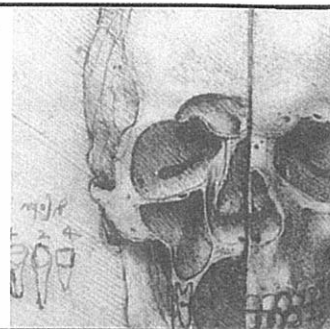
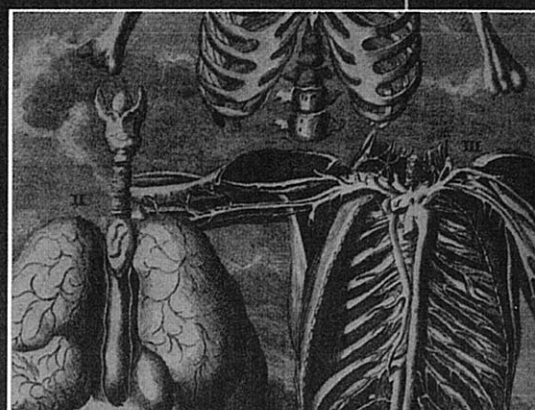
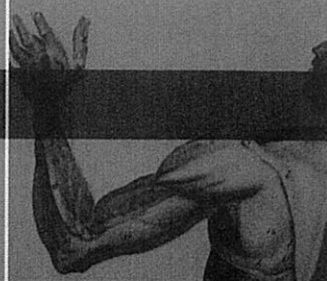




AUSTRALIAN MILITARY MEDICINE



AUGUST 2002 - Volume 11 - Number 2



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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.

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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 by 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 high resolution (300dpi) TIFF 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 high resolution (300dpi) TIFF or 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.

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EDITORIAL

Rumours of war....

AS WE APPROACH the first anniversary of the terrorist attacks of 11 September, the Australian Defence Force remains actively involved in Afghanistan, the Persian Gulf and central Asia, as well as East Timor, Bougainville and the Solomon Islands, and in the seas to our north. For all three Services, this continues to be one of the largest Defence Health Service undertakings since the Vietnam War. The other factor that has influenced the way we view our security is the anthrax letter attacks in late 2001 in the United States. These attacks have demonstrated the vulnerability of Western countries to such attacks. In this issue, both the effects of the 'white powder' incidents on the Australian public health system and the further developments of the health response to chemical, biological or radiological attack are considered. The third paper with this theme reviews developments of pretreatment agents' protective against mustard poisoning.

As we move into September 2002, there are also rumours of war. The United States is keen that the long-term concerns about Iraq's potential weapons of mass destruction be addressed. Whether this will involve the return of weapons inspectors, limited conflict or all out war is difficult to predict. What is even more difficult to predict is what the ADF's health involvement will be. My December editorial should be an interesting one as we look back over the next few months.

The Defence Health Symposium 2002, AMMA's conjoint meeting with the Defence Health Service, the Australian Disaster Medicine Group and the Australian Centre for Post-traumatic Mental Health, was a roaring success. With over 620 attendees, there was a myriad of excellent papers presented, ample opportunity to catch up and network, and a good infusion of over 50 new members into AMMA. I am also very happy to see a range of papers coming to Australian Military Medicine for publication.

In addition to the papers mentioned earlier, this issue addresses a number of key military medical themes, including medical research, health policy, occupational health and Naval history. The future of Defence medical research, the nutrition of our

recruits, new Japanese encephalitis vaccines and chemical protective agents, are all addressed. Critical analysis of current Defence health policy considers cervical cancer screening, influenza vaccine and surgical smoke. Finally, the challenge of providing Naval health care during the Tudor period provides some important lessons for today.

As always, an excellent series of papers, which are available to universities and other subscribers, including Defence, through the Australasian Medical Index and Meditext. *Australian Military Medicine* is also working towards being fully peer-reviewed by 2003. In this issue, we see a number of articles that have been peer-reviewed. If you can assist in this process, please complete the enclosed form and return to the Editor. The other initiative is to look back ten years to the beginning of the Journal and to reprint some of the articles from that time. The first of these is James Ross' article on influenza vaccination from 1992.

If possible, the next six months promises to be more challenging than the last. The rumours of war will continue and may crystallise, and uniformed shortages will continue to challenge. At the very least, there should continue to be a myriad of topics for future papers, reviews, editorials and letters to the Editor.

Andy Robertson

PRESIDENT'S MESSAGE

ONCE AGAIN, WE AS A WORLD SIT ON THE PRECIPICE. Whether the protagonists are right or wrong is not for me to comment. But it seems increasingly likely that before too long the world will be engaged in another hot war. Whether Australia is involved remains to be seen.

It is just over 10 years since we last faced the prospect of a war that involved the potential for the use of chemical, biological and nuclear weapons. The frantic efforts that were involved in 1990 to adequately protect Australia's forces from these threats led to an increased awareness of the problems that are faced. That awareness has been redoubled by the events of the last twelve months. One of the observations that will be able to be made of the current efforts will be how much better is preparedness in these areas.

Since 1990, Australian forces have been working at an operational tempo that is unprecedented since Vietnam. Not only have they faced the land deployments in Rwanda, Bougainville and East Timor, which have involved the efforts of all three Services, but our Naval forces have been operating to protect the borders of the sea-air gap to the northwest, as well as deploying to the hostile Antarctic regions to protect Australia's fishing interests.

In all these activities, the ability to deploy Health Services in support of the forces (and in the case of Rwanda as the primary mission of the deployment) has been vital to success. Our Health Services are stretched, and the challenges in providing adequate support are enormous. There has, however, been significant progress in developing the infrastructure within which the Health Services can deliver care.

What has been the Australian Military Medicine Association's contribution to these efforts? Since 1990, the Association has held 11 annual scientific conferences, including our co-hosting of the Defence Health Symposium earlier this year.

Our conferences are widely acknowledged as being of the highest standard, with papers presented on a wide range of military health related subjects. They provide an opportunity for us to get together and explore options for improving the delivery of health care to military forces, wherever deployed. At least as importantly, they provide a venue for informal networking where ideas, flights of fantasy or passions can be discussed, debated, rebutted, or perhaps form the

germ of a seminal idea that could revolutionise military health care. They also strengthen the bond between us all as professional healers.

The Association also publishes its journal three times a year, and, thanks to the hard work of our Editor, the articles are of ever increasing quality.

It is through these various mechanisms that the military health profession in Australia will be able to continue to advance and improve its ability to deliver the highest quality health care into operational areas so as to minimise mortality and morbidity amongst those who place their lives on the line in the defence of our country.

DEFENCE HEALTH SYMPOSIUM

The recent Defence Health Symposium held in Sydney, and co-hosted by AMMA, was clearly a resounding success. Over 600 delegates attended, including many from overseas. The papers, many from AMMA members, were of a very high standard. The opportunity to share knowledge and ideas among us all was unprecedented.

At the Symposium dinner, we announced the conferring of Honourary Life Membership on Air Vice Marshal Eric Stephenson for his long and outstanding contribution to military medicine. The announcement was greeted with acclamation.

AMMA also had the opportunity to advance its membership base, and it was pleasing that we attracted over 50 new members during the Symposium. The challenge for the Association and Council is to support and maintain that membership.

The Symposium was the Association's 11th Annual Conference, and as such the holding of a separate conference in our traditional month of October will not occur.

CONFERENCE 2003

In 2003, AMMA will revert to its normal routine of holding a conference in October. We will go to the equable climes of South Australia, with the opportunity to sample the fruits of the local vines. The dates will be 17 to 19 October, so it is now time to put pen to paper and start writing those erudite contributions to scientific progress for presentation at the Conference.

FUTURE CONFERENCES

AMMA has been approached by a number of other associations and organisations to join in co-hosting future conferences. Council will be considering this in a strategic context in the next couple of months. There are positives and negatives in relation to such proposals.

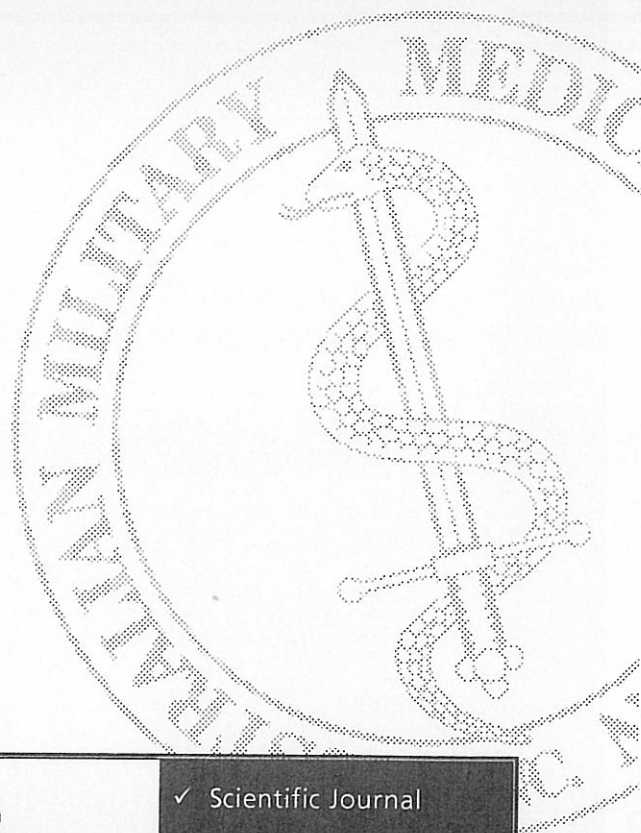
As the Defence Health Symposium demonstrated, there is great opportunity in advancing the membership base of the Association, as well as elevating the profile of the Association. On the down side are the prospects of diluting the independence of the Association, diluting the sponsorship base, and having ever-different dates for our Conferences. Members who might have ideas in relation to the concept of regular co-hosting of conferences are invited to contact a member of Council and put their thoughts and ideas for consideration.

ASSISTANT SURGEON GENERAL—NAVY

Commodore Peter Habersberger RANR has recently retired as Assistant Surgeon General – Navy. Peter has had a long association with the Navy, both as a clinician (in cardiology) and manager (both through the former office of the Director General Naval Health Services and the office of the Surgeon General). Peter has also been a member of the Association since its inception, and was instrumental in organising the Association's first conference. I am sure all members of the Association will wish Peter all the best for the future.

The new Assistant Surgeon General—Navy is Commodore Graeme Shirtley. Graeme is a radiologist in private practice in Sydney and has been the senior Naval Health Reserve officer in Sydney for several years, working with the Fleet Medical Officer in Maritime Headquarters managing the provision of Reserve personnel support to Health Service requirements.

Russell Schedlich



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ORIGINAL ARTICLES

Enhancing Resistance to Sulphur Mustard Injury: Expression of Glutathione S-Transferase in Human Keratinocytes – Developing a Model to Explore Pre-Exposure Strategies*

Sam Ross and Peter J Gray

ABSTRACT

THIS PAPER DESCRIBES the rationale for current work undertaken at the Chemical, Biological, Radiological and Nuclear Defence Centre (CBRN DC) investigating the feasibility of pre-exposure approaches to counteracting the toxicity of the chemical warfare agent sulphur mustard (HD). HD is a vesicant that causes severe, slow-healing lesions in skin, lungs and eyes. The work described is focused on endogenous glutathione S-transferase (GST), a phase II detoxifying enzyme expressed by many eukaryotic cell types. Elevated levels of GST have been found in some tumour lines resistant to alkylating chemotherapy drugs, which are biochemically similar in action to HD. It is possible that a capacity to resist DNA damage caused by such drugs could also represent resistance to DNA damage caused by HD. Human keratinocytes in vitro have been chosen as a biochemical model for the skin, a major target of HD. The aim of this ongoing study is to determine whether phase II enzyme inducers can increase levels of GST in these cells. A cell survival assay has been developed for this model. A GST assay protocol was devised, utilising a microplate spectrophotometer with kinetics functions. These techniques constitute a system that is proving useful in the testing of reagents for toxicity and GST induction in keratinocytes.

