations as well as the interpretation of the data by the clinician in the form of a provisional and differential diagnoses. Other items such as the treatment plan and specific orders and instructions are included in one form or another.

For purely clinical purposes, this paper-based system has proven relatively effective over time. Clinicians are trained to work with little or no recorded information, relying on their basic clinical skills. While the patient's medical records are 'nice to have', the reality is that, even in the best run hospitals, records are often not available when you would like them.[13]

Current health information systems in use tend to support administration and organisational goals rather than support patient care activities. Van Bemmel et al. see computerized patient records as the key to making the transition to health information systems that support patient care.[14] A number of arguments against a computerized medical record revolve around unauthorized use of the information and security issues. Halamka describes a number of measures to ensure security of computerized medical records by a sequence of measures ranging from access protocols, data encryption, physical protections, audit processes and software measures at the servers level to ensure protection.[15] They had not detected any unauthorized access in the first six months of use.

Van Bemmel et al. argue the goals for the use of computerized patient records include

support to direct patient care (information access and decision support), assessment of quality and outcome, planning and research and education.[14]

Current Information Technology in Military Health Care

Both the United States Department of Defense and the Australian Defence Force have set up programs to introduce automated health information systems across their enterprises. In the case of the USA, there are 20 different information technology programs listed from the web site of the Office of the Secretary of Defense, Health Affairs[16]. Included in these are Composite Health Care System II (CHCSII), the program that will lead to a computerized patient record for the dependency of the military health service (noting that this includes dependents of service people and veterans), and the Theater Medical Information Program (TMIP), which will deliver a health information system for the operational environment.[16]

In Australia, the HealthKEYS project will deliver a: 'single, efficient and effective Health Management Solution that best meets the health information needs of health services units, providers, individuals, senior executives, commanders and line managers within the ADF'[17].

The Future

What does information technology have to offer future military health care? It is easy to be skeptical about this issue when information technology has been aggressively marketed but still the average military health professional has very few health specific information tools. In 1998, the United States Army Medical Department conducted a seminar to discuss the possible use of telemedicine on the battlefield. They invited personnel who were serving across the echelons of care. There was some interest in the 'sexy' technology such as teleradiology systems and the like but the overwhelming need from the front line was for reliable voice communications (unpublished data). As the 1st Brigade becomes used to operating in a digital environment with the Battle Command Support System the same results would perhaps be obtained. Having said that, I believe it is somewhat short sighted, naive and, I would even suggest, foolish to view information technology as a distraction that will go away and to ignore it's potential advantages. We do so at our own risk, perhaps summed up by Gunther Grass when he said: 'Information networks straddle the world. Nothing remains concealed. But the sheer volume of information dissolves the information. We are unable to take it all in.'[18]

In other words, if we do not look to define exactly what information is required when and where, we will have so much information available that we will not be able to find the key pieces.

The Future of the ADF Health Services

The JP 2060 Study outlines the future capabilities and directions that are thought to be required for operational health support to ADF operations in the future.[19] It argues the view that to achieve the ADF Health Services vision (to achieve a world class Military Health Service for the ADF) and mission (to optimize the health of ADF personnel), there are five key outcomes, three of which are described as enabling and two as supporting. The enabling outcomes are a fit and healthy force, prevention of casualties and treatment of casualties. The supporting outcomes are to develop health capabilities and manage and sustain the health service. What are the information requirements for these outcomes and how is this information best obtained?

Fit and Healthy Force. This outcome commences with recruiting and involves ensuring individuals are as well prepared as possible to participate in military operations. The availability of a comprehensive medical history via a computerized medical record system would have clear benefits to recruiting doctors in performing recruiting medicals. Information technology hardware is no longer an impediment to such a system and it is not unreasonable to suggest that such systems will become common place within a generation (technophiles would say this is an overly conservative time-frame).

Once a member is recruited, there is still potential for information technology to assist this outcome. The current approach in the ADF is for generic approaches to physical fitness training, standards and assessment. Negroponte discusses the prospects for using individualized information in a commercial sense.[5] Physical fitness programs should likewise be tailored to an individual, based on factors such as current and past health, injuries, occupation, physical fitness level, physique and other factors. It is not difficult to accept that an automated information system, drawing data from disparate sources such as medical and personnel records and applying a predetermined algorithm to decide action required would be an effective and efficient method of producing large numbers of individualized fitness and health programs in a short period of time. Monitoring progress of a large number of individuals through their

personalized program would also be more easily done with automated systems.

Casualty prevention. This outcome is concerned with identification, assessment and control of health threats that confront ADF personnel in both operational and non-operational environments. The outcome is heavily reliant on accurate and timely information. The actual threat from the environment, as well as data on potential water and food sources should be able to be obtained from geographical information systems, communicable diseases information from the Centre for Disease Control and or local health authorities via web access and the conventional and non-conventional weapon threat from classified sources. The assumption underlying this is that the data has been collected and entered by someone, somewhere and it is available when required. To achieve this assumption someone needs to be sorting through the data available from all sources, cataloguing and indexing it much like current search engines do in order for users to retrieve what they need, when they need it.

Prevention also revolves around health surveillance and casualty prevention programs. The bulk of the data for these functions are collected during clinical encounters. It is labour and time intensive to transfer data by hand from clinical notes to other systems and this is why the ADF Health Status Report highlights the need for a health indicator data collection system as a strategic priority (accessed from www.defence.gov.au/index.html). An automated system driven by entries in a computerized health record would increase the quantity of data available. If it were able to be organised and analysed relatively easily, the resulting information would be of greater value in identifying the factors related to preventable casualties. For example, the current approach for health surveillance is to obtain data on a weekly basis. To truly identify emerging threats within a time frame that can be acted on, especially with potential non-conventional weapons or communicable diseases, requires more frequent review of clinical presentations, focusing more on symptoms being reported than the clinician's diagnosis. This can be achieved feeding the symptoms reported in clinical encounters into a database that is continuously analysed by an automated agent looking for trends in frequency of reporting of 'symptoms of interest'.

More futuristic in concept but perhaps closer than we realise in fact is the use of physiological monitoring systems to track the physical and mental well being of each individual. Aggregated data about the physical readiness (from the perspectives of fatigue, hydration, nutrition) can be provided to Commanders in order to select the task unit most appropriate for a given task. Such a monitoring system can also be used to provide remote triage capability when the individual becomes a casualty. The United States Army is working on this capability as the Warfighter Physiological Status Monitor program.[20]

Develop Health Capabilities. This outcome is related to personnel, facilities and organisations. It includes research into health related areas as well as education and training at both the individual and collective level. Information technology and its use in education could be the subject of a paper in its own right; however, the linking of continuing education and clinical audit type programs to computerised health records in order to individualise training for the clinician based on types of cases seen and perhaps, more importantly, what they are not seeing offers more effective ongoing education than current programs. Clinical research should be fed from the clinical records from the perspective of areas to examine and also data collection to test hypotheses.

Manage and Sustain the Health System. Class 8 supplies are consumed as patients are treated. It follows that as the treatment is documented, the class 8 requirements can be calculated with reasonable accuracy. This provides for automated replenishment of stores in a timely manner (assuming that the items are physically available). Financial management is clearly amenable to automated systems; however, the potential to make better use of financial information to identify the true cost of preventable illnesses and injuries can be realised by linking the financial processes to the clinical process more effectively.

Casualty Treatment. I have saved this for last as I view it as the central outcome in terms of establishing a comprehensive, integrated and automated health information system. My view is this is where much of the data entry required by most aspects of the other outcomes enters the system and all other outcomes need a feed of data or information from the clinical encounter.

In many instances there is no reason why the member should not enter some of the relevant data. For instance, in an automated injury data collection effort, the member can enter the relevant background data while waiting to be seen or while they are having their initial ice treatment. Most of the data required here is relatively straight forward (who was in control of the activity, what happened, weather, time etc) and often not recorded by the clinician because it has not direct bearing on the management of the casualty in most cases. Parameters such as blood pressure, body height or weight, when collected can be automatically assessed in

light of previous readings and significant trends identified.

As a clinician, I am also not surprised that this is also perhaps the hardest 'nut to crack'. As mentioned, my clinical training is such that I can assess and treat patients with no records available to me. Therefore, it is hard to convince me that there will be great gains in my ability to provide health care to the majority of my patients simply by providing me a computerized version of their complete health record. To expect me to record my clinical notes electronically is also going to be met with resistance. First, there is the issue of depersonalizing the consultation by having to enter data into a computer. Second, there is time. To enter clinical notes electronically requires more time than the hand written note, simply because very few clinicians are fast keyboard operators. Hand written consult notes can be abbreviated and formatted as the writer sees fit. Tied to this is the fact that many clinical encounter applications are optimized for data retrieval not data entry in order to allow faster and more comprehensive search and data management functions. This means they have preset formats and allow a narrow set of terms to be used. Clinicians used to writing in 'free text' in their own style and using abbreviations will resist the relatively rigid stricture of computerised health records.

A key challenge is to make the interaction between the provider and the system acceptable in terms of time, convenience and effect on the consultation process. Data entry technology perhaps holds the key, with advances in writing tablets and voice recognition software promising to overcome some of the barriers to use of computers in real time during clinical encounters.

Doctrine and Policy Development

All the outcomes require underpinning policy and doctrine to be developed and published. Much of this is on line already through the DEFWEB. The Military Health Manual is a good start at cataloguing these documents in the terms of the outcomes they relate to (defweb.cbr.defence.gov.au/dpemhm/). I would suggest that this effort can be improved by the addition of a section where draft policy is published as it is being prepared and staffed to allow for interactive comment from a wider range of people than is currently possible. I believe the earlier the people who are expected to work with policy and doctrine are able to see the policy and comment, the easier to introduce and implement the changes associated with the product. The current system that relies on electronic mail is clearly faster than using conventional mail; however, even faster and more responsiveness can be achieved by a web based system. The other advantage is that discussion can be more wide ranging and thorough by allowing all to see comments by others. This process does take some time for users to get used to and participation is not guaranteed; however, it does provide a better chance for the 'coal face' to develop a sense of ownership in policy if they see it and have a chance to influence during development.

Information Technology in Future Military Health Care Scenarios

The following vignettes convey the author's impressions of how it could (should) be if the Defence Health Services harnesses the potential of information technology and applies it the provision of a high quality military health care service.

In 5 Years

Scenario 1. Miss Josephine Recruit applies to join the General Reserve as a medic. The recruiting medical officer reviews her history electronically with her permission through her GP's practice. He downloads her vaccination history since birth, notes that she had juvenile asthma but has needed no medication for the last 8 years but is otherwise well.

She has an uneventful induction training period and is accepted into the RAAMC as a medic. She is issued her medical assistant training package on a CD ROM and allocated a user identification and a password to access the on line test material. She returns to her unit and over the next three months works her way through the material. As she completes modules, she completes the on line tests under supervision. She will continue to work through the course modules up to advanced medical assistant status.

Scenario 2. George Smith arrives at Kapooka to commence induction training. His medical record from recruiting is accessed on arrival. His immunization history was available and has been entered on his ADF electronic health record. He receives the vaccinations required to be up to date and his BMI is noted to be at the upper limit of normal. His physical training history is checked and it is noted that he struggles with running. Over the next few weeks he presents with shin splints from running. Pack marching causes minimal symptoms. He is commenced on a swimming and cycling program by the PTI's to improve his fitness level. Over the next three weeks his legs settle and he returns under PTI supervision to pack marching successfully. After a further 3 weeks of the swimming/cycling and pack marching he

returns to the running track. After a period of leave he reports to his new unit - an infantry battalion. The Unit orderly room registers him as having marched in on the system and his medical record is reviewed by the health information system. This notes that he has vaccinations overdue and an alert is sent to the RAP to review his record. In doing this, his history is reviewed and the period of shin splints is drawn to the MO's attention. George is called in for review and warned of the risk if he attempts to keep pace with unit PT. He is referred to the PTIs for a program to build up his exercise capacity and monitor his shins. He completes the program and resumes full PT with the Unit the next month.

10 Years

Scenario 3. LCDR Afloat is serving as the medical officer on board the HMAS NEWSHIP in the South-West Pacific. The ship is due to arrive in port in two days time. LCDR Afloat enters a request on his ship board system for the latest health intelligence on the port. It is stored on his terminal until the ship's communication system can send the request. The information is received later that evening and is waiting for the doctor that morning. It reveals significant new cases of arboviral illnesses in the port area. After further research through the electronic health library on the ship's network, LCDR Afloat assesses the crew is at significant risk during their port visit from the arbovirus. The ship's crew is warned to take precautions against mosquito bites in their stop over. Seven days after leaving port he enters a query into his system to check that there has been no increase in symptoms consistent with arboviral infections. The system tells him there hasn't been.

Scenario 4. Australia is involved in peace support operations in an area of the world that has recently undergone a bloody civil war. There were numerous unconfirmed reports of use of non-conventional weapons during the conflict, with both parties known to have access to chemical and biological munitions and delivery systems. Monitoring has not revealed any grossly contaminated areas. The health surveillance system is checking for symptoms such as tiredness, malaise and lethargy occurring in geographical clusters. An area is identified where there is an association between serving in that area and presentation within 24 hours feeling tired, washed out and a range of non specific symptoms. Further investigation reveals this area had been contaminated by persistent chemical agents within the previous 12 months. Patients with symptoms were counseled and a long-term monitoring system was put in place.

Scenario 5. Simultaneously with Scenario 4, Australia has small contingents serving in operations elsewhere. Their food and water sources are all centrally procured and distributed from Australia. The health surveillance system alerts HQ AST that there is a rise in gastrointestinal illness in each theatre. Investigations reveal a contaminated batch of water as the source of the problem and within 12 hours of the first cases the batch is withdrawn.

20 Years

Scenario 6. Members who served in Scenario 4 are claiming that all people who served have similar symptoms and they must have all been exposed. In reviewing their service history and medical records, it is clear that the members identified as being exposed in Scenario 4 have one constellation of symptoms, those from other areas have a different set and those who served in both areas have a mix. The people affected are clearly identifiable from their electronic record and their situation, including management options are sent electronically to their primary care provider as well as to the individual where possible.

Scenario 7. An infantry section is patrolling an urban area on a peace enforcement mission. They are each equipped with body worn computers, physiological monitors, GPS and radios. The medic with the patrol (now SGT Recruit from Scenario 1) has visibility of where each of her section is as well as the ability to check their vital signs at any time. The aggregated picture of the section's physical and mental status is being fed to the section commander and up the chain of command. As they cross a street, they take fire from two directions. The section all receives an alert from the system that two members have been hit by bullets. The medic can see where they are located and her system indicates that both are still alive, one with a chest wound, the other with a leg wound. SGT Recruit contacts them by radio and confirms they are still able to talk and gets a description of their wounds. The chest wound patient was wearing ballistic protection however the bullet was deflected at an edge and entered the side of his chest. It seems to be a graze, and certainly his vital signs indicate a minimal injury. The patient with the leg wound reports significant arterial bleeding and this is reinforced by his BP that is reported to be 100/60 according to his status monitor. The medic conveys the situation to the section commander and gets the all clear to proceed. SGT Medic directs first aiders to dress the chest wound while she attends the member with the leg wounds.

The casevac requests are compiled by the Section 2IC's system after interrogating the

section commander and the medic's systems, and the Commander and the medic review the message. The message is sent as soon as the two of them have reviewed and approved it. At the same time the medic's system is preparing to send a stores consumed report based on the medications used by her and the dressings and fluids etc administered. The patients current status, including description of injuries, treatment and location are checked by the AME team as they travel to the scene. Once in the air and heading to the level 3 facility, the relevant details are sent via the AECC to the triage officer at the Joint Force Health Support Unit who will receive the two patients. The surgical teams are warned out and as the operating rooms are clear they are prepared to do the initial wound surgery on arrival.

Conclusion

The information revolution is characterized by rapid development in information and communications technology. Even though the all important bandwidth availability may become less of a factor by technology, there will still be finite limits of how much information can be moved at once, and as technology increases the limit, the amount of information we want to move will increase.

Watson and Crick perhaps started the next age in 1953 when they unraveled the structure of DNA. This has led to work on the identification of the human genome and perhaps the start of what might be called the 'genome age'. Further progress in this area will unlock perhaps the most basic data element of all - the genetic coding for individuals. The possibilities that arise from this may perhaps be the subject of an AMMA Annual essay in the years to come.

On information: Information can tell us everything. It has all the answers. But they are answers to questions we have not asked, and which doubtless don't even arise.

On computers: Computer science only indicates the retrospective omnipotence of our technologies. In other words, an infinite capacity to process data (but only data - i.e. the already given) and in no sense a new vision. With that science, we are entering an era of exhaustivity, which is also an era of exhaustion.[21]

References

1. Nietzsche F. The Wanderer and His Shadow, aph. 278. 1880.
2. Reagan R. Guardian 1989 Jun14.
3. Salim H. Networking in Africa: A brief analytical overview.1997 (Accessed at http://www.sas.upenn.edu/African_Studies/Comp_Articles/hadi.html)
4. Toffler A, Toffler H. Athena's Camp: Preparing for conflict in the Information Age. 1997 (Accessed at http://www.rand.org/publications/MR/MR880/MR880.fm.html)
5. Negroponte N. Being digital. 1995 (Accessed at http://archives.obs-us.com/obs/english/books/nn/bdcont.htm)
6. History of the information revolutions and communications technology timeline. (Accessed at http://myron.sjsu.edu/caesars/COMM.HTM).
7. Hovenga E, Kidd M, Cesnik B (Eds). Health informatics: An overview. London: Churchill Livingstone; 1996.
8. Downes L, Mui C. Unleashing the killer app. Boston: Harvard Business School Press; 1998.
9. Buckley ET, Franke III HG, Milton AF. Army After Next technology: Forging possibilities into reality. Military Review - US Army Command and Staff College March/ April 1998. (Accessed at http://www-cgsc.army.mil/milrev/English/MarApr98/buckley.htm)
10. Cebrowski AK, Garstka JJ. Network-Centric Warfare: Its origin and future. US Naval Institute Proceedings 1998; 124(1). (Accessed at http://www.usni.org/Proceedings/Articles98/PROcebrowski.htm)
11. The Army After Next Program. (Accessed at http://www-ari.army.mil/aan.htm)
12. Echivarria A. Tomorrow's Army: The challenge of nonlinear change. Parameters (US Army War College Quarterly) 1998; Autumn.
13. Manktelow N. Privacy under the knife. e Commerce News 2000 Dec 5. (Accessed at http://it.mycareer.com.au/e-commerce/20001205/A58266-2000Dec5.html)
14. Van Bemmel JH, van Ginneken A, Stam B, van Mulligen E. Virtual electronic patient records for shared care. MEDINFO 98. Amsterdam: IOS Press; 1998.
15. Halamka JD. Web technology for emergency medicine and secure transmission of electronic patient records. MD Computing 1998;15(4).
16. Office of the Secretary of Defense - Health Affairs (Accessed at http://www.tricare.osd.mil/infomgt/infotech.html).
17. Defence Health Service. DHS Newsletter 1999 Dec.
18. Grass G. Interview in New Statesman & Society (London, 22 June 1990). (Accessed from Microsoft Bookshelf 1998)
19. United States Army. Warfighter Physiological Status Monitor program. (Accessed at http://dcdd.amedd.army.mil/infopapers/WPSM%20info%20paper1aug00.htm).
20. Spahni S, Scherrer J, Sauquet D, Sottile P. Middleware for Healthcare Information Systems. MEDINFO 98. Amsterdam; IOS Press; 1998.
21. Baudrillard J. Cool Memories. (Accessed from Microsoft Bookshelf 1998)