[Abbreviations: GSH – reduced glutathione; GST – glutathione S-transferase; HD – sulphur mustard; kbp – kilobase pairs; LDH, lactate dehydrogenase; MW – molecular weight; NHEK – neonatal human epithelial keratinocytes; NR – Neutral Red dye]

INTRODUCTION

Sulphur mustard (bis(2-chloroethyl) sulphide; HD), sometimes referred to as “mustard gas”, is a bifunctional alkylating agent that has been used as a chemical warfare agent, first in Ypres in 1917 and most recently in the Iran-Iraq conflict in the 1980s^{1,2}. It is a vesicant, causing dose-dependent injuries to skin, eyes and airways on contact, and is also capable of causing systemic toxicity. Although its cytotoxic properties have been extensively documented (reviewed in references 3 to 5)³⁻⁵, the details of the biochemical mechanism through which it causes its characteristic injuries is still poorly understood. As a result, there are no specific medical pre- or post-exposure treatments. The only way to protect the body from HD is by physical barrier; in practice, this entails the use of protective clothing to cover all skin surfaces and a respirator/self-contained air supply. Such protective

gear is cumbersome and imposes a high physiological burden on the wearer.

APPROACHES TO COUNTERING SULPHUR MUSTARD INJURY

The search for specific therapies to counteract the consequences of HD exposure has pursued two courses, seeking reagents that will mitigate cellular damage by HD if administered prior to exposure, or antidotes that will reverse the damage sustained once HD exposure has taken place. Both approaches, however, have been hampered by aspects of the toxicology of this agent. The molecular and biochemical mechanisms by which HD induces cell injury that leads to the characteristic lesions is poorly understood. In contrast, the detailed knowledge of the anticholinergic action of nerve agents has led to the development of pre- and post-exposure strategies that target specific

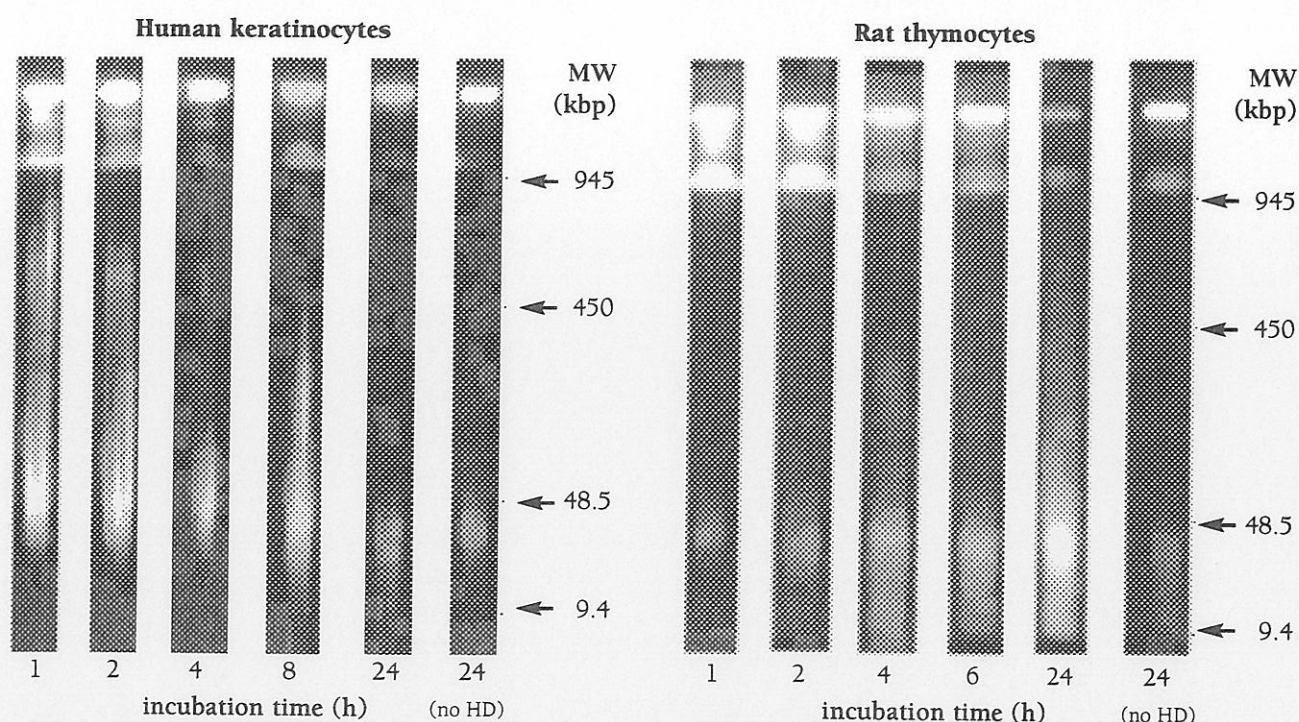
1. Dr Ross and Dr Gray are research scientists at the CBRN Defence Centre, Platforms Sciences Laboratory, Defence Science & Technology Organisation, Australia. This paper was presented at the 2002 Defence Health Symposium.

elements affected by the chemical action of organophosphates. It is known that HD is a potent alkylating agent that readily attacks DNA, forming mono-functional adducts and crosslinks^{6,7}. One theory proposes that DNA damage is the initial event, leading to activation of poly(ADP)ribose polymerase and NAD⁺ depletion, leading to inhibition of glycolysis and cell death⁸. Another suggests that HD readily reacts with intracellular glutathione, which leads to loss of protection against free radicals, and inactivation of enzymes that regulate calcium homeostasis⁹. Neither of these schemes has been proven conclusively. Possible post-exposure antidotes that have been investigated include poly(ADP)ribose polymerase inhibitors¹⁰, calmodulin antagonists¹¹, NAD⁺ precursors^{12,13}, anti-inflammatory drugs¹⁴ and povidone iodine^{15,16}. However, the pathogenesis of HD injury presents an obstacle to this approach. Following exposure to HD, there is a dose-dependent latent phase, lasting from hours to days, during which a

casualty experiences no symptoms³. HD is highly lipophilic; in vapour or liquid form, it is rapidly absorbed by body tissues. Decontamination is only possible following exposure to liquid, and then it must be carried out within a few minutes of contact in order to be effective³. Studies undertaken at CBRN DC have demonstrated that breakdown of nuclear chromatin, an indication that the cell is irretrievably committed to cell death¹⁷, can be detected as soon as one hour after exposure to an *in vitro* equivalent of a vesicating dose of HD in rat thymocytes¹⁸ and normal human keratinocytes (NHEK) (Figure 1). It is therefore probable that, in the case of HD injury, by the time gross pathological changes become apparent, cellular damage is well advanced and may be beyond the reach of reversal of the biochemical changes that have taken place. In view of the difficulty associated with administering any post-exposure antidote, the pursuit of pre-treatment options appears to be the most realistic approach.

FIGURE 1: Breakdown of nuclear chromatin following exposure to HD.

NHEKs (*left*) and thymocytes (*right*) were incubated with 100 mM HD. NHEKs were embedded in agarose (4×10^6 cells per sample) prior to incubation with HD, and thymocytes were embedded after incubation. At 1 to 24 h agarose blocks were incubated with 10 mg/ml RNase at 37°C for 1h, then Proteinase K was added to 0.25 mg/ml and the samples incubated overnight. High MW DNA degradation was analysed by pulsed field electrophoresis as described in [18].



GLUTATHIONE S-TRANSFERASE, AN ENDOGENOUS DETOXYFIFYING ENZYME

Glutathione-S-transferases (GSTs) catalyse the reaction between reduced glutathione (GSH) and a broad range of electrophilic molecules (reviewed in references 19 and 20)^{19,20}. Several distinct GST subunit types that are the products of separate genes have been identified. Subunit types are distinguished by their substrate binding specificities, and proportions present in different cell types – mammalian cytosolic GSTs have been grouped into the classes: alpha (AGST), mu (MGST), pi (PGST), sigma (SGST), theta (TGST), zeta (ZGST) and omega (OGST). GSTs are thought to have an important role in mitigation of toxic injury to cells; conjugation of highly reactive electrophilic species with GSH decreases the detrimental reactivity of such

substances towards cellular macromolecules. They belong to a larger group of detoxification enzymes referred to as phase II enzymes, which are generally involved in detoxification pathways by catalysing the elimination of reactive intermediate metabolites of carcinogenic molecules^{21,22}.

Increased levels of GST activity have been found in many tumour and leukemia cell lines, where it has been correlated with resistance to various chemotherapy drugs, including alkylating species such as melphalan²³⁻²⁵. Keratinocytes express the GSTP isoform^{26,27}. Since GST has been inferred to have a role in resistance to alkylating agents, and HD is an alkylating agent that readily attacks DNA, it is possible that manipulation of GST activity in the skin might represent a strategy to moderate cellular damage caused by HD exposure.

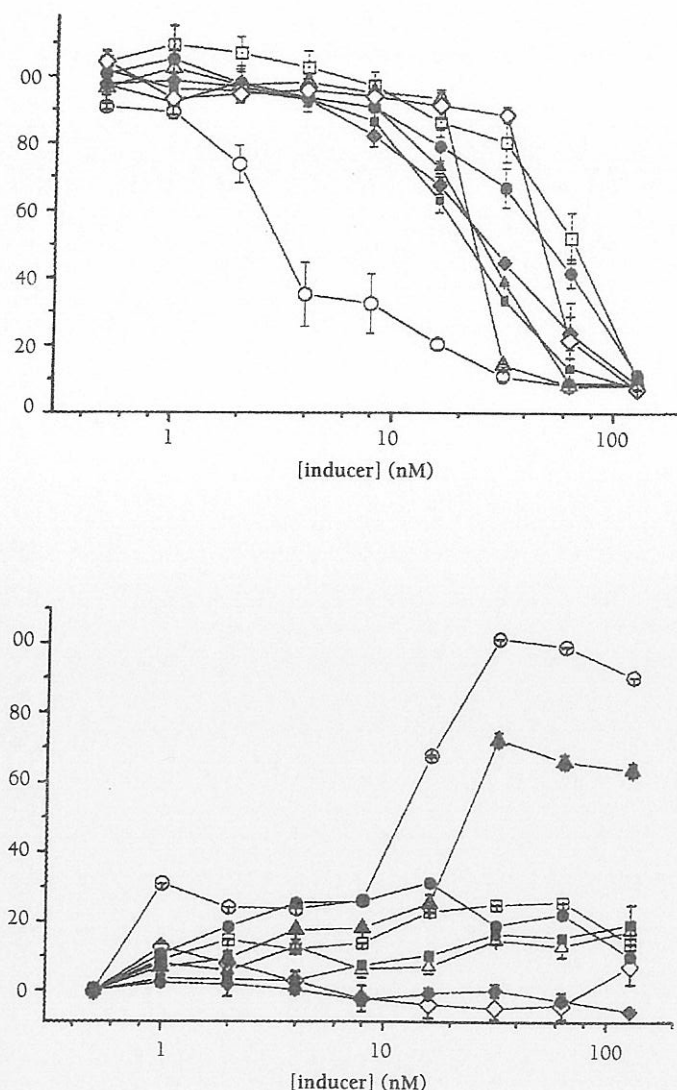


FIGURE 2: Assay of phase II enzyme inducers for toxicity to keratinocytes.

Neutral Red uptake assay (above): NHEKs were plated into 48-well culture plates (18,000 cells per well) and allowed to recover for two days in serum-free medium. Inducers were solubilized in dimethyl sulfoxide or ethanol, and diluted into medium to required concentrations (final concentration of solvent in medium 0.1% v/v). Cells were incubated with inducers for 24 h, then incubated with Neutral Red (30 mg/ml in serum-free medium) for 3h. Samples were extracted by extraction with 50% ethanol/1% acetic acid (0.4 ml per well), and NR quantified by measuring A540nm.