History

Dual Roles: Poisonous Sea Creatures and Their Role in Neuromuscular Research - Implications for Military Medicine[1]

Major General John Pearn AM RFD (Rtd)[2]

The discipline of military medicine necessitates an understanding of the neuroanatomy and neurophysiology of the motor unit. Nerve gases and their antidotes effect the third link, the neuromuscular junction, of the four-link chain which comprises the motor unit. Similarly, agents such as botulinum toxin with their bioterrorist potential also act at this site. Certain paralytic diseases for which military personnel receive vaccination (principally poliomyelitis) involve the first link in this chain[1]. Envenomation by a range of poisonous creatures causes weakness or paralysis by damaging the second, third or fourth links of this basic structure.

The "motor unit" was the term coined by the Noble Laureate, Sir Charles Sherrington, in 1930, to define the functioning unit of motor neurones based in the spinal cord, medulla or mid-brain; their emergent axon; the neuromuscular junctions and the array of muscle fibres which contract following depolarisation[2].

It is a delicious paradox that poisonous sea creatures _ which inadvertently can also cause human death and disability _ have been the agents by which neurophysiology and the discipline of toxinology has been advanced. In particular, the role of both venomous molluscs and toxic fish has been central to an understanding of the fundamental actions of the motor unit. Called by Sherrington "The Final Common Path", an understanding of the function of the motor unit is central to the management of victims envenomed by a variety of land and sea creatures; and the prior protection or post-exposure clinical management of military personnel exposed to nerve gases.

Intoxications, envenomations or viral infections at any point along this four-link chain result in the subjective symptom of weakness; and the objective signs of hypotonia, flaccidity and paralysis. All who care for those presenting with acute weakness or paralysis needs raise a differential diagnosis which involves diseases along this four-link chain. The history of the advancement of knowledge - concerning the structure and function of the motor unit - has depended on the use of both molluscs and fish and their venoms, as experimental tools.

Differential Diagnosis - Acute Weakness And Paralysis

Any patient who presents with acute paralysis, weakness, hypotonia or flaccidity necessitates the raising of a differential diagnosis which includes the diseases that target one or more of the four links which comprise the motor unit chain[3]. Such diseases range from Sarin intoxication to snakebite; and from poliomyelitis to polymyositis[4].

In 1669, the Dutch medical student, Jan Swammerdam, conducted the first experiments on nerve-muscle preparations, thus ushering in the modern era of experimentation[5] which has provided an understanding of the motor unit. This in turn makes possible the interpretation of the symptoms and signs of envenomed and intoxicated patients today.

A significant milestone in the modern era of neuromuscular research was von Haller's discovery, in Gottingen in 1757, that vertebrate muscles possess intrinsic irritability and contractility which are independent of any supplying nerve. Haller, a great polymath, was also a poet. One of his oft-quoted stanzas reads:

"Of Nature's inmost heart no human mind can tell
Happy, indeed, is he who knows its outer shell"[6].

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1 Pearn JH. Dual roles: Poisonous sea creatures and their role in neuromuscular research - Implications for military medicine. *Aust Miil Med* 2001;10(2): 82-85.

2 Major General John Pearn AM RFD MD FRACP FACTM is the former SGADF. He is contactable C/- Office of the Professor of Paediatrics & Child Health, Department of Paediatrics & Child Health, Royal Children's Hospital, Brisbane Qld 4029

Claude Bernard (1813-1878) provided the final experimental proof that the contractility of muscles was due to electrical effects in the muscle fibres themselves. In 1856 he used curare to paralyse nerves in vertebrate nerve-muscle preparations - and then demonstrated that the muscles could be stimulated to contract normally by direct electrical stimulation. These experiments formed the basis of our present-day understanding of post-envenomation rhabdomyolysis, muscular dystrophy and viral polymyositis.

Claude Bernard's life illustrated the importance of both broad perspective and focussed application in the prosecution of biological research. He wrote:

"Put off your imagination, as you take off your overcoat, when you enter the laboratory; but put it on again, as you do your overcoat, when you leave the laboratory. Before the experiment and between whiles, let your imagination wrap you round....."[7].

It is this broad imagination, this wider love of nature, which is so important in research into envenomation and intoxication by poisonous creatures; and in an understanding of the pathophysiologic effects which result from exposure to agents such as anticholinesterase inhibitors and competitive antagonists which act at the motor end place of voluntary muscles.

There exists a paradox that some of the world's most venomous creatures have provided the research tools by which the action of their venoms can not only be understood, but by which the evolving knowledge of the motor unit has developed.

Molluscs

Members of the Phylum Mollusca have been used extensively in the delineation of the structure and function of the motor unit. The giant squid, Loligo forbesii, has a single giant axon (Figure 1). It was used, from 1939, by the Nobel Laureates (1963), Sir Alan Hodgkin, A.F. Huxley and the Australian, Sir John Eccles, to define the depolarisation chain in the axon; and the discovery of sodium and potassium channels in the membrane of excitable tissues[8]. In 1949, Sir Bernard Katz joined the team and introduced the voltage clamp technique. This research tool facilitated the discovery of other ionic channels in both nerve and muscle[9].

Figure 1: The Giant Squid, Loligo forbesii, whose single giant axon was the research tool used by Sir Alan Hodgkin, A.F. Huxley and Sir John Eccles in their discovery of ion channels and their role in the transmission of the depolarisation impulse along nerves. A 1994 Isle of Man postage stamp.

Another cephalopod, the Blue-ringed Octopus (Hapalochlaena sp.) was found to contain tetrodotoxin (TTX) (Figure 2), a low molecular weight substance which was found to block the sodium channel in neural tissues.

Figure 2: The Australian Blue-Ringed Octopus, Hapalochlaena maculosa, common in all eastern and northern Australian in-shore waters. Its saliva is a potent source of tetrodotoxin (TTX). An Australian 1984 postage stamp.

Tetrodotoxin was originally extracted from puffer fish (Figure 3). It occurs also in a Costa Rican frog and in poisonous newts (Family Salamandridae). Venoms from another family of molluscs, the cone shells (Conidae) have been used to define and study calcium channels in excitable tissues.

Figure 3: The Tiger Puffer Fish, Takifugu rubripes, an initial source of tetrodotoxin (TTX), used to block the sodium channel in excitable tissues. Tetrodotoxin is used as a basic research tool in the investigation of new venoms and toxins. From a 1966 Japanese postage stamp.

Omega-conotoxins are small polypeptides from Conus species, of which Conus geographus is the best known (Figure 4). Work currently being undertaken under the leadership of Professor Richard Lewis at the Centre for Drug Design at the University of Queensland has demonstrated that certain conotoxins act selectively on calcium channels in dorsal root ganglia; and thus possess the potential for novel pharmacological approaches to control severe and intractable pain.

The effects on acute short-term memory loss, consequent upon eating marine mussels contaminated with domoic acid, have been described following outbreaks of shellfish poisoning in Nova Scotia in 1987[10]. The resultant intoxication syndrome, Amnesic Shellfish Poisoning, is distressing for the victims and perplexing for first aiders and doctors who manage these clinical effects. This toxin, derived from dinoflagellates of the genera Nitzchia and Pseudonitzchia, is concentrated in the tissues of filter-feeding bivalves (Class Pelecypoda) such as oysters, clams and mussels.

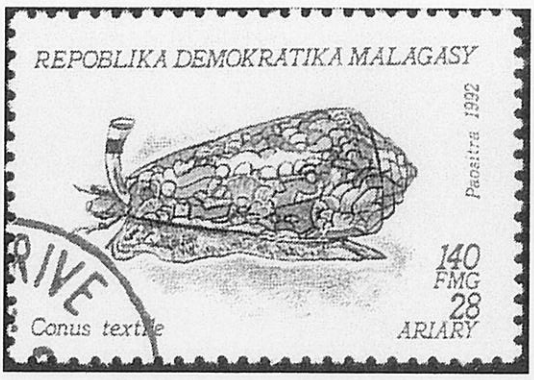


Figure 4: A 1992 stamp from the Malagasy Democratic Republic, showing a shell of the Family Conidae. The venom of cone shells contains, inter alia, omega-conotoxins which have a selective calcium channel blocking effect on the neurones in the posterior root ganglia. Conus geographus has also caused human deaths by causing acute paralysis.

Fish

Certain coral reef and pelagic fish may concentrate a planktonic toxin, ciguatoxin, which is a cause of the dramatic human intoxication, ciguatera[11]. Both the Pacific and Caribbean ciguatoxins cause their sensory, motor and autonomic effects[12] by locking the sodium channel in the "open" position.

Historically, it was believed that the eating of terrestrial or marine snails of the family Turbinidae caused the enigmatic syndrome of ciguatera. The Spanish explorer in Cuba, Don Antonio Parra, in 1787 first described this intoxication. He used the local Creole word "cigua" to describe the marine or terrestrial gastropods which were believed to be its cause[13]. In 1774, when Captain James Cook sailed on H.M.S. Resolution to the south-west Pacific (near the island of New Caledonia), his crew became intoxicated with ciguatera following the eating of "Sea Bream". His surgeon, the 28 year old William Anderson RN, subsequently described the dramatic symptoms which afflicted both the crew and the ship's dogs in that episode.

Because both tetrodotoxin and ciguatoxin lock the sodium channel (in the "closed" and "open" positions respectively), they can be exploited in experimental studies of any new or unknown poison, toxin or venom - to test whether such new poisons act on the sodium channel.

Early research on the third link in Sherrington's motor unit, the neuromuscular junction, was undertaken following studies of the acetylcholine receptor of certain fish. The electric organ of the electric eel, Electrophorus eleotricus and the electric ray (Torpedo sp.) contain the highest known concentrations of acetylcholine receptors[9]. This work was extended when it was found that alpha-bungarotoxin, from the Banded Krait, Bungarus multioinctus, would bind selectively and irreversibly to the acetylcholine receptors of voluntary muscles. Radioactive bungarotoxin is thus used to facilitate the identification of and counting of acetylcholine receptors both for clinical studies of suspected myasthenia gravis and for neuromuscular research more generally.

Many molluscs, jellyfish, crabs, corals, ticks, scorpions, spiders and snakes possess poisons or venoms, the majority of whose actions remain unknown to science. Their further study holds great promise for development and better diagnostic tests; and certain novel therapies for human disease and envenomation.

Acknowledgments
I thank Dr Ken Winkel, Director of the Australian Venom Research Unit at the University of Melbourne; Lt Colonel Peter Leggat RAAMC, Deputy Director of the School of Public Health and Tropical Medicine at James Cook University, Townsville; and Captain James Roche RFD, RAAMC, of Sydney, for much encouragement.

References

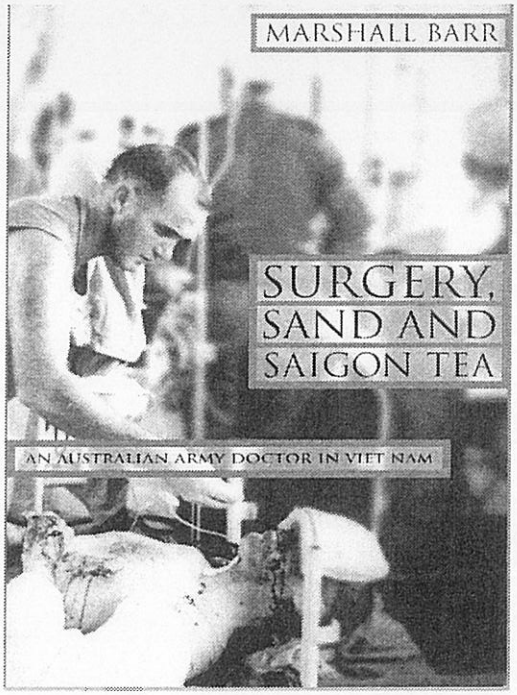
1. Pearn JH. Poliomyelitis: The role of the military in the final campaign. Mil Med 2000; 165:726-729.
2. Sherrington CS, Eccles JC. Numbers and contraction-values of individual motor-units examined in some muscles of the limb. Proc Roy Soc 1930; 160B: 326-357.[1]
3. Pearn JH. Differential diagnosis: The challenge of chronic fatigue. J Chron Fatigue 2000;7(4):17-31.
4. Pearn J. The discovery of neuronpathy as a cause of progressive paralysis in childhood. The historical origins of modern differential diagnosis in neuromuscular disease. J Neurol Sci 1984; 64: 99-107.
5. Swammerdam Jan. The Book of Nature [Bybel du Natuur] London, Printed for C.G. Seyffert, 1758: 122-124.
6. Garrison FH. Albrecht von Haller (1708-1777) In: An Introduction to the History of Medicine. Fourth edition Philadelphia, W.B. Saunders Coy., 1929: 317-8.
7. Garrison FH. Claude Bernard (1813-1878). In: An Introduction to the History of Medicine. Fourth edition Philadelphia, W.B. Saunders Coy., 1929: 545.
8. Hodgkin AL. Ionic movements and electrical activity in giant nerve fibres. Proc Roy Soc Lond (Biol) 1958; 148: 1-37.
9. Bowman WC. Pharmacology of neuromuscular function (2nd ed.). London: Wright; 1990: 22,26,30,33,75,101,140-141.
10. Perl TM, Bedard L, Kosatsky T, Hockin JC, Todd EC, Remis RS. An outbreak of toxic encephalopathy caused by eating mussels contaminated with domoic acid. N Eng J Med 1990; 322: 1775-80.
11. Pearn JH, Lewis RJ, Ruff T, Tait M, Quinn J, Murtha W, King G, Mallett A and Gillespie N. Ciguatera and mannitol: Experience with a new treatment regimen. Med J Aust 1989; 151: 77-80.
12. Pearn J. Neurology of Ciguatera. J Neurol Neurosurg Psychiatry 2001; 70(1): 4-8.
13. McKenzie A. The Role of Obnoxious species in the elucidation of nerve and neuromuscular transmission. Meditheme 2000; 19: 76-7.

[1] This paper formed the keystone of the award of the Nobel Prize for Physiology and Medicine to Sherrington in 1932.

Book Reviews

SURGERY, SAND AND SAIGON TEA
An Australian Army Doctor in Viet Nam[1]

Marshall Barr[2]



(Reproduced with permission from Allen and Unwin)

SURGERY, SAND AND SAIGON TEA is one of Allen and Unwin's latest releases. This book is a candid and frank look at Australian service in Vietnam from a Citizen Military Force (Reserve) anaesthetist's point of view. Although Marshall Barr prefaces his Vietnam memories with short accounts of his life prior to Vietnam and the preparations in Australia, the book is principally focused on his Vietnam service in Vung Tau and is based on diaries he kept during the period. Marshall Barr has constructed a very honest and enthralling book. Whether the thirty or so years has give him time to reflect or whether he needed personally to 'tell it like it was', Barr has produced a 'warts and all' look at the Vietnam war from the 8 Field Ambulance in Vung Tau. Unlike many Australian troops in Vietnam, he was fortunate in having had the opportunity to visit other units scattered across southern Vietnam. He spent time with the Australian Task Force at Nui Dat, with Australian Civilian Teams at Long Xuyen and Bien Hoa, and with American units in Saigon and Tay Ninh. He even managed to get down to RAAF Butterworth in Malaysia and then had to pay for a commercial flight to get back to the war.

This is not a book of bravado, as we have sometimes seen portrayed in some of the literature and films of period, but a sincere and truthful recollection of a long and often stressful posting. Barr is often critical of others but freely and, sometimes, humorously portrays his own shortcomings. He poignantly portrays the importance of friendship and companionship in the field while frankly noting his and others over-dependence on alcohol and tobacco to get them through the day. He also reflects on the psychological damage caused to unprepared troops by the traumas of war.

From a military medical viewpoint, Barr's book encapsulates a number of important lessons which we should not have to constantly relearn. Whether it is the importance of standard operating procedures, the need for highly trained resuscitation teams, the need for professional anaesthetic support or fitness for flying in those being evacuated, Marshall Barr has illustrated how these can be combined to produce an effective military health care team - a team which was put to the test by the Tet offensive in February 1968. Barr does not glorify the work they did but manages to convey the appreciation he had for all the hard-working doctors, medics and nursing officers who carried out their roles in often highly difficult and stressful circumstances. He has also clearly illustrated the close relationships and, in some cases, interdependence of the various United States and Australian forces' medical

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1 Review by Andy Robertson

2 Barr M. Surgery, sand and Saigon Tea. Crows Nest: Allen and Unwin; 2001. ISBN 1-86508-463-8. RRP $29.95

3 Available from the AMMA Library

assets and the well-developed liaison between Australian military and civil aid personnel.

Marshall Barr continues to practice as a Consultant Anaesthetist at the Royal Berkshire Hospital in England. His keen interest in history - he is the Honorary Editor of the History of Anaesthesia Society - has assisted him in writing an absorbing autobiographical view of the Australian medical officer in war. As COL Don Beard (rtd) notes in the Preface, Marshall Barr often underrates himself and beneath the light hearted exterior was a dedication to the wounded Australian soldier and a desire to constantly improve the medical services provided to the troops in the field.