Lactate Dehydrogenase assay (below): cells were plated into 96-well culture plates (9,000 cells per well) and treated with inducers as above, then the assay was carried out according to the manufacturer's instructions. Assays were carried out in quadruplicate.

KEY:

- dimethyl maleate
- dimethyl itaconate
- 1-nitro-1-cyclohexene
- sulfuraphane
- ◆ 5,6-dihydro-2H-pyran-2-one
- △ 8-naphthoflavone
- ◇ 3-butylatedhydroxyanisole
- ▲ t-butyl hydroxyquinone

TOXICITY OF GST INDUCERS TO HUMAN KERATINOCYTES

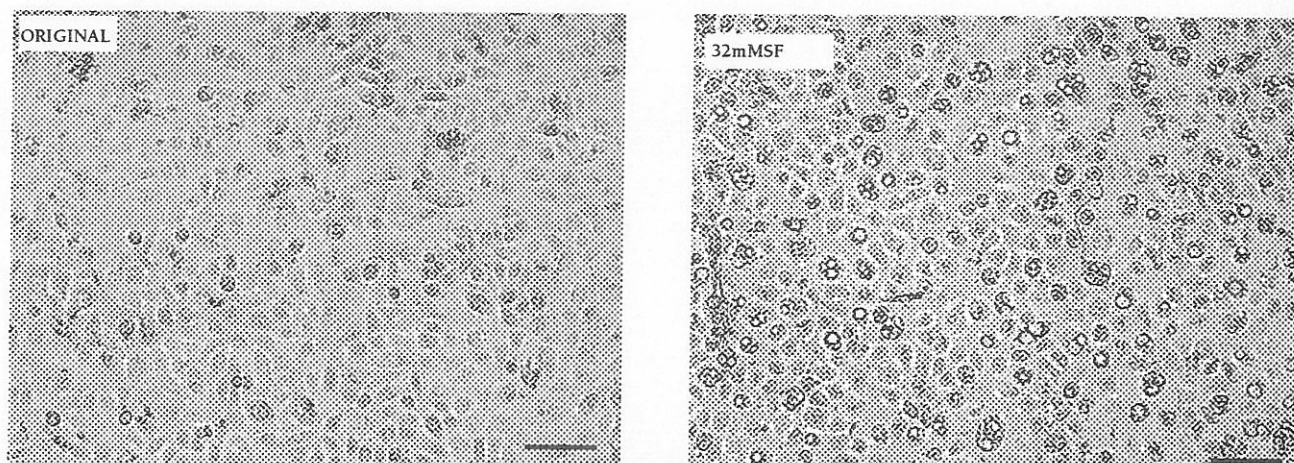
Several classes of reagent have been identified, which are able to induce increased expression of phase II detoxifying enzymes, including GSTs (discussed in references 28 to 31)²⁸⁻³¹. However, some of these inducers have demonstrated cytotoxicity towards some cell types^{32,33}, and so it was necessary to develop a method for establishing the dose limits for use with cultured NHEK. Morphology, plasma membrane integrity and active uptake of dyes by metabolically active cells are properties that have all used to assess cell viability³⁴. For NHEK, a protocol exploiting the uptake of the dye Neutral Red (NR)

was developed. This assay relies on the active uptake of the dye by the lysosomes of uninjured cells³⁵.

To date, several inducers have been tested for cytotoxic effects towards NHEK: dimethyl maleate, 1-nitro-1-cyclohexene, b-naphthoflavone, dimethyl itaconate, 5,6-dihydro-2H-pyran-2-one, 3-butylated hydroxyanisole and t-butylated hydroxyquinone (Figure 2). The upper limit of concentrations at which these reagents demonstrate toxicity towards NHEK is 5 – 10 mM. However, NR uptake clearly showed that 1-nitro-1-cyclohexene reduced viability to approximately 50% at only 5 mM – this reagent is probably too toxic to consider for further investigation.

FIGURE 3: Morphological changes in keratinocytes exposed to sulforaphane.

Light microscopic examination of NHEK x 100. Cells were incubated in serum-free medium alone (*left panel*) or medium containing 32 mM sulforaphane (*right panel*) for 24 h. Black bar at bottom right of each panel represents 0.1 mm.



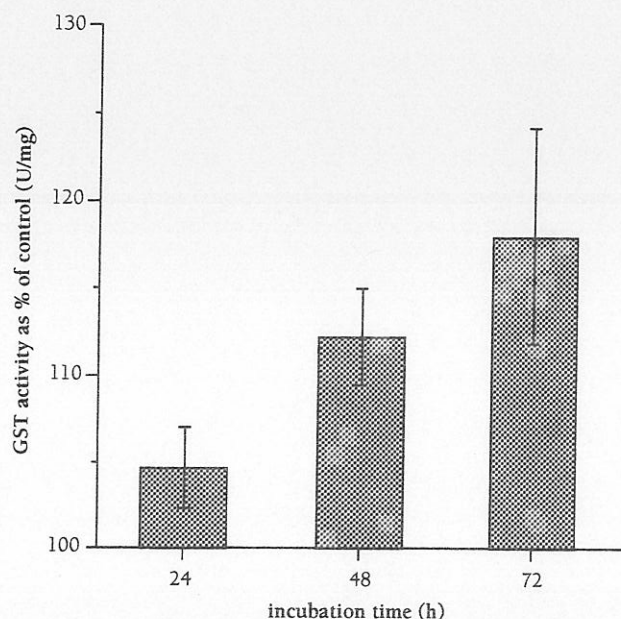
Results from a commercial kit (purchased from Roche) measuring cell survival by detecting leakage of lactate dehydrogenase (LDH) were found to be misleading for this cell model. Comparison of results obtained from the two different methods showed that the LDH detection did not correlate with the NR assay for all inducers tested, and was not correlated with obvious morphological changes observed by light microscopy. An example of this is shown at Figure 3. Cells incubated with 32 mM sulforaphane were clearly showing abnormal morphology, with formation of large vacuoles, whilst NR

uptake indicated viability reduced to 33%; however, the LDH assay did not reflect this (cytotoxicity ~16%). Therefore, after preliminary testing the LDH release kit was discarded.

MEASUREMENT OF GLUTATHIONE S-TRANSFERASE IN KERATINOCYTES

A colorimetric assay for GST was devised, utilising the substrate preference of GSTP for 1-chloro-2,4-dinitrobenzene. GST catalyses the conjugation of reduced glutathione to 1-chloro-2,4-dinitrobenzene to give a product with an absorbance maximum at 340 nm³⁶.

The assay procedure was scaled so as to run multiple samples simultaneously in a 96-well microplate format, using a Multiskan Ascent spectrophotometer equipped to perform kinetics calculations.



Initial assays showed an increase in GSTase activity in NHEK incubated with 5 mM sulforaphane, which was statistically significant after 48 h (Figure 4).

FIGURE 4: GST activity in keratinocytes incubated with sulforaphane.

NHEK were seeded to 25cm² culture flasks so that they were ~80% confluent at harvest. All assays were in triplicate. Cells were incubated with 5 mM sulforaphane in serum-free medium. To collect samples, cells were scraped into cold 0.25M sucrose, sonicated (2 x 10 bursts, 50% intensity) and centrifuged at 100,000 g for 1h at 4°C. The supernates were collected for assay. Protein determination was done using BioRad's DC Reagent kit (BSA as standard). GST activity was measured by mixing 150 µl starter solution (2.5mM glutathione + 1mM CDNB in 0.1 M potassium phosphate buffer, pH 6.5) with 100 µl sample in a 96-well microplate plate, and monitoring A340nm at 25°C. 1 unit of GST activity = conjugation of 1 mmole of CDNB with glutathione per minute (at pH 6.5, 25°C).

CONCLUSIONS

NHEK in culture are being used as a model to assess the feasibility of using GST, an endogenous detoxification enzyme, as a means of ameliorating cell damage caused by exposure to the chemical warfare agent HD. An assay protocol suitable to this cell type to measure has been developed to measure cell survival. Several inducers of phase II detoxifying enzymes have been assayed for cytotoxicity towards NHEK; on the basis of these tests, at least one inducer has already been

rejected for further consideration as it is too toxic to NHEK to be of use. An assay to measure GST activity in NHEK has been successfully developed and adapted to run in a microplate format, thus allowing the simultaneous testing of replicates of multiple samples. Initial tests show that sulforaphane can induce increased GST activity in NHEKs. These assay systems should prove useful in ongoing assessment of the ability of such reagents to increase cell resistance to damage by HD.

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ORIGINAL ARTICLES

The 1998 Army Recruit Health and Diet Survey

Christine K. Booth and Ross A. Coad¹

ABSTRACT

Objectives: To determine the adequacy of Army recruits' usual diet before commencement of training. To identify problems which may be addressed in future preventative health programs.

Design: Recruits completed a health and diet questionnaire, were weighed and donated a fasting blood sample for measurement of cholesterol, fasting triglycerides, apolipoprotein B, homocysteine, ferritin and vitamins (total antioxidant capacity, folate, thiamin, riboflavin and vitamin B6).

Participants: Recruits on their first day of Army recruit training were invited to participate. Participants recording an implausible level of energy intake or who did not complete the questionnaire were excluded. The final sample included 107 (males = 91) for dietary survey and 184 (males = 159) for biochemistry tests.

Main outcome measures: Nutrient intake, food risk score, body mass index, biochemical vitamin status, cardiovascular disease risk factors.

Results: Recruits mostly had ideal body weight, had a high rate of smoking (26%) and high participation in organised sports. The average diet was too high in fat and unbalanced with respect to the recommended core food groups. Recruits were at risk of eating insufficient calcium, magnesium and zinc and folate, thiamin and riboflavin deficiencies were revealed. Females were at risk of iron deficiency. Half had at least one risk factor for cardiovascular disease.

Conclusions: Nutrition education should aim to lower the prevalence of cardiovascular risk factors and address the special dietary needs of female personnel. Education strategies need to build an awareness of the association between lifestyle factors and increased risk of cardiovascular disease as well as improving the eating habits of personnel.

Key words: Army recruits, military, risk factors, dietary intake, nutritional status

INTRODUCTION

THE US MILITARY is sufficiently concerned about modifiable cardiovascular (CV) risk factors amongst active-duty service personnel to have implemented nutrition and health promotion initiatives during the 1980's¹ and follow-up nutrition assessment programs² have shown the benefits of changes implemented in the service messes. Service personnel eating in messes are more likely to eat the recommended servings.

Medical Simulation Centre has developed expertise in medical simulation of fruit and vegetables than the general US population³ and over the past decade have reduced their fat intake and lowered their serum cholesterol². Evaluation of US Navy health promotion

efforts in two longitudinal cohort studies of life-style factors, an eight year study (n = 640) and an eleven year study (n = 1576), demonstrated significant positive effect on fitness and health behaviours⁴.

Recent information concerning the eating habits of ADF personnel is not available. However, during the 1980's ADF personnel eating in barracks were apparently consuming excessive salt and fat. Problems identified at the time included a low rate of attendance at messes, provision of food from commercial fast-food outlets and over consumption of food by sedentary and active ADF members^{5,6}.

The ADF Health Status report identified the development of an ADF health promotion program with a

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focus on injury prevention, mental health and CV health as a priority activity⁷. The present study complements this activity by determining the adequacy of the dietary intake of Army recruits prior to commencing their training and highlighting problem areas, which may become the basis for future health promotion programs.

METHODS

Participants

During the period, March – May 1998, Army recruits arriving at Army recruit training centre (ARTC) were invited to take part in a health and diet survey. Approximately 184 recruits (159 males and 25 females) took part in the survey during their first day at the Kapooka Army Base. Most recruits (90%) were school leavers aged between 17 and 25 years (range 17 to 36 years). Three recruits were university graduates and 13 had graduated from a college of higher education. Participants completed a health and diet questionnaire, had their weight and height recorded and donated a fasting blood sample. The questionnaire consisted of 15 demographic and medical questions and a 152-food semi-quantitative food frequency questionnaire (FFQ), which had been validated against a three-day food diary⁸. The experimental procedures were approved by the Australian Defence Medical Ethics Committee (ADMEC protocol 133/97). Written consent was obtained from each participant after the details of the study were explained.