This book is excellent reading and is highly recommended as an addition to the library of anyone who has a keen interest in either military medicine or military history.[3]

Roden Cutler, V.C. - The Biography[1]

Colleen McCullough[2]

In this her first attempt at non fiction, Colleen McCullough has excelled. Not only does she tell the life story of a great Australian, she also explores the question - what makes the man? Is it family values, education, soldiering, life tragedies, politics, diplomacy or sheer heroism? For this man, she leaves us a little up in the air with the question only half answered.

The book is divided into nine sections including maps and black and white photographs. The middle seven sections deal with a chronological account of Roden Cutler's life from humble beginnings in suburban Manly to Governor of New South Wales and whose achievements and popularity challenge the endeavours of Arthur Philip and Lachlan Macquarie.

In the first section, she attempts to define heroism by interviewing other Victoria Cross survivors and exploring some of the myths surrounding modern celluloid heroes. She concludes that heroes are people who tend to put the needs of others before themselves. She uses this section as a king of preface to provide a background and also to give a clue as to the general theme of the biography. The final section of the book asks the question - can such a man really exist? Again she returns to the original theme of heroism.

The biographical details, especially in the middle section of book, are heavily supplemented with an extremely well explained political history of Australia. In particular she details how the paradoxes of party politics including such people as Evatt, young Menzies and a garrulous McMahon were all to have a significant influence on Cutler and provide him with the steps to build his diplomatic career. I found the explanation of the Suez crisis a very simplistic account of what was a very complex affair.

McCullough also provides the reader with a detailed geographical description of places in Australia, implying that she is aiming for an international readership. I found this refreshing from an Australian author as many assume the reader would be well aware of the location of places well known to many Australians, but the reader needs to consult an atlas - not so in this book.

Her style is extremely readable and like all good books is hard to put down, though I must confess I am a student of Australian history and a bit of a hero worshipper. McCullough also uses an oral history obtained from interviews with Cutler, which adds depth to the narrative. She disperses his comments throughout the text to give a personal insight into events that would be otherwise rather descriptive.

We do not find out a lot about Cutler's personal habits, particularly his likes and dislikes, except his love of Rudyard Kipling. The author uses this fact quite cleverly when Cutler is posted to Pakistan - Kipling Country. Indeed, she uses the line from Kipling's famous poem `If' to provide a motto for Cutler - `if you can walk with Kings - nor loose the common touch!' Maybe this is her subtle way of enticing the reader to explore the whole poem and discover other criteria postulated by Kipling to support his hypothesis - `but what is more you'll be a man my son'. This poem may well give us an insight into answering the question - `what makes this man?'

Cutler has his fair share of life tragedies which include the early and untimely death of his father, the loss of his own leg smashed by bullets from a Vichy French machine gun, his fight for survival with horrific post operative complications and the tragic and sudden death of his wife in the prime of middle age, off

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1 Review by Bruce P. Waxman

2 Sydney: Random House; 1998. ISBN 0-09-183933-5. RRP $35.00 Hard Cover

of which the author uses to illustrate the depth of his resolve.

In conclusion, McCullough suggests the reader may find all this too hard to believe. How can someone like this really exist? A man with all the innate qualities of heroism, willpower, uncanny knowledge, good humour, fidelity and most importantly humility. What was the driving force? What was his motivation? McCullough does not really give us an answer but rather quotes the myth of Sir Galahad `That heroism endures as long as the soul remains untainted'. She therefore comes full circle finishing on the note of heroism as an explanation for Cutler's outstanding qualities.

I wonder however, whether she has missed an important point. Indeed she gives us a clue as to what is behind this great man. Could it be his mother? A consistent theme throughout the whole biography is the way Cutler worshipped his mother and is always attempting to support her needs. It may be that great men are nurtured by love and devotion to the powerful woman in their life. It may be that these maternal qualities and characteristics are reflected in men who are great achievers providing them with ambition and motivation.

Why not read the book and work it out yourself - you will not be disappointed!

Iceblink: The tragic fate of Sir John Franklin's lost polar expedition[1]

Scott Cookman[2]

It has been called the greatest disaster in the history of polar exploration. Led by Arctic explorer Sir John Franklin, two state-of-the-art ships and 128 hand-picked men - the best and the brightest of the British Empire - sailed from Greenland on July 12, 1845 in search of the elusive Northwest Passage. Fourteen days later, they were spotted for the last time by two whalers in Baffin Bay. What happened to these ships - and to the 129 men on board - has remained one of the most enduring mysteries in the annals of exploration. Drawing upon original research, Scott Cookman provides an unforgettable account of the ill-fated Franklin expedition, vividly recreating the lives of those touched by the voyage and its disaster. He has faithfully reconstructed the voyage, from its ships, its Commanders and the men of the Discovery Service, to the factors that ultimately decided their fate. Some of these factors could be, and were, expected and suitable preparations made. These include the extreme weather and being trapped in ice (although possibly not for 18 months). Others factors were not and Cookman suggests a human culprit whose activities may have been integral in triggering the deaths of Franklin and all 128 of his men.

The North West Passage exists or rather the North West Passages exist. They exist, however, in one of the most inhospitable parts of the planet. The first successful passage did not occur until 1906, some 60 years after Franklin's attempt. Indeed, Cookman notes that, while humankind has made 8 successful trips to the moon, it has only traversed the North West Passage 7 times. Against this back drop, Cookman describes a voyage of idealism, national pride, endurance and, at times, amazing bravery. He also captures the atmosphere of a ship trapped in ice for over a year and a half, with coal and food supplies dwindling, with underpowered engines, with officers and fit sailors dying rapidly and mysteriously, and the last desperate bid across the ice and frozen seas to the outposts of northern Canada - a bid destined to fail. In his final Afterword, Cookman notes that 'No disaster is a bastard. Most, in fact, have many fathers' (pp. 198). He summarises the many factors that were to doom this voyage to failure - from its overriding focus on the technology of the time, its large crew, an unknown bacteria called *Clostridium botulinum*, and to Franklin's luck (or lack of it).

This book was loaned to me by an Army colleague with a passion for arctic exploration. As this was not usually an area of strong interest for me, I approached this book with some trepidation. Rather than a rehashed pastiche of old Scott stories, this is a fascinating look at the Discovery Service of the Royal Navy in the mid 19th century, its interaction with the environmental challenges and the role of

[1] Reviewed by Andy Robertson

[2] Cookman S. Iceblink: The tragic fate of Sir John Franklin's lost polar expedition. New York: John Wiley & Sons; 2000. ISBN 0-471-37790.

military medicine and preventative health in ensuring these voyages were, generally, successful. It is well worth reading and there are a number of important lessons to take home, from not going necessarily with the lowest contractor to personnel selection for operational duties. **Ice Blink** is the name 19th century sailors gave polar mirages, caused by light reflected off polar ice.

Conference Reports

RACS Annual Scientific Meeting 2001 - Military Surgical Section[1]

Rob Atkinson

The Military Surgical Section of the RACS Annual Scientific Congress was held in Canberra on 10 May and 11 May 2001. The section was convened by Richard Nugent from Canberra. Two papers were also presented in the Trauma Section, which has a close relationship with the Military Section. These were LTCOL John Crozier presenting on 'Blunt trauma to the liver' and LTCOL Jeff Rosenfeld presenting on 'Neurosurgery by non-neurosurgeons'.

On the afternoon of 10 May 01, I introduced a mini-symposium on the surgical role in the 'Military Operations other than War'. We were fortunate to have Robin Coupland as our Foundation Speaker. He has published a book for the International Committee of Red Cross on War Surgery, which has been used by many of us on deployment. He gave an overview on International Humanitarian Law. This was followed by a series of presentations on our experience in 'Military Operations other than War'.

CAPT Pete Riddell detailed his experience in Afghanistan as member of the International Committee of Red Cross team. WGCDR Gordon Morrison spoke on Rwanda and COL Peter Sharwood discussed Bougainville. LTCOL John Crozier presented on the tsunami in Papua New Guinea and LTCOL David McNicol, Orthopaedic Surgeon, gave a presentation on East Timor with UNTAET. He outlined a vision for the future, with which we all agreed, where the military surgical endeavour could possibly be combined with the humanitarian aid as the peace keeping mission unfolded and the military aspects decreased.

I finally presented on the interface between the International Committee of the Red Cross and the military, pointing out in summary that we are approaching the same position, namely the peaceful development of a community, albeit from different directions. In a democracy such as ours, our values very much reflect those of the International Committee of Red Cross, which was supported by all.

Our formal dinner in the evening was combined with the History Section and was a splendid occasion at the War Memorial. Peter Stanley, the senior Historian, was our guest and the Foundation Speaker for the Military History Section.

The next day, I presented on the anti-personnel landmine effects through the 'Surrogate Project' at the Defence Science and Technology Organisation at Salisbury. COL Peter Sharwood presented on the surgical experiences on East Timor and LTCOL Rob Presley presented on the gunshot wound that he had treated in East Timor. Rob Presley, a professional marksman with experience with various weapons, was able to clearly demonstrate the problems with the safety mechanism of the Austeyr. COL Peter Byrne presented on the difference between Vietnam and East Timor, spanning his lengthy military career. Robin Coupland's talk extended from wounds from the Red Cross field hospital to international law. In essence, he drew on his large experience, which had resulted in his publication. BRIG Duncan Lewis, who spent nine months in command on the border on East Timor in 2000, presented on his experiences on casualty care from a Commander's perspective.