Biochemical analysis

Subjects fasted overnight. The next morning before breakfast a 25 mL venous blood sample was drawn. Blood was processed within one hour of collection by centrifugation then washing and dilution of red blood cells into appropriately buffered solutions. Plasma and red blood cell samples were transported frozen to a central laboratory for analysis. Vitamin B6 (pyridoxal 5'-phosphate) and riboflavin status were assessed by use of automated functional enzyme methods⁹, red blood cell thiamin was measured by microbiological assay¹⁰, total plasma homocysteine was measured by High Performance Liquid Chromatography method¹¹ and total antioxidant capacity (TAOC) was measured by automated colorimetric assay using reagents supplied by Randox Laboratories, UK. Plasma lipids (cholesterol and triglycerides) were measured by auto-

mated enzymatic assays using manufacturer-supplied reagents (Roche Diagnostics, New Jersey, USA). High density lipoprotein (HDL) cholesterol was measured by the same technique following precipitation of low-density lipoprotein (LDL) and very low-density lipoprotein with polyethylene glycol. Ferritin and apolipoprotein B were measured by particle-enhanced nephelometric assay using manufacturer-supplied reagents (Behring BNA, Dade Behring, Germany).

Data analysis

Nutrient intake was calculated using the DIET/1 NUTRIENT calculation software (Xyris Software, Brisbane, Australia), which used the NUTTAB 92 database, a database of Australian foods. This database does not include values for folates, vitamin B6 or vitamin E. Participants with a ratio of energy intake to basal metabolic rate of less than 1.10 and those who completed the FFQ incorrectly were excluded from dietary data analysis¹². Individual food risk scores were calculated by comparing the individual's intake of the food groups (fruit, vegetables, dairy products, meat and cereal products) against the 'Core Food Groups' of the National Health and Medical Research Council (NHMRC)¹³. A score of '0' indicated that recommendations for all five groups were met and a score of '5' indicated that no food-group recommendations were met.

Statistical analyses were performed with SPSS (Statistical Package for the Social Sciences, version 9.0, 1999, SPSS, Inc., Chicago, IL). Descriptive statistics, including means, medians, standard deviations, 2.5th and 97.5th percentiles were used to compare dietary intake with the recommended dietary intakes (RDI)¹⁴ and the National Nutrition Survey¹⁵. These also allowed comparison between biochemical measurements with clinical cut-offs. Where required, data were transformed (natural log) to normalise the distributions. Significance was accepted at $p < 0.05$ and in regression analyses an r^2 value ≥ 0.25 with $p < 0.05$. Multiple linear and binomial logistic regression analyses were used to assess associations between variables. Comparison of means was achieved by use of the independent t test and Levene's test for equality of variances. The distribution of nutrient intakes below the RDI was determined, and combined with probability statistics to calculate the number of subjects likely to have reported intakes below their individual

requirements. This approach recognises that the RDI overestimates nutrient requirements of almost all individuals in the population¹⁶.

RESULTS

Health questionnaire

The questionnaire revealed an apparently healthy group of young people with a high rate of smoking (26%) and high participation in organised sports (80%). Although 62% of recruits had more than two standard drinks in the week prior to the survey, the reported average daily intake of alcohol was 0.5 standard drinks. Vitamin or nutritional supplements were taken by 13% of recruits. The incidence of upper respiratory tract infection was 26% in the fortnight preceding the survey. The average body mass index of recruits was 21 (SD = 2, range 15 to 27) and only

three recruits had a BMI > 25. Eighteen recruits (10%) reported a family history of heart disease.

Dietary intake

Figure 1 summarises the overall dietary balance by presenting the distribution of food risk scores. Figures 2 and 3 present the mean intakes of vitamins and minerals, respectively.

Nutrient intake was not associated with age, gender, BMI, education nor any of the biochemistry measures. Table 1 compares the mean daily energy and nutrient intakes of recruits with the results from the 1995 National Nutrition Survey. Table 2 provides an estimate of the adequacy of micronutrient intake and Table 3 presents the mean dietary intake, by food groups, of the recruits. No associations were found between dietary intake and biochemical measurements.

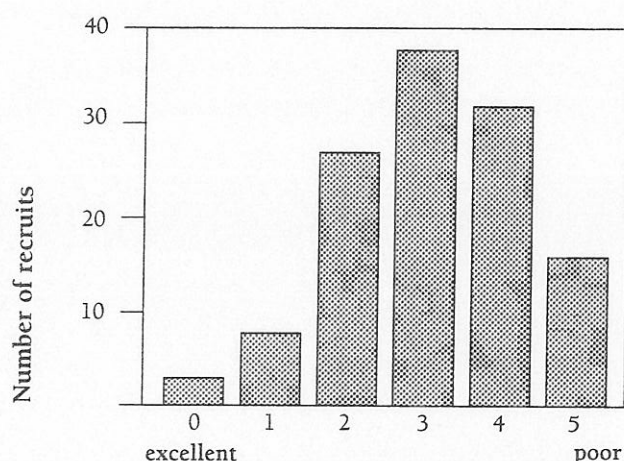


FIGURE 1: Distribution of food risk scores (n = 107).

FIGURE 2: Mean and SD for daily intake of vitamins. The columns extend from 0 to the mean of the values and the bars represent the SD. Results are presented as a proportion of RDI. [RDI = recommended dietary intake.]

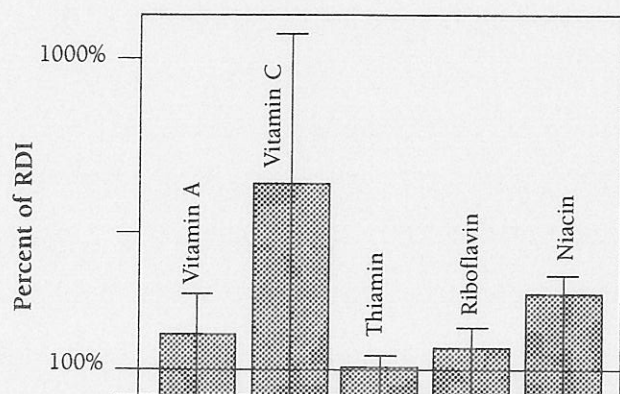


FIGURE 3: Mean and SD for daily intake of minerals. The columns extend from 0 to the mean of the values and the bars represent the SD. Results are presented as a proportion of RDI. [RDI = recommended dietary intake.]

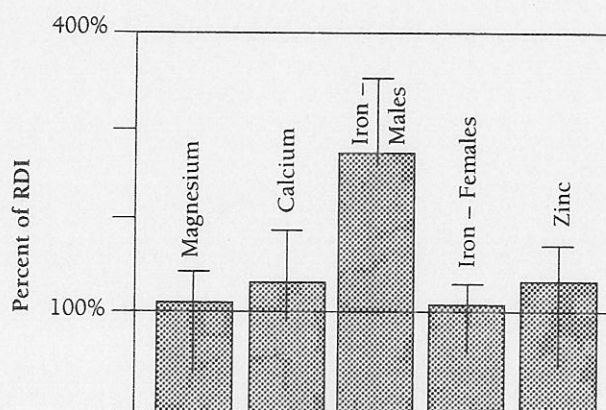


TABLE 1: Mean and SD for daily energy and nutrient intakes compared with the National Nutrition Survey and RDI. (* Males n = 91, females n = 16. Age range 17 – 36 yr, mean age 21 ± 3.5 yr. † The data collected in the present study was by use of a food frequency questionnaire and data collected by the National Nutrition Survey was by a 24 hour recall method. Data for the National Nutrition Survey are presented for all persons aged 19 and over with an energy intake to BMR ratio ≥ 0.9 and for all persons aged 19 to 24 years. [RDI = recommended dietary intake; EI = energy intake; BMR = basal metabolic rate.]

	Sex	Recruits*	National Nutrition Survey †		RDI ¹⁴
			Aged 19 and over EI ≥ 0.9 BMR	Aged 19-24	
Energy (MJ)	M	12.0 ± 3.0	11.8	13.3	9.8 - 11.2
	F	10.2 ± 3.0	8.4	8.4	8.5 - 9.7
Protein (g)	M	127 ± 34	116	128	55
	F	107 ± 29	81	78	45
Carbohydrate (g)	M	321 ± 105	321	376	
	F	289 ± 82	233	243	
Fat (g)	M	116 ± 33	106	119	
	F	93 ± 50	77	75	
Alcohol (g)	M	6.3 ± 7.2	20	15	
	F	3.7 ± 4.1	9	7	
Fibre (g)	M&F	29 ± 12	25	23	30
Magnesium (mg)	M	423 ± 149	404	390	320
	F	405 ± 157	310	273	270
Calcium (mg)	M&F	1214 ± 498	919	929	800
Iron (mg)	M	18 ± 6	17	18	7
	F	15 ± 5	13	12	14
Zinc (mg)	M&F	16 ± 5	13	14	12
Vitamin A (mg retinol equivalents)	M&F	1413 ± 616	922	1065	750
Vitamin C (mg)	M&F	241 ± 198	102	135	40
Thiamin (mg/1000kJ)	M&F	0.21 ± 0.05	0.15	0.2	0.1
Riboflavin (mg/1000kJ)	M&F	0.30 ± 0.11	0.19	0.2	0.15
Niacin (mg niacin equivalents/1000kJ)	M&F	4.72 ± 0.79	4.09	4.4	1.6

TABLE 2: Dietary assessment of micronutrient adequacy

Nutrient	Sex	Mean Intake: RDI (%)	Proportion below RDI (%)	Probability Estimate of Inadequacy* (%)
Vitamin A equivalents	M&F	188	9	3
Thiamin	M&F	209	0	0
Riboflavin	M&F	197	4	1
Niacin equivalents	M&F	295	0	0
Vitamin C	M&F	602	2	1
Calcium	M&F	152	18	10
Magnesium	M	132	26	7
	F	150	19	10
Iron	M	254	0	0
	F	110	50	19
Zinc	M&F	136	19	6

(*The distribution of nutrient intakes below the RDI was determined and combined with probability statistics to calculate the number of subjects likely to have intakes below their individual requirements. This approach recognises that the RDI overestimates nutrient requirements of almost all individuals in the population¹⁶. RDI = recommended dietary intake)

TABLE 3: Mean daily dietary intakes by food group*. (* Food group intakes are expressed as number of serves. Serving size is indicated in parentheses).

Food group	Mean	Median	SD	Minimum	Maximum
Alcoholic beverage (10g ethanol)	0.5	0.4	0.56	0.01	3.7
Non-alcoholic beverages (100 mL)	6.9	6.0	3.9	1.4	20.0
Cereals (1/2 cup raw, 2 slices, 2 biscuits)	4.9	4.3	2.7	1.9	22.5
Dairy (250 mL milk, 30 g cheese)	2.8	2.4	1.6	0.1	8.1
Egg (1 whole)	0.3	0.3	0.36	0	3
Oils & butter (1 tablespoon)	1.3	1.1	1.0	0.02	6.6
Fish (120 g)	0.27	0.12	0.28	0	1.7
Fruit (1 whole, 2 small)	1.7	1.4	4.5	0	8.4
Fruit juice (250 mL)	1.0	0.57	1.4	0	8.0
Pulses (1/2 cup)	0.2	0.01	0.26	0	1.3
Meat (120 g, 1/4 chicken)	1.9	1.8	0.9	0.2	5.1
Nuts (1/2 cup)	0.24	0.13	0.27	0	1.3
Confectionery (50 g bar)	0.53	0.36	0.59	.03	4.2
Vegetables (1/2 cup)	5.1	4.7	2.8	0.4	16.6

Biochemistry measures

Table 4 presents the mean results for the biochemistry measures compared with clinical cut-offs. Apart from plasma ferritin where females had lower values ($t = 4.836$, $p < 0.01$), males and females had similar results for all measurements. When the Army recruits were compared with a group of blood donors of similar

age¹⁷ (mean = 23.1 ± 3.8 yr, 388 males and 491 females), the recruits (mean = 21 ± 3.5 yr, 91 males and 16 females) had poorer thiamin ($t = 4.325$, $p < 0.01$) and riboflavin ($t = 7.385$, $p < 0.01$) status and better vitamin B-6 status ($t = 10.304$, $p < 0.01$). No associations were found between age and biochemical measurements.