That afternoon, COL Don Beard gave a presentation on Korea, then and now, as he has just returned to Kapyong in North Korea with LTGEN Peter Cosgrove as part of the 50 year celebrations. COL Ross Blair from New Zealand presented on his experience, particularly in relation to the New Zealand commitment in East Timor. BRIG Bran Pezzutti gave an erudite presentation on military anaesthetics and CAPT Ian Jones presented on obstetrics and gynaecology in active service from Bougainville to East Timor. COL John Crompton presented on ophthalmology in the military and MAJ Andrew Ellis finished the day with a presentation on the education of military medical personnel using the surrogate models at Royal North Shore Hospital.

[1] Abstracts are published in ANZ J Surgery 2001: 71(Suppl.); A64-65, A91-92. The author of abstract MS1 is R Atkinson and not R Coupland as listed. MS4 was not presented.

AMMA Awards and Grants

Enter Now

Weary Dunlop Award

The Weary Dunlop Award, named after our first life member, is awarded to the best original paper presented at the Annual Conference and is worth $500. The Conference Organising Committee for 2000 decided that a panel of past winners should do the judging of this award, and Council has agreed that this should become the practice for the future.

Patron's Prize

The Patron's Prize is awarded by the Association's Patron to the best paper published in a refereed journal during the year and is worth $250.

Journal Editor's Prize

The Journal Editor's Prize is awarded by the Editor of Australian Military Medicine for the best paper published in the journal and is worth $750.

Essay Prize

The topic for the 2001 Essay Prize is "The future role of IT in military health". The topic for the 2002 Essay Prize will be announced at the 10th Annual Scientific Conference.

Research Grants

The AMMA Research Grant is provided to assist in research being undertaken by members of the association in aspects of military health, and is worth up to $1,000, which may be granted in full, in part, or divided between several applicants.

Closing Date

Applications for the 2002 awards are required to be submitted to the Secretariat by 30 June 2002.

More Information

Contact details for the AMMA Secretariat and Conference Managers, Leishman & Associates Tel: 03 6234 7844 or Fax: 03 6234 5958, Email amma@leishman-associates.com.au. Visit the AMMA Website for the latest information at http://amma.trump.net.au/

10th Annual Scientific Conference

19-21 October 2001
Gold Coast International Hotel
Surfers Paradise Queensland

Conference Highlights

Keynote Address
Medical Aspects of Space Flight
Colonel James Bagian USAFR

Welcome Cocktail Reception Poolside

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Guest Speaker
Brigadier Pat McIntosh

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28 presentations
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Abstracts from the Literature

Submitted by James Ross

Rosenberg E, Caine Y. Survey of Israeli Air Force line Commander support for fatigue prevention initiatives. Aviat Space Environ Med 2001;72(4):352-356.

Background: Sustained and continuous high intensity military operations have increased in scope in recent years. These mandate ever more sophisticated efforts to prevent and ameliorate aviator fatigue. Successful implementation of new fatigue countermeasures requires thorough pretesting among experienced aviator opinion leaders: based and squadron commanders. Methods: Anonymous and voluntary survey questionnaire containing background material and Likert-scale questions regarding 14 primary through tertiary fatigue prevention initiatives current in the aeromedical literature or unique to the IAF was distributed to all base and flight squadron commanders in the IAF. Results: Of the commanders, 38% returned fully completed questionnaires. The most popular primary prevention initiatives (garnered 87% support) dealt with reservist aviators: 1. Requiring reserve pilots to arrive at the squadron at least 3 h before night flights to facilitate napping time, and 2. Improving scheduling coordination of those reservists employed as civilian aircrew. The chief (88% support) secondary prevention countermeasure endorsed was to utilise stimulant drugs such as caffeine or amphetamine to sustain the alertness of fatigued aviators. Leading the list of tertiary prevention initiatives (75% support) was the suggestion that squadrons debrief the incidence of aviator fatigue, as well as their success in the area of time-management when debriefing high tempo exercises and operational missions. Conclusions: Commanders differentially supported a wide range of fatigue countermeasures. Use of stimulant drugs achieved the broadest support. Instituting specific measures to facilitate alertness in reservist aviators was also a priority. Surveying the degree of commander support for new prevention initiatives provides the basis fort prioritisation of scarce resources, should improve line cooperation, and provides important experience-proven feedback for researchers and policy makers.

Comment: *A worthwhile approach: asking the operators what they think works and where more investment should go. Nearly all the strategies received more than 50% support - only the mandating of a minimum 6 hours sleep a night was really dismissed. That 88% supported the use of stimulants was the most revealing. It seems the IAF has a lot of familiarity with stimulants, and they are a 'quick fix' to maintain mission readiness.*

Brickfield F, Pyenson L. The impact of stroke on world leaders. Mil Med 2001;166(3):321-322.

Purpose; Earlier studies by our unit documented frequent disability in world leaders resulting from stroke but did not quantify the incidence of cerebrovasular accidents. We sought to identify the frequency and impact of strokes in world leaders. Methods: Using various sources, we identified world leaders who sustained strokes while in office from 1970 to 1999 and tabulated information on symptoms and subsequent ability to lead. Results: Twenty leaders were identified who had sustained strokes during the study period, for an incidence of 0.444 strokes per 100 leaders/year. Half of the affected leaders lost their political power within the year; most had persistent disabilities, which included motor, speech, cognitive, and emotional deficits. Conclusion: Strokes in world leaders may be slightly less common than expected based on studies of Western populations of similar age, but they are often devastating to a political career. Nonetheless, loss of political power is not inevitable.

Comment. *From the CIA. It is really surprising, given the pressure political leaders are under, that the stoke incidence appears lower than the expected in western populations. That may be explained by other genetic and cultural differences. However, what is more amazing is that anyone is able to maintain head of government status following a CVA. It is clearly easier to get into power than to lose power in many countries.*

Memish Z, et al. The cost-saving potential of prevaccination antibody tests when implementing a mass immunisation program. Mil Med 2001;166(1):11-13.
A seroprevalence study of hepatitis A virus, hepatitis B virus and varicella-zoster virus was carried out among Saudi Arabian National Guard soldiers with the objective of determining the cost-saving potential of prevaccination antibody tests when implementing an immunisation program for the soldiers. A systematic sampling of 450 blood samples from 1350 soldiers who donated blood at our hospital was carried out. Antibody tests were performed using the enzyme-liked immunosorbant method. The seropositivity rates for antibodies to HAV, HBV and VZV were 97.5, 17.8 and 88.5% respectively. Comparing the cost of pre-vaccine screening with that of universal vaccination, it was estimated that savings of 76% and 32% could be effected for HAV and VZV. Conversely, screening for HBV before immunisation could increase the cost of vaccinating against the disease by 49%. A seroprevalence study could be a useful cost-saving approach to a mass immunisation program against endemic, natural immunity-conferring diseases.

Comment: *The outcome will clearly be dependent on the natural level of seroconversion in the community being dealt with. The HAV positivity will be a little less than 98% in Australia, methinks.*

Weaver J, McAlister W. Vision readiness of the Reserve Forces of the US Army. Mil Med 2001; 166(1):64-66.
In 1996 and 1997, the Army conducted an exercise to assess the ability to rapidly mobilise the reserve forces. In accordance with Army requirements, each soldier was evaluated to determine if he or she met vision and optical readiness standards. Of the 1947 individuals processed through the optometry section, 40% met vision requirements without correction and 32% met vision requirements with their current spectacles. The remaining 28% required examination. A major impediment to processing reserve units for deployment is the lack of vision and optical readiness. In the mobilisation for the Persian Gulf War, significant delays were incurred because of the time required to perform eye examinations and fabricate eyewear. However, as a result of this exercise, current prescriptions will be available in the event of mobilisation. To ensure readiness, all units should perform such exercises periodically.

Comment: *Yep, eyes are and always will be a big problem. The exercise of testing all reservists is a mammoth job, and then maintaining accuracy of prescription another problem. 'Just in time' testing may well be the preferred option for reservists still, because of the logistic hurdles.*

Kortepeter M, Krauss M. Tuberculosis infection after humanitarian assistance, Guantanimo Bay, 1995. Mil Med 2001;166(2):116-120.
Upon redeployment to Fort Lewis, Washington, from operation Sea Signal in Guantanimo Bay, Cuba, 55 of a military police unit was identified as positive for Purified Protein Derivative (PPD). A case-control study was conducted to document the number of converters and to identify risk factors among the soldiers for PPD conversion while in Cuba. Forty-six of the soldiers (3.7% of the unit) met the criteria for PPD conversion as a result of deployment. Forty-four converters and 84 controls completed surveys. Logistic regression showed that statistically significant independent risk factors for PPD conversion included working around coughing migrants (odds ratio = 6.73, Confidence interval = 2.2-20.4) and birthplace outside of the USA (OR 4.89, CI 1.3-18.5). Contact in the psychiatric hospital (OR 0.22, CI 0.05-0.900 and contact with migrants with known tuberculosis (OR 0.16, CI 0.05-0.54) appear to be protective factors, possibly because known tuberculosis patients and hospitalised patients most likely would be on treatment and rendered noninfectious. With the US military's involvement in humanitarian and refugee operations in countries highly endemic for tuberculosis, service members are at increased risk of acquiring tuberculosis infection. Detection of tuberculosis infection and appropriate treatment should become a higher priority within the US military.

Klein L, Kasper M. NATO medical support to crisis response operation - A strategic view. Internat Rev Armed Forces Med Services 2000;73(3):165-169.

Comment: *The rather quixotic, even mercurial translations rendered in this publication act to limit its value. Nevertheless, it is worthwhile to persevere, as this is a way to observe activities within the continental component of NATO. This article describes some changes to the principles underlying NATO medical support. Much parallels changed thinking in Australia. For instance, standard of care should as far forward as is possible, be equivalent in operational setting to peacetime, with a seamless flow through the treatment hierarchy, and a reduced forward health logistic footprint. There is then a description of medical policy and doctrine. There is definitional opacity here,*

with policy topping the hierarchy, below which sits joint doctrine and component doctrine - while here we have policy sitting under doctrine. Then command and control in the joint environment. The wording is revealing: coordinate, establish, support. Little in the way of command and control here. It is apparent that single nation medical support is preferred, or at worst, one nation providing all the 'nucleus' and other nations supplementing this. The idea of true multinationality is a long way off.

Fenner P, Harrison S. Irukandji and Chironex feckeri jellyfish envenomation in tropical Australia. Wilderness Environ Med 2000;11(4): 233-240.

Objective: To compare the temporal distribution of Irukandji and Chironex fleckeri stings, the demographics of victims, the prevailing physical conditions an the time of the sting, and the prevalence of unsuitable first aid strategies. Methods: Retrospective assessment of 478 Chironex and 544 Irukandji stings in Queensland and the Northern territory of Australia. Results. Adolescent and young adult males were the most common victims of Irukandji (medial age 21 years) and Chironex stings (median age 16 years). Most Chironex stings occurred on the legs, while Irukandji stings were most common on the arms. Vinegar was correctly used to remove tentacles in 90.5% of Chironex stings, whereas inappropriate treatments were used in the remaining cases. Chironex stings were reported in every month in the Northern territory, and in all months but June and July in Queensland. The peak prevalence for Chironex stings occurred in January in both areas, while the number of Irukandji stings peaked in December in Queensland and in May in the Northern Territory. Chironex stings were more common on still, cloudy days, whereas Irukandji were more common on still, clear days. Irukandji stings were more frequent than Chironex stings on rough days (p= .0005). Chironex and Irukandji stings were similar with respect to tides, moon phases, and rainfall. Conclusions. This study failed to predict exact weather patterns or other contributing factors to reduce the risk of stings to an acceptable level, but did identify several factors that increase the incidence of stings. The 'stinger-free' season reported on Chironex warning signs is inaccurate and should be changed to warn bathers that Chironex may be present year round, particularly in the Northern Territory.

Comment: *This article, together with the accompanying one describing the venom characteristics of the box, blubber and Irukandji jellyfish, have advanced the understanding of these envenomation complexes. The box jellyfish is the most dangerous jellyfish in the world, with Australia averaging one death every two years. The ever increasing presence of the Australian military in the north should bring more focus on the management of this conditions.*

Chang E, et al. Planning for an annual episodic mass gathering: emergency department and clinic utilisation in Yellowstone. Wilderness Environ Med 2000;11(4):257-261.

Objective: Planning and providing emergency and primary care for a large transient population of visitors and employees in a national park can be problematic. Furthermore, planning for emergency and primary health care needs of visitors and itinerant workers in a wilderness area national park has not been well documented. A study was performed to analyse emergency and primary health care utilisation in a national park. Methods. Data was gathered from all patients presenting to lake Hospital Emergency Department in Yellowstone in 1995, and a retrospective chart review was performed. Results. Two distinct populations with different health care needs were identified. Conclusion. Utilisation analysis revealed differences between conventional mass gatherings and the mass gatherings in Yellowstone. Because of the unique conditions and populations found in a wilderness area, conventional mass gathering emergency medical service models may not be an appropriate model for planning health care in a national park. Analysis of utilisation data can help plan resources for emergency and primary health care for a park population.

Comment: *I was looking for the comment on getting consent for each participant to have their reports reviewed for this study. Didn't get a mention. I trust the ethics were considered at some stage. Low utilisation at 5.2 visits per 10000 visitors, compared to other quoted studies at 16-32 per 10000 visitors. Of course, the demographics will vary, as will activities that will influence injuries and illness.*

Walter, E et al. Influenza A in a basic training population: Implications for directly observed therapy. Mil Med 2000;165(12):941-943.

Purpose; To describe our evaluation of basic trainees exposed to influenza A and our experience with mass prophylaxis. Methods: Using a structured interview, 101 individuals were evaluated for symptoms of influenza A. Nasopharyngeal wash specimens were obtained from symptomatic troops; amantidine prophylaxis was prescribed for all. Diagnosis

was confirmed using a rapid influenza assay or shell vial culture. After completing prophylaxis, the group was reevaluated to determine medication compliance and perceived side effects. Results: At baseline, 80 trainees reported symptoms. Three additional cases of influenza were identified, two using the rapid assay. Reported compliance with the amantidine prophylaxis was 46.5%. Conclusions: Nonspecific complaints that could be consistent with viral infection were numerous in this basic trainee cohort. The rapid assay allowed us to expediently identify additional patients, who were then removed from the cohort to limit further transmission. Compliance with prophylaxis was poor; thus directly observed therapy is recommended.

Comment: *The US military has been vaccinating recruits against Influenza for many years - since an episode in the US Air Force academy in the 1970s which stopped the academy in its tracks for several weeks. No epidemiological studies were done to evaluate the benefits and costs of the vaccination program: it just became entrenched. We have recently seen some good studies on young healthy working population in the Northern hemisphere that suggest there is a cost benefit in vaccinating such a group. The likelihood is that an institutionalised group such as recruits would also benefit. Would be a great study to do...*

As for this study, how you differentiate symptoms of Influenza A from symptoms of Influenza B and many other viral infections - I do not know. Of 80 trainees with 'symptoms', only 2 actually had infection confirmed. It is not determined by this study that in recently vaccinated troops there is any advantage in giving prophylaxis, but the paper glosses over this issue.

Pope R, Schumacher J, Creedon J. The effectiveness of the parachutist ankle brace in reducing ankle injuries in an Airborne Ranger battalion. Mil Med 2000;165(12):944-948.

The purpose of this study was to determine if the parachutist ankle brace (PAB) decreases the number and severity of ankle injuries in an airborne Ranger battalion. A retrospective study was performed covering a 38 month period. A computer database was used to track all jump injuries with a diagnosis of ankle pain, sprain, or fracture. The frequency was calculated for ankle injuries per 1000 jumps and the average length of medically restricted duty per ankle injury. A total of 13782 static line parachute jumps were conducted during the study period. Without the PAB, 35 ankle injuries were seen (4.5/1000 jumps) with 9 fractures and 316 days of medical restrictions. Using the PAB, 9 ankle injuries were seen (1.5/1000 jumps), with 3 fractures and 71 days of medical restriction per 1000 jumps. The correct use of the PAB appeared to significantly decrease the incidence of ankle injuries in this battalion.

Comment: *The study was limited because of some difference in the jumps performed by the PAB versus the non-PAB wearers. There were more jumps onto airfield in the latter group. There was no information on prevailing conditions, other equipment and so on. Thus, this study is indicative only, but certainly worth a second look.*

Submitted by Andy Robertson

Srinivasan A, Kraus CN, DeShazer D, et al. Glanders in a military research microbiologist. N Engl J Med 2001;345(4):256-8.

Comment: *This is the first reported human case of glanders in the English medical literature since 1949. It was, unfortunately, laboratory acquired at the US Army Medical Research Institute of Infectious Disease. A couple of interesting points. Diagnosis may be difficult, and conventional phenotypic identification testing inaccurate. We also now know the disease responds well to imipenem and doxycycline.*

Fidler DP. Facing the global challenges posed by biological weapons. Microbes Infect 1999;1(12):1059-66.

This review article examines the growing concern about the threat posed by the use of biological weapons by States or terrorist groups. The article analyzes the nature of the perceived risk from bioweapons, the historical attempts to control them, and the emerging policy and legal framework designed to deal with the bioweapon threat.

Comment: *This is one of the more balanced articles on biological weapons - balanced and with an excellent section on arms control. The Indiana University School of Law was probably not the first place I would have looked for a sensible contribution to the biowarfare discussion.*

Hyson JM Jr, Whitehorne JW. The "Amex" cast aluminum denture of World War I. J Hist Dent 2001 Jul;49(2):89-91.

In 1917-18, the U.S. Army revived a denture technique first introduced in 1866 by Dr. James Baxter Bean, the Confederate dental

surgeon who established the first military maxillofacial hospital trauma ward in Atlanta, Georgia, during the American Civil War - the cast aluminum wartime denture.

Comment: *Must have been a great look. Any comment from the dentists?*

Mellor AJ. Helicopter medical retrieval in Sydney, New South Wales. J R Nav Med Serv 2000;86(3):167-9.