TABLE 4: Biochemical assessment of nutrient adequacy.

(* Of the 8 participants with low plasma ferritin concentrations, 4 were female. TAOC = total antioxidant capacity; HDL = high-density lipoprotein; LDL = low-density lipoprotein; EGRAC = erythrocyte glutathione reductase activity coefficient, a functional measure of riboflavin status; EASTAC = erythrocyte aspartate transaminase activity coefficient, a functional measure of vitamin B6 status.)

	Mean and SD (n = 184)	Clinical Cut-off	Proportion outside clinical range (% , n)
TAOC (mmol/L)	1.71 ± 0.19	≥ 1.60	28.6%, 52
Total Cholesterol (mmol/L)	4.5 ± 1.03	≤ 5.2	24.6%, 45
Triglycerides (mmol/L)	1.02 ± 0.40	≤ 1.30	9.8%, 18
HDL-Cholesterol (mmol/L)	1.08 ± 0.28	≥ 0.9	2.2%, 4
LDL-Cholesterol (mmol/L)	2.99 ± 0.93	≤ 3.50	24%, 44
Apolipoprotein B (g/L)	1.05 ± 0.31	≤ 1.30	19%, 35
Apolipoprotein B:LDL-C	0.23 ± 0.05	< 0.26	30%, 55
Ferritin (g/L)	80.2 ± 56.1	> 15.0	4.4%, 8*
Total Homocysteine (mmol/L)	13.5 ± 11.5	< 10.0	55.7%, 101
Red Cell Thiamin (nmol/L)	283 ± 97	≥ 190	13.2%, 24
EGRAC (ie riboflavin)	26.1 ± 16.6	≤ 40	17%, 31
EASTAC (ie Vitamin B6)	74.9 ± 21.1	≤ 120	0

DISCUSSION

The average daily diet of the recruits provided 12000 kJ (males) and 10000 kJ (females) as protein (18%), carbohydrate (44%), fat (36.5%) and alcohol (1.5%). This represents an average diet, which is too high in fat according to the National Goals and Targets for Improving Health¹⁸. Figure 1 shows that the recruits' diet is biased towards an unbalanced eating pattern. Although the recruits were at low risk of eating insufficient vitamins, riboflavin, thiamin and folate deficiencies were identified. The Army recruits may have had worse thiamin and riboflavin status than a group of their peers from the general Australian population. Some recruits (male and female) were at risk of eating insufficient calcium (10%), magnesium (10%), and zinc (6%) and females were at risk of eating insufficient iron (19%).

The dietary intake of the recruits was compared with the dietary intake of adults of the same age recorded during the 1995 National Dietary Survey. Although the National Dietary Survey provides insufficient data to allow statistical comparison and the two surveys used different dietary assessment tools, some observations can be made. The energy and macronutrient intakes (protein, carbohydrate, fat) of recruits appears similar to the general public, their intake of vitamins and minerals might be higher and their alcohol consumption might be lower than the general public. This is potentially positive, because it suggests that the recruits eat better than the general public. Such a finding is consistent with this group (recruits) being selected for their high level of physical fitness and good body mass index.

Thiamin has been considered to be one of the marginally adequate nutrients in the Australian diet. It was believed that thiamin enrichment of flour to the concentration of 6.4 mg/kg, which commenced in 1991, would alleviate the problem of poor thiamin status in the Australian population¹⁹. However, the finding of significant prevalence of thiamin deficiency amongst first-time blood donors¹⁷ and Army recruits suggests that the benefit of this public health measure requires reassessment.

One in four female recruits had reduced iron stores. This finding, coupled with the apparently poor dietary intake of iron by female recruits, suggests that female soldiers are at risk of iron deficiency. This comes as no surprise, because a 1995 review of iron

status in Australia identified teen-aged girls and women of child-bearing years as having high rates of iron deficiency²⁰.

The antioxidant status of 29% of recruits was shown to be less than optimal. Evidence is accumulating that oxidative stress contributes to the pathogenesis of chronic diseases such as atherosclerosis and that it slows recovery from a period of vigorous physical activity. Because it is difficult to isolate the individual contributions of the various antioxidant systems in the body, the measurement of the total antioxidant capacity (TAOC) may be the most relevant measurement to assess antioxidant status. A lower than normal TAOC can therefore result from either a primary reduction in antioxidant resistance or a secondary reduction as a result of increased antioxidant stress. The method used in the present study is influenced by urate, albumin, ascorbate, glutathione, vitamin E and bilirubin. One criticism of the method concerns the non-stoichiometric response of the assay to the different antioxidants²¹. A further problem is that of defining an appropriate clinical cut-off. Our laboratory has not established an optimal reference interval for the assay. In the present study a manufacturer's reference has been used.

Possibly the most important finding concerns folate status. Elevated homocysteine, which has been identified as an independent risk factor for peripheral, cerebral and coronary vascular disease, is inversely related to folate status. Moderately elevated homocysteine concentrations may be the first biochemical marker of insufficient intracellular folate. Recent studies suggest that the cut-off for a healthy plasma homocysteine concentration (ie minimal risk for CV disease) may fall below 10-15 mmol/L²². More than half (56%) of recruits had homocysteine values > 10 mmol/L.

Apart from elevated homocysteine, additional CV risk factors were identified amongst the recruits. One in four had elevated cholesterol, 19% had elevated apolipoprotein B and 10% had elevated triglyceride concentration. Of these results, apolipoprotein B is possibly the best predictor of risk. A predominance of small, dense LDL (LDL-III) in plasma is predictive of coronary risk²³ and the concentration of apolipoprotein B tends to increase with increased concentration of LDL particles. The ratio of apolipoprotein B to LDL-cholesterol provides an estimate of the absolute number of LDL particles, which is known to be an independent risk factor for coronary heart disease.

Elevated fasting plasma triglyceride concentration (>1.5 mmol/L) in the presence of elevated apolipoprotein B to LDL-cholesterol ratio (>0.26) is highly predictive of the presence of small dense LDL particles²⁴. Five percent of recruits had both elevated plasma triglyceride concentration and elevated apolipoprotein B to LDL-cholesterol ratio.

The estimated dietary intake of foods and nutrients by recruits did not predict the apparent prevalence of vitamin deficiency and CV risk factors. This is not unexpected because the FFQ tool is best used to identify trends in eating patterns rather than individual nutrient intakes. The lack of correlation between estimated dietary intake and biochemical measures highlights the need to include blood tests as part of nutritional status monitoring. Moreover, non-dietary factors such as cigarette smoking and level of physical activity may be contributing to the observed biochemical status^{25, 26}.

The authors recommend that nutrition education be targeted at lowering the prevalence of CV risk factors among Army personnel and addressing the special dietary needs of female personnel. Education strategies need to build an awareness of the association between lifestyle factors and increased risk of CV disease as well as improving the eating habits of per-

sonnel. Furthermore, it is recommended that a uniform through-career approach to nutrition education should be adopted at Defence policy level and that such a program should be routinely monitored by use of surveys such as that reported here.

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DECLARATION

There was no conflict of interest with respect the conduct of this survey. This survey was sponsored by Defence Health Services and funded by the Department of Defence in accordance with the Defence Science and Technology Organisation's research tasking process. The sponsor had no involvement in the conduct of the survey, nor gave direction regarding the publication of the report. DSTO management authorisation was required before the manuscript could be submitted for publication.

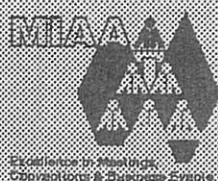
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ORIGINAL ARTICLES

Screening for Cervical Cancer

Karen Leshinskas¹

INTRODUCTION

RECENT ADVANCES IN TECHNOLOGY have resulted in the emergence of a new method of screening for cancer in women. There is an existing widely established method that has good reliability. The new method has been evaluated overseas and has been widely adopted as an acceptable alternative to the older widely established method.

Current Australian health policy is that the new test alone cannot be trusted to confer the same degree of accuracy as the old test.¹ If doctors or women wish to use the new test an additional cost is involved.

The old test (also known as the Papanicolaou or 'P' test) and the new test (also known as the Thin Prep or 'T' test) may have to be repeated due to unsatisfactory technique. If the technique is satisfactory, then either a negative or positive result is given. If the test is negative, the woman is advised to have the test repeated again in two years in most cases. If the test is unsatisfactory, it must be repeated and a negative result obtained. If the test is again unsatisfactory, the woman is referred to a specialist for assessment. The specialist will determine by special technique if the woman has the disease or not. If the test is positive the woman is referred to a specialist for assessment to determine if she has the disease or not.

POLICY

The ADF has been advised to continue using the old test and to test more often than recommended. There appeared to be little basis for this opinion and the resultant departure from national policy raises ethical issues.

National policy is based on studies in civilian populations. These populations may differ from the Australian Defence Force (ADF). Therefore, an attempt should be made to review the methods and make an informed decision in terms of best possible outcome for the females concerned and thus the ADF.

METHODOLOGY

The problem lends itself to decision tree analysis utilising Bayes's Theorem. References have been sought

from numerous sources. Where possible ADF data has been utilised.

The test results from both tests from Unit 1 (sample of 571) were compared with the test results from Unit 2 (sample of 86). The two samples were comparative. Therefore, it can be assumed that Unit 1 is a representative sample of the ADF. Unit 1 results were of a larger number, so will be more valid in statistical comparisons. For Unit 1, P testing was previously well established and T testing was introduced in 1998. P testing resulted in 15% unsatisfactory tests, whereas T testing resulted in only 4% unsatisfactory tests.

Following unsatisfactory tests, the test must be repeated. Following repeat testing, all unsatisfactory and positive tests are referred. P testing, when satisfactory, tested 68% negative and 32% positive at Unit 1. T testing, when satisfactory, tested 81.72% negative and 13.98% positive also at Unit 1. Follow up data on presence or absence of disease was not available for the ADF samples. The results of previous studies have a lot of information on presence of disease after testing²⁻⁵.

A comprehensive study has determined the sensitivity and specificity of the tests and, from this, we can use Bayes's Theorem to determine the probabilities of disease (state of nature) given the results of the tests. Health Insurance commission statistics⁶ (and ADF data) also confirm that the overall prevalence of the disease is 3.6%⁷. Thus the studies also show reasonable representation of Australian data.

Australian population data⁸ put the number of females aged 15 to 70 at 6,650,055. The recorded number of P tests in Australia was 1,325,680 in 1999⁶. As a maximum (many P tests need to be repeated due to an unsatisfactory result and some females need P tests six monthly), this represents only 19.9% of the Australian female population. Given that the current recommendation is for every eligible female to have tests every two years, at best only 39.87% of females are having P tests every two years. Thus, given this situation, it is highly likely that the rates of disease in the Australian population are underestimated.

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P TESTS

We are given the 'true positive rate' as 81.6%. The true positive rate is defined as true positives/(true positives +

false negatives).⁹ This equates to a probability of 0.8160.

We are also given the true negative rate as 95.8% (true negatives/(true negatives + false positives)).⁹

P TEST	DISEASE	
TEST	POSITIVE	NEGATIVE
POSITIVE	0.816	0.042
NEGATIVE	0.184	0.958
	0.036	0.964

BAYE'S THEOREM¹⁰:

$$P(A|B) = \frac{P(B|A)*P(A)}{P(B|A)*P(A)+P(B|A^*)*P(A^*)}$$

Thus, we want to know the probabilities of disease given the results of the test and we know the probabilities of the test given disease.

Disease present = D+; Disease absent = D-; P test positive = P+; P test negative = P-

$$\begin{aligned} P(D+|P+) &= \frac{P(P+|D+)*P(D+)}{P(P+|D+)*P(D+)+P(P+|D-)*P(D-)} \\ &= \frac{0.816*0.036}{0.816*0.036 + 0.042*0.964} \\ &= 0.4205 \end{aligned}$$

$$\begin{aligned} P(D-|P+) &= \frac{P(P+|D-)*P(D-)}{P(P+|D-)*P(D-)+P(P+|D+)*P(D+)} \\ &= \frac{0.042*0.964}{0.042*0.964 + 0.816*0.036} \\ &= 0.5795 \end{aligned}$$

$$\begin{aligned} P(D+|P-) &= \frac{P(P-|D+)*P(D+)}{P(P-|D+)*P(D+)+P(P-|D-)*P(D-)} \\ &= \frac{0.184*0.036}{0.184*0.036 + 0.958*0.964} \\ &= 0.0071 \end{aligned}$$

$$\begin{aligned} P(D-|P-) &= \frac{P(P-|D-)*P(D-)}{P(P-|D-)*P(D-)+P(P-|D+)*P(D+)} \\ &= \frac{0.958*0.964}{0.958*0.964 + 0.184*0.036} \\ &= 0.9929 \end{aligned}$$

Constructing the conditional probability table:

P TEST	DISEASE	
TEST	POSITIVE	NEGATIVE
POSITIVE	0.4205	0.5795
NEGATIVE	0.0071	0.9929

If the P test is negative, then there is a 0.9929 probability that the disease will be absent, and a probability of .0071 that it will be a false negative. If the P test is positive, then there is 0.4205 probability of disease being present, and 0.5795 probability of disease being absent (false positive).

T TESTS

We are given the 'true positive rate' as 92.6%. True positive rate is defined as true positives/(true positives + false negatives). This equates to a probability of 0.9260. We are also given the true negative rate as 95.8% (true negatives/(true negatives + false positives)).

T TEST	DISEASE	
TEST	POSITIVE	NEGATIVE
POSITIVE	0.926	0.042
NEGATIVE	0.174	0.958
	0.036	0.964

BAYE'S THEOREM¹⁰:

$$P(A|B) = \frac{P(B|A) \cdot P(A)}{P(B|A) \cdot P(A) + P(B|A^c) \cdot P(A^c)}$$

Thus, we want to know the probabilities of disease given test and we know the probabilities of test given disease. Disease present = D+; Disease absent = D-; T test positive = T+; T test negative = T-.

$$\begin{aligned} T(D+|T+) &= \frac{T(T+|D+) \cdot T(D+)}{T(T+|D+) \cdot T(D+) + T(T+|D-) \cdot T(D-)} \\ &= \frac{0.926 \cdot 0.036}{0.926 \cdot 0.036 + 0.042 \cdot 0.964} \\ &= 0.4516 \end{aligned}$$

$$\begin{aligned} T(D-|T+) &= \frac{T(T+|D-) \cdot T(D-)}{T(T+|D-) \cdot T(D-) + T(T+|D+) \cdot T(D+)} \\ &= \frac{0.042 \cdot 0.964}{0.042 \cdot 0.964 + 0.926 \cdot 0.036} \\ &= 0.5484 \end{aligned}$$

$$\begin{aligned}
 T(D+|T-) &= \frac{T(T-|D+)*T(D+)}{T(T-|D+)*T(D+)+T(T-|D-)*T(D-)} \\
 &= \frac{0.074*0.036}{0.074*0.036 + 0.958*0.964} \\
 &= 0.0029 \\
 T(D-|T-) &= \frac{T(T-|D-)*T(D-)}{T(T-|D-)*T(D-)+T(T-|D+)*T(D+)} \\
 &= \frac{0.958*0.964}{0.958*0.964 + 0.074*0.036} \\
 &= 0.9971
 \end{aligned}$$

Constructing the conditional probability table:

T TEST	DISEASE	
TEST	POSITIVE	NEGATIVE
POSITIVE	0.4516	0.5484
NEGATIVE	0.0029	0.9971

If the T test is negative, then there is a 0.9971 probability that the disease will be absent, and a probability of .0029 that it will be a false negative. If the P test is positive, then there is 0.4516 probability of disease being present, and 0.5484 probability of the disease being absent (false positive).

For unsatisfactory tests, there is no information available as to whether there are differing rates of disease amongst this group. Thus, the same rates of disease versus no disease for each test will be used.

When the female is referred for assessment following a positive test (or repeated unsatisfactory), she undergoes a procedure and consultation. If the disease is found to be present following this assessment, then she will have minor surgery. Minor surgery will result in one day in hospital and approximately seven days sick leave. If the disease is not detected in time, which will be the consequence of all false negative tests or no testing when disease is present, then the woman will have to have major surgery.

The average daily income of women in the ADF is \$314.78. This was calculated using ADF 1999 census data¹¹ and the DMPLS ready reckoner¹². This figure was used in the calculation of 'loss to the ADF' for an individual in hospital or on sick leave.

CALCULATING PAYOFFS (IN 2000 \$AUD)

Cost of performing a P test

$$\begin{aligned}
 &= \text{Test cost} + \text{Doctors wages (1/2 hour)} \\
 &= \$18.50 + \$35.00 = \$53.50
 \end{aligned}$$

Cost of performing a T test

$$= \$27.00 + \$35.00 = \$62.00$$

Cost of performing both tests (current cost) = \$80.00

Referral for assessment

$$\begin{aligned}
 &= \text{Procedure Cost} + \text{Consultation cost} \\
 &= \$49.70 + \$150.00 = \$199.70
 \end{aligned}$$

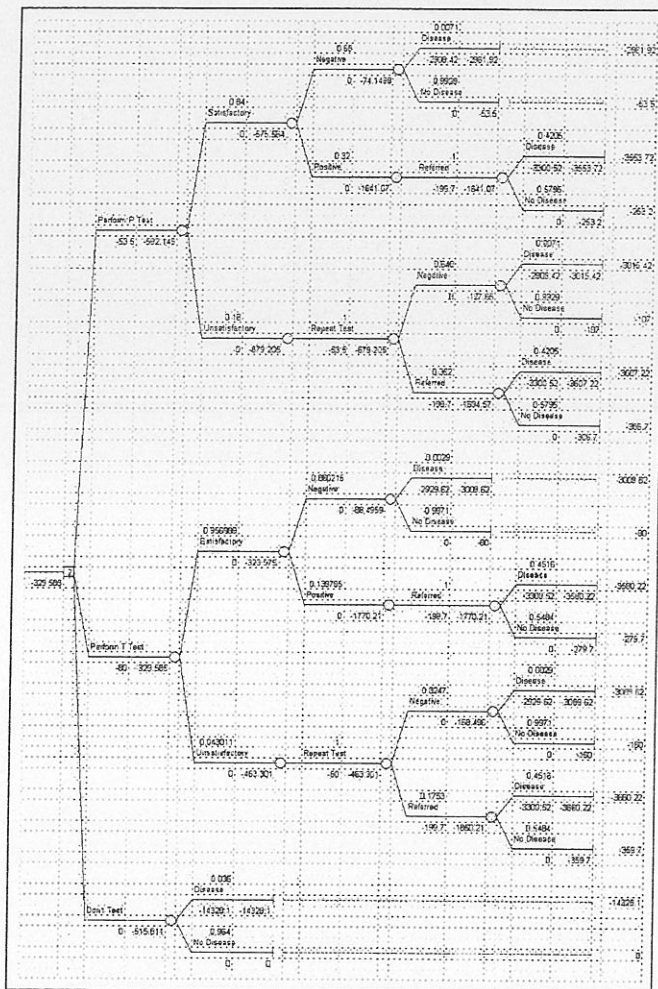
Minor surgery

$$\begin{aligned}
 &= \text{Surgery} + \text{anaesthetic} + \text{consultations} + \text{theatre} \\
 &+ \text{hospital cost} + 7 \text{ days} \\
 &= \$169.75 + \$127.31 + 2* \$150.00 + \$500.00 \\
 &+ \$300.00 + 7* \$314.78 = \$3300.52
 \end{aligned}$$

Major surgery

$$\begin{aligned}
 &= \text{Surgery} + \text{anaesthetic} + \text{consultations} + \text{theatre} \\
 &+ 7 \text{ days hospital costs} + 30 \text{ days sick leave} \\
 &= \$791.25 + \$593.44 + 6* \$150.00 + \$500.00 \\
 &+ \$2100.00 + \$9443.40 = \$13428.09
 \end{aligned}$$

These values can be placed onto a decision tree.



Thus the costs to the ADF of a false negative are:

X	Y
YEARS	COST
1	-2908.42
2	-5763.34
3	-8618.26
4	-11473.18
5	-14328.10
6	-17183.02
7	-20037.94
8	-22892.86
9	-25747.78
10	-28602.70

This demonstrates that if it is decided that testing would occur every year then the cost to the ADF for one female developing cancer in that time is \$2908.42. If it is decided that an appropriate interval is two years, then the costs per female developing cancer in that time is \$5763.34 and so on. Lengthening periods of time between testing will impact the overall cost to the ADF. We can individually calculate the expected monetary value of testing at each interval. The costs increase with time. Thus, the more frequent testing is done, the better. It is difficult to determine what frequency is too frequent or not necessary, and perhaps should be the subject of another, more involved paper.

We know that the 5-year mortality rate for this disease is 14%. Thus, left undiagnosed and treated for five years, 14% will develop cancer and die. If diagnosed in this late stage, the costs of treatment are much greater. The costs of treatment steadily rise the longer the disease is left to develop into cancer. If we assume that the ADF will utilise national policy of two yearly testing, the proportionate cost of a false negative can be calculated.

If we try to determine the line for PAP smears, we know that they will cost \$53.50 (= Y intercept), thus we know one point on the line (0,53.50) and the second point is (5, 13428.09).

Using: $Y = aX + c$ and substituting for $X = 0$, $Y = 53.50$.

Substituting to find a: $14328.09 = a \cdot 5 + 53.50$;
 $a = 2854.92$

The disadvantages of testing too frequently are:

- Increasing health care costs for unknown additional benefit. While the reported abnormality rate of the ADF is higher than the abnormality rate of the general population, in the general population only 19% of females undergo testing each year, hence there is likely to be underreporting of the true incidence of the disease. The tests are reliably sensitive (>99%), so at this stage there would appear to be no reason to increase frequency of testing for the ADF in general.
- Initial and ongoing outlays that the system may be unable to support. The EMV reduces (becomes more negative) with increasing time between testing, thus overall costs increase with increasing frequency.
- Reduced compliance and acceptance amongst the female population. Having to return for a higher frequency of testing will reduce the acceptance of the testing.

- Not a great deal is known about the time delay for the development of invasive cancer. Previous studies have put the time delay at approximately seven years from first affected. Obviously the purpose of the test is to catch the early form of the cancer before it becomes invasive.

RESULTS

The decision tree above is the decision tree for this problem. The expected monetary value (EMV) decision rule selects the decision alternative with the largest expected value to the ADF. The EMV decision rule has selected decision two as the best option. This is primarily because there are less unsatisfactory tests and less false negative tests with test T. From an expected monetary value perspective, it is better to not test than do P tests (\$515.18 vs \$592.15).

CONCLUSIONS

The ADF reports a higher rate of positive P and T tests than the general Australian population. This, however, may be the result of under-reporting (under-testing) in the Australian population.

When analysed in this manner, T tests have the highest expected monetary value when compared to P tests and no testing. The EMV for T tests is \$329.58, a P test is \$592.15 and no testing is \$515.81. Thus, the ADF could afford to pay up to \$250.00 for T tests and still be at a higher EMV than either not testing or P tests.