Undoubtedly the main attraction of this job is the interest of never knowing what will happen next! Primary response to an MVA allows one to experience the atmosphere and deal with clinical situations in an alien setting. This broadens ones perspective and has taught me never to be tempted to criticise a paramedic bringing a patient into a resus room. The same is true of interhospital transfers where tact and diplomacy can be tested as well as clinical skills. On the negative side the unpredictability can be difficult domestically (a primary at 1755 means you will be at least two hours late home) and there can be long and dull days when nothing happens. A lot of time is spent transporting post arrest patients from one hospital to another to find an ICU bed. In military medicine, it is difficult to envisage a future conflict when severely injured casualties would not require transport both locally and over long distances. This job provides an ideal opportunity to become confident with transporting critically ill patients.

Comment: *Why are we not involved in some form of strategic alliance with helicopter retrieval services? It strikes me as being excellent ground for skill development.*

AMMA Update

News and information for members of the Australian Military Medicine Association

Successes

The following AMMA members have achieved success through honours, awards, promotions, publications, etc.

Members will note that these items are not complete. The Editor needs sources of information from the three Services and from our civilian members as well, so that this section of your journal can truly reflect the cross-section of our membership. Updates can be faxed to CAPT Andy Robertson on (02) 6266 2314 or emailed to andyandlaura@bigpond.com

Defence Force Promotions

The following AMMA members have been selected for promotion in the Defence Forces:

- CMDR Jenny Graham to CAPT
- LTCOL Darrell Duncan to COL
- LEUT Andrew Davidson to LCDR
- LEUT Sarah Sharkey to LCDR
- LEUT Morag Ferguson to LCDR

Defence Force Movements

- WGCDR Amanda Dines will post as CO of Air Health Wing.
- LTCOL Duncan to COL HLTH
- COL Wells, GPCAPT Austin & LTCOL Gill to DHSB late 2001.

Retirements

- LTCOL Graham Durant-Law has retired and will be involved in consulting and reserve work.
- LEUT James Provan has retired and will take up a general practice job in WA.

Awards & Grants

AMMA have a number of awards and grants available to members. Deadline for all awards is 30 June 2002.

For those wishing to do a research project within defence, the project must be approved by ADMEC (The Australian Defence Medical Ethics Committee). Information kits for new researchers are available from the ADMEC Executive Secretary on

Tel: (02) 6266 3818
Fax: (02) 6266 4982

Research Grant - $1000

A grant presented towards new or ongoing research.

Journal Editors Prize - $750

For best paper by an AMMA Member published each year in the AMMA Journal.

Patron's Prize - $250

Best article published in a peer-reviewed journal by an AMMA member – must be a health related article.

Australian Military Medicine Prize - $500

Best essay by an AMMA Member on a chosen topic. The topic for 2002 will be decided at the 2001 conference.

For further information contact the AMMA Secretariat or visit the website.

AMMA Contacts

For all general AMMA inquiries contact the Secretariat.

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Website: http://amma.trump.net.au/

AMMA Website

Visit AMMA's website at: http://amma.trump.net.au/

The web site is constantly evolving and any contributions are welcome.

AMMA Conferences

2001 Conference

The 10th AMMA Scientific Conference will be held on the Gold Coast from the 19-21 October 2001 at the Gold Coast International Hotel.

The full registration brochure has been posted to all AMMA members.

If you require extra brochures or more information please call Leishman & Associates on (03) 6234 7844 or visit the web site http://amma.trump.net.au/

Journal

Journals for 2001/2002 will be published as follows:

Issue	Copy Deadline
Dec 2001	31/10/01
Apr 2002	28/02/02
Aug 2002	30/06/02
Dec 2002	31/10/02
Apr 2003	28/02/03

All queries regarding the Journal should be directed to the Editor:
Andy Robertson

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Conference and Meeting Calendar

Date	Conference	Venue	Contact No.
16-19 Sep 2001	13th National Casemix Conference	Hobart	Conference@conlog.com.au
17-21 Sep 2001	Australian Radiation Protection Society Conference	Gold Coast	(07) 3406 8014
12-15 Oct 2001	Pharmacy Australia Congress	Melbourne	(02) 6283 4793
19-21 Oct 2001	**10th AMMA Conference**	**Gold Coast**	**(03) 6234 7844**
4-9 Nov 2001	AMSUS Meeting	San Antonio, Texas	http://www.amsus.org/meetings/current.html
8-11 Nov 2001	Society of Hospital Pharmacists	Hobart	(03) 6234 7844
20-22 Nov 2001	Canadian Operational Medicine Conference	Halifax, Nova Scotia	(02) 6266 4483
22-24 Nov 2001	Paediatric Update	Westmead, NSW	(02) 9845 0521
26 Nov - 07 Dec 2001	Medical Officer Underwater Medicine Course	HMAS Penguin, Sydney	(02) 9960 0300
12-13 Apr 02	ARC International Resuscitation Conference	Melbourne	(03) 9249 1214
25-27 Jul 02	**Defence Health Symposium - Co-hosted by AMMA**	**Sydney**	**(02) 6266 4483**
27-29 Aug 02	RACMA/ACHSE Congress	Perth	(08) 9489 4800
10-15 Nov 02	AMSUS Meeting	Louisville, KY	http://www.amsus.org/meetings/current.html

AMMA ON THE NET

Conferences:	Medical Conferences	http://www.pslgroup.com/medconf.htm
Journals:	Medical Journal of Australia	http://www.mja.com.au/
	New Scientist	http://www.newscientist.com/
Military Medicine:	AMSUS	http://www.amsus.org/
	Armed Forces Infectious Diseases Society	http://www.wramc.amedd.army.mil/afids/links.htm
	Association of Military Osteopathic Physicians and Surgeons	http://www.amops.org/
	Finnish Museum of Military Medicine	http://www.travel.fi/int/mmm/
	Henry Jackson Foundation for the Advancement of Military Medicine	http://scoop.hjf.org/
	International Association of Military Flight Surgeon Pilots	http://www.geocities.com/Pentagon/2265
Professional Colleges:	ANZCA	http://www.anzca.edu.au/
	RACGP	http://www.racgp.org.au/
	RACMA	http://www.racma.org.au
	RACP	http://www.racp.edu.au/
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INSTRUCTIONS FOR AUTHORS

Australian Military Medicine welcomes articles and other contributions on all aspects of military health care. Articles submitted may be subject to peer review. Articles must be offered exclusively to *Australian Military Medicine* for publication. Articles which have been published elsewhere will only be considered if prior approval has been received from the original publisher and they are of importance to the field of military medicine. All accepted manuscripts will be subject to editing.
Contributions should be sent to:

The Editor
Australian Military Medicine
16 Gaylard Place
GORDON ACT 2906
andyandlaura@bigpond.com

MANUSCRIPT REQUIREMENTS

One hard copy and one electronic copy of the manuscript should be submitted. The typed copy should be typed double-spaced and single-sided on A4 paper. The electronic copy should be on disk or sent be e-mail. The text in both hard and electronic copies should be unformatted. The electronic copy may be in any common word-processor format.

Contributions should be between 500 and 5000 words in length. Letters to the Editor should not exceed 500 words or 10 references. The Editor may consider any contributions outside these limits. Any articles reporting on human subjects involved in experiments must contain evidence of approval by the relevant institutional ethics committee.

The title page should include the article title; list of authors, including details of their full name, military rank, postnominals, position and institutional address; and, preferably, an abstract of the article (150-200 words). Contact details for the principal author, including postal address, e-mail address, telephone and fax numbers, should also be included.

Headings and sub-headings should be consistent throughout the article and conform with articles previously published in the Journal. No text, references, or legends to figures or tables, should be underlined.

Illustrations, figures and pictures should not be embedded in the document. Their intended position, however, should be clearly indicated. Illustrations and pictures should be saved as separate documents in TIFF, GIF or JPEG formats. **Tables** may be embedded in the paper.

Photographs may be black-and-white or colour. They should be provided in soft-copy, preferably as JPEG files, but may be provided as hard-copy. Slides must be converted to soft-copy graphics files or to photographs.

Abbreviations mean different things to different readers. Abbreviations are only to be used after the complete expression and the abbreviation in brackets has appeared. For example, the Australian Defence Force (ADF) may then be referred to as the ADF.

SI units are to be used for all articles. Any normal ranges should also be included.

References should be in accordance with the "Vancouver" system (see *MJA* 1991; 155: 197-202, or www.mja.com.au/public/information/uniform.html). References in the text should be numbered consecutively as they are cited and should appear as superscript numbers (e.g. text[1,2]). References are collated at the end of the article. Annotation of the references should accord with the abbreviations used in *Index Medicus*. Where there are seven or more authors, list only the first three then use *et al.* Authors are responsible for reference accuracy. An example of the reference system is as follows:

1. Quail G. Asthma in the military. *Aust Mil Med* 2000; 9(3):129-137.
2. Bowden M. Black Hawk Down. New York: Atlantic Monthly Press; 1999.

Reprinting of articles may be authorised by the Editor, with the author's consent, if an acknowledgment, quoting both the Journal and the original date of publication, is printed with the article.

Australian Military Medicine Association

Statement of Objectives

The Australian Military Medicine Association is an independent, professional scientific organisation of health professionals with the objectives of:

- promoting the study of military medicine
- bringing together those with an interest in military medicine
- disseminating knowledge of military medicine
- publishing and distributing a journal in military medicine
- promoting research in military medicine

Membership of the Association is open to doctors, dentists, nurses, pharmacists, paramedics and anyone with a professional interest in any of the disciplines of military medicine.
The Association is totally independent of the Australian Defence Force.