There is no reason to increase the frequency of testing for the ADF, given the high negative predictive values of the tests. Increasing the frequency of testing may also be an unpopular decision amongst the recipient female population.

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A VIEW FROM THE FRONT

The Future of Defence Medical Research Lionel K.H. Lee¹

ABSTRACT

PROGRESS IN THE LIFE SCIENCES will be driving scientific progress in the 21st Century the way physics did for the 20th Century. The new revolution in Biotechnology indicates that the warrior of the future will be drawn from a society very much influenced by this development. Bio-sensors may detect potential threats of all kinds. Biologically inspired materials could provide light protective armour. Trauma therapeutics will enhance survival from wounds. The future prospects of defence health research involve studying the changing situation of the modern battlefield, the new threats to which the combatants are being subjected and the overwhelming potential of discoveries in the life sciences and biotechnology. By this, defence health research will achieve three main purposes, enhance the safety and health of service personnel, maximise their survival on the battlefield and improve their combat performance.

INTRODUCTION

At the dawn of the new millennium, it has been said concerning progress in the life sciences that the 21st century will become the age of new Biology. Biology will be driving scientific progress for this century, the way Physics did for the 20th Century. It was thus not just pure coincidence that the first draft for the human genome project was completed in Feb. 2001. This landmark breakthrough will yield so much promise for new discoveries in the life science.

The warrior in 2020 will be drawn from a society that has been armed by biotechnology. They will have increased strength, endurance and a superior resistance to disease and ageing. By then Bio-sensors may be able to detect threats of all kinds. Biologically inspired materials could provide light protective armour. Trauma therapeutics will enhance survival from wounds. Against such a backdrop of future promise, there is so much opportunity for those of us engaged in defence health and medicine to harness these new discoveries for the benefit of defence health.

DEFINING RESEARCH PROGRAMMES

The central focus of R & D activities of the Defence Medical Research Institutes (DMRIs) is the war-fighter operating as individuals or in teams. There are three main purposes:

- To enhance the safety and health of the service personnel.
- To maximise their survival on the battlefield.

- To improve combat performance.

In order to make a greater and significant contribution, researchers need to understand three trends:

- The changing situation of the modern battlefield
- The threats to which the combatants are being subjected
- The overwhelming potential in the recent discoveries in the life sciences and biotechnology.

There should be a push-pull relationship in defining needs for research. The main sponsors of the research, which are the operational staff of the army, navy and airforces and particularly from the Medical Corps, articulate the requirements. At the same time, creative ideas should also be articulated by the research scientists and engineers (RSEs) in whom domain knowledge reside. From such a relationship, innovative solutions to problems will result.

APPRECIATING THE BATTLEFIELD

The modern battlefield presents an ever-changing landscape and challenge. It will be fought with increasing tempo and precision. Large battle formations will be replaced or complemented by small group forces spread over a wider dispersion. Modern weapons are much more lethal and devastating. The threat of chemical and bio-weapons with their asymmetric impact is real. Precision weapons and improved mobility bring along a technical complexity to the battlefield.

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All this points to an overwhelming individual burden challenging physical and cognitive endurance. Operations other than war, terrorism and long intensity conflicts will force the defence health services to move out of their traditional scope of looking after operational forces to attending to civilians victimised by these conflicts.

THREATS TO THE COMBATANTS

Against such a challenging environment, the soldier, airman and sailor remain extremely vulnerable to threats to safety, health and performance. Examples of such threats are listed in Table 1. DMRIs offer the potential to protect them.

TABLE 1: Threats in a Battlefield Environment

Category	Threats
Environment	Heat, Cold, G-Forces, Altitudes, Hypoxia, Undersea, Submarine
Materials	Toxic Chemicals, Radiation, Infections and Biological agents, Laser, Explosives, High Velocity Missiles, Non-lethal weapons, Infrasound
Metabolic	Physical Exhaustion, Fatigue, Dehydration, Sleep Deprivation
Mental/Cognition	Fear, Chronic Anxiety, Information Overload, Battle Stress

HARNESSING THE LIFE SCIENCES INITIATIVES

Recent advances in the field of genetics, genomics and proteomics will alter the approach, diagnosis, treatment and prevention of diseases. With genetic profiling, the effect of individual genetic elements on disease and fitness can be determined. Genomics-based therapeutics approaches will become the norm.

Assuming that the issues relating to personal privacy can be overcome, the military has a unique opportunity to collect and use genetic data. It would be of great value to the military to increase the epidemiological monitoring of troops and to add genetic information to such studies. Because genetic information offers clues to improving human performance, it could provide the army with means of increasing combat effectiveness. Then applying artificial intelligence techniques, such

as neural networks and machine learning processes, we should be able to data-mine the wealth of genetic and epidemiological data. The challenge is in the ability to organise these efforts and intelligently tap this potential wealth of information purposes of manpower selection and preventive medicine.

EXPLOITING BIOTECHNOLOGY

The rapid growth of the biotechnology industry is evident from the statistics in Table 2¹. In 1985 approximately 1,500 biotechnology patents were granted in the United States. By 1998, the number had increased more than 9000. Between 1994 and 1999, market capitalisation more than doubled from US\$45 billion to almost US\$97 billion, which is more than the estimated US\$75 billion for the entire US defence industry¹ at that time.

TABLE 2: Biotechnology Industry Statistics in the USA 1993-1999 (in US\$ billions)

Year	1993	1994	1995	1996	1997	1998	1999
Sales	5.9	7.0	7.7	9.3	10.8	13.0	13.4
Revenues	8.1	10.0	11.2	12.7	14.6	17.4	18.6
R&D	4.9	5.7	7.0	7.7	7.9	9.0	9.9
Market Capitalisation	N/A	45	41	52	83	93	97
Number of Companies	1,231	1,272	1,311	1,308	1,287	1,274	1,283
Number pub listed coys	225	235	265	260	294	317	327
Number of employees	79,000	97,000	103,000	108,000	118,000	141,000	153,000

What is driving this unprecedented growth? Mainly, the prospects in the health care industry. But this growth has tremendous potential for applications to defence especially to defence health. To keep pace

with the unprecedented rate of discovery, the armed forces will have to establish new, effective partnerships with the emerging biotechnology industry¹, participate in research, leverage research and developments

in the commercial sector and develop its capability to act on the opportunity as they arise. The DMRIs can serve as a catalysts and conduits to assist the Armed

Forces in building this capability. There is extensive opportunity and scope to apply the new frontiers of Biotechnology for military purposes (Fig 1).

FIGURE 1: THE BIOTECH SOLDIER – The possible applications of biotechnology for military use

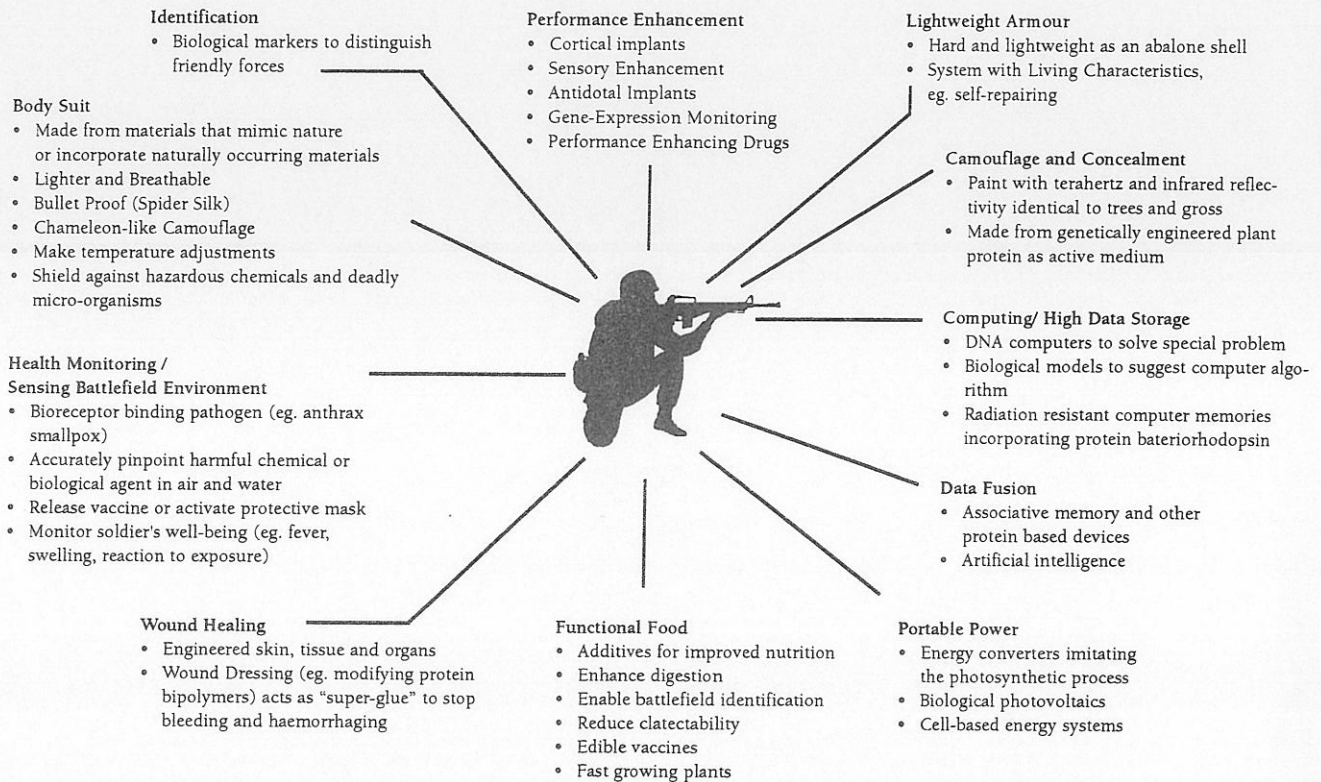
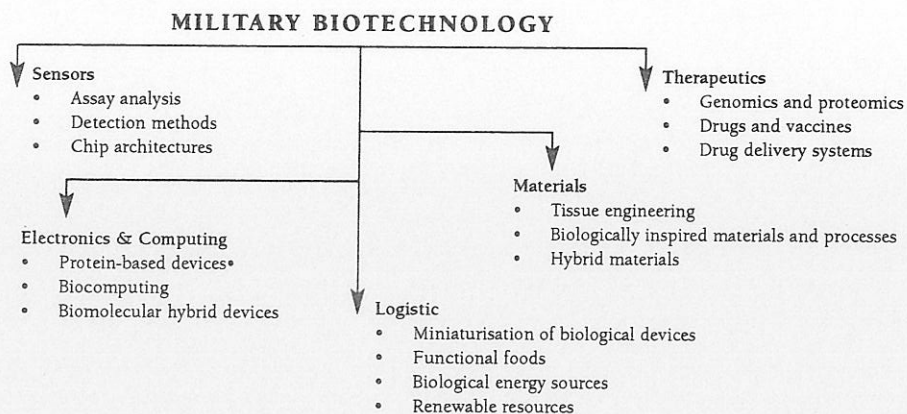


FIGURE 2: Military Biotechnology



BIO-SENSORS

The operational environment carries unseen and not so obvious threats to the combatant. Unsafe air, water and food should be detected early for prevention and intervention to counter these threats to become effective.

The advances in microelectronic mechanical systems (MEMS), microfluidics and nanotechnology open up the exploitation of using bio-sensing as early warning devices of environmental threats or from biological and chemical attacks. Small bio-sensors will

probe the environment for specific threats through chemical, biochemical or biological assays. DNA chips provide the potential for miniature devices to diagnose a variety of disease threats with speed and specificity. These will be simple, small and robust for field use.

BIO-MATERIALS

There is a need to protect the war-fighter and should the protection be breached and wounding occurs, there is a need to repair the wounds. Bio-materials and bio-inspired materials have the potential to change the mindsets as to how these two requirements of protection and repair can be achieved. Bio-materials are biologically produced materials. Tissue engineering and stem cell research will offer inherent advantages over synthetic materials for wound healing. They are self-replicating. On the other hand, synthetic materials soft or hard, bio inspired materials could be used in vivo or in vitro. An example would be inspiration of the spider web to make strong and resilient scaffolds or the abalone shells for body armour.

BIO-COMPUTING

Bio-computing integrates computer science and biology. It builds computational models of biological systems or to use biological processes as enablers to develop new computational techniques. For example, artificial neural nets are computer algorithms that mimic the way neurons process information.

THERAPEUTICS

New technologies will lead to the development of new drugs and vaccines, which through the pharmacogenetics will be tailored to suit individual soldiers. There will be cheaper means of discovering and testing new drugs. With micro and nano-technology, advanced drug delivery systems can be developed to introduce drugs via micro-needles or implanted

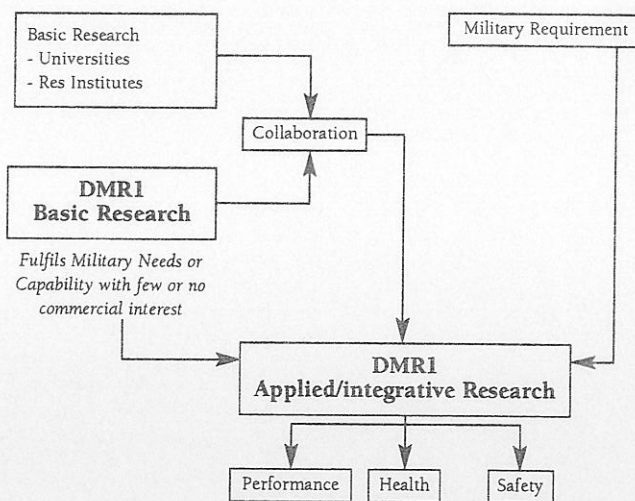
devices. Drugs and vaccines can also be introduced through genetically processed foods.

CONCLUSION

Advances in the Life Sciences and Biotechnology are often made possible through a broad front, multidisciplinary approach. For example, research in bio-materials involves the disciplines of biology, nanoscience, medicine and biomimetics. This is where the DMRIs provide value add service to the armed forces they serve.

DMRIs are poised in our niche for integrative/applied research to bring together the new science and technology from basic research and point them towards fulfilling military needs and requirements. In this way, we will be exploiting the advances in life sciences and biotechnology and so improve the performance, safety and health of the men and women in our armed forces.

FIGURE 3:
Role of Defence Medical Research Institutes



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A VIEW FROM THE FRONT

White Powder Incidents:

Did we manage and could we manage again?

Peter Channells¹

ABSTRACT

THE USE OF BIOLOGICAL WEAPONS has been around since before the siege of Kaffa in 1346 when the Tartars catapulted plague infected bodies over the ramparts. The potential for terrorists to use biological agents against a civilian population has been well understood by security agencies for some time. However, until the tragic use of anthrax through the mail system of the United States last year, the full implications and reality of such incidents was not well understood by mainstream policy makers and budget guardians.

Australia has a very well developed and practiced emergency response system at both the state and national levels. Agencies fully understand their roles and responsibilities and significant effort had been exerted as part of the 2000 Sydney Olympics to prepare for potential chemical, biological or radiological incidents. The "white powder" hoaxes of late 2001, however, presented a very different challenge for public health officials and the Australian emergency management system, which, despite some early problems, managed well. Officials were faced with a high level of uncertainty, an unclear level of risk, unfamiliar coordination arrangements, a very nervous public and reactive media. Paradoxically, while we do not want such terrorist incidents to occur again, without more incidents it will be difficult to maintain an effective level of preparedness.

INTRODUCTION

White powder incidents is a shorthand reference to the hoaxes and mis-identifications that occurred following the real anthrax laced letters that were sent in the United States after September 11, 2001. These letters resulted in a world wide scare campaign by opportunistic, but not very original individuals sending a range of inert substances that they alleged were anthrax through the mail. The impact of these incidents was considerable. First responder agencies were stretched, laboratories were swamped, postal services interrupted, and the public inconvenienced. It also generated considerable media hype and panic such that flour on a bread roll became a white powder incident, which resulted in the mid-flight grounding of a flight from Brisbane to North Queensland and decontamination of the passengers.

This paper doesn't go through a chronology of the over 3000 recorded white powder incidents that we had in Australia. It instead focuses on how Australia's emergency response system is structured and how we might maintain an adequate level of preparedness for managing a repeat or similar situation.

Before discussing preparedness for managing bioterrorist incidents, it is important to have an understanding of the context, just what is being prepared for, and why. We need to examine the threat and risk environment. To do this we need to look at the known offensive use of bio-agents as weapons; the potential for the use of such weapons; and the consequences on a population if such weapons were to be used.

We know that the use of biological agents as weapons is not new. For example, in ancient Athens, Solon used the purgative herb, hellebore, to poison the water supply during the siege of Krissa, and the siege of Kaffa in 1346 saw the Tartars catapult plague infected bodies over the ramparts. However, the number of times that such weapons have been used is few. In recent times, the most notable incidents have been the deliberate contamination of a salad bar with salmonella in 1984 in the United States, the failed use of botulinum toxin by the Aum Sect in 1995 in Japan and, of course, the use of anthrax.

While the number of actual incidents is few, this needs to be balanced by the potential to use such agents.

1. Mr Peter Channells is responsible for Disaster Management within the Department of Health and Ageing. He is the secretary of the Australian Disaster Medicine Group.

There has been much publicity around the Russian former bio-weapons program and the current Iraqi bio-weapons program. There is also regular reporting about the interest of terrorist groups in acquiring bio-weapons. Many of the potential agents are readily available. Anthrax is a common soil bacteria causing annual outbreaks in cattle, viral diseases are endemic in some countries and, more recently, genetic sequences have become commercially available.

To examine the consequences, we need look no further than the disruption and panic that followed the anthrax letters in the United States and the subsequent hoaxes there and in other countries including Australia. Nobody could have predicted the impact that five letters, amongst millions of mail items, could have had. The Brentwood mail centre is still closed.

The last part of the context matrix is the ability to rapidly detect a bio-agent. Currently there is no bio-detection system equivalent to those available for chemical and radiological agents.

In summary, the technology, capability and perhaps more significantly, the intent to use a bio-weapon exists and the consequences from the use of a bio-weapon are significant. A risk assessment of these parameters is the basis for the actions taken by policy makers and emergency managers.

CURRENT ARRANGEMENTS

In Australia, the constitutional responsibility for the safety of citizens rests with the state or territory in which they live. The Commonwealth provides support and coordination for prevention and preparedness measures and assists with response and recovery operations when requested. This system has led to all states and territories having well established agency-specific and multi-agency emergency plans at all functional levels within the state or territory. Through Emergency Management Australia (EMA), the Commonwealth supports the states and territories and coordinates Commonwealth assistance on a routine basis as well as under specific response plans in times of emergency/disaster.

All plans are regularly reviewed and exercised, using a network of key people, to the point that there is a high level of confidence that our emergency managers can efficiently deal with any situation. In terms of the paper's theme, the management of white powder incidents marks the beginning; the

point from which we can judge quite clearly how well our preparedness has been maintained.

The questions remain, how does a population prepare? Can it prepare at all? How does it maintain that preparedness?

PREPAREDNESS

In terms of non-terrorist incidents, the Australian emergency management system has been able to effectively respond to any emergency that has so far presented in Australia. So the answer to the questions of whether a population can prepare and remain prepared has to be yes, at least for non-bioterrorist incidents. Can we extend this current system to cover bioterrorist incidents, or is there some fundamental aspect of a bioterrorist incident that makes that approach impossible?

All disasters have features that are unique and that require different responses. For example, structural collapse (crush injuries and complicated casualty extraction procedures) versus fires (burns and respiratory injuries requiring years of treatment) versus chemical accidents (contaminated casualties, specialised medical treatments). In the case of bioterrorist incidents, the differences are that:

- There will generally be no incident site and therefore no or little need for the usual emergency responders (police, fire & ambulance). An alert medical person and capable laboratory will be the ones to discover the incident when patients present and health authorities will take the lead in managing it.
- The tools used to combat the incident will be a pill and a needle. These are not normally available in the quantities needed to treat the numbers of casualties that will result from a bioterrorist incident and/or they may not be licensed to be used for that purpose.
- It is difficult to prepare in an optimal fashion for a terror incident¹. There is too low an incidence of such events to justify the enormous financial outlay it would take to prepare every community for every event. Equally, there are too few incidents for a community to acquire enough collective experience to make a significant impact on a response to the next incident.
- It is likely that a covert release of a biological agent will not be recognised until enough cases are observed and reported to allow recognition of an

unusual event. Given that people will present with flu like symptoms to widely dispersed medical facilities, this problem is greatly compounded.

Having considered the differences between bioterrorist incidents and other emergency incidents, there are also many similarities. All are unforeseen, they create disruption and destruction, they cause casualties and they are, by definition, beyond the capacity of local resources to manage. Viewed in this light, Australia's success in managing non-bioterrorist incidents should give us a sense of confidence that our emergency management system can handle a bioterrorist incident by simply building in arrangements to address those aspects specific to a bioterrorist incident.

SPECIFIC ASPECTS OF BIOTERRORIST INCIDENTS

The main aspects that need to be incorporated are:

- access to intelligence information;
- an alert health system;
- laboratory capability;
- availability of appropriate treatments; and
- a nationally coordinated and consistent communications arrangement.

Before consequence managers can begin to prepare for a bioterrorist incident, it is critical that the health sector and other consequence managers have an understanding of the capability and intent of terrorist groups and access to warnings of specific potential incidents.

As stated earlier, it is likely that the first indication that there has been a bioterrorist incident will be the presentation of patients in medical facilities. Therefore, it is critical that staff of those facilities have sufficient awareness that they do not automatically rule out the possibility that a deliberate release of an agent has occurred.

Having identified the possibility, the capacity to rapidly analyse a sample to identify if an unusual agent (e.g. anthrax) is present becomes the next critical step. Should such an agent be present, that information needs to be communicated widely within the health sector and other relevant agencies (such as

police), treatment of the patient needs to begin and other patients identified.

In Australia these aspects have been addressed through appropriate membership on relevant committees such as the National Chemical Biological and Radiological (CBR) Working Group and its state and territory equivalents. National education and training material and courses have been developed for use by national and state/territory agencies. Specific CBR incident management plans have been developed at all levels, from facility to state and national, and these arrangements are regularly exercised.

Laboratory capability is being addressed through the acquisition of equipment, training, and links to facilitate the rapid uptake of new developments in the diagnostic field. In the area of treatments the Commonwealth Department of Health and Ageing is establishing a stockpile of relevant pharmaceuticals; facilitating the development of national treatment protocols and supporting national coordination through groups such as the Australian Disaster Medicine Group, Communicable Diseases Network Australia and the Public Health Laboratory Network. Similar activities are being undertaken in the agricultural sector through the Commonwealth Department of Agriculture, Forestry and Fisheries Australia and its state and territory equivalents.

Recognising the significant role that communications will have in managing an incident, the Department of Health and Ageing manages the National Emergency Media Relations Network. During the white powder incidents, the Department's media team enacted their national information networks, met with the press officers of the national security network and coordinated a consistent approach by all media spokespeople, as well as handling the hundreds of calls from the public, agencies and journalists.

CONCLUSION

A bioterrorist incident in Australia will undoubtedly create significant problems. Australia, however, does have an excellent emergency response system that is being built on to ensure it is capable, and stays capable, of managing a bioterrorist incident.

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REVIEW ARTICLES

Further Development of the Health Response to Chemical Biological and Radiological Emergencies: "A Multi-multi-Agency Response"

Dr Michael Hills¹

FROM 1998 TO 2000, the need for a civilian health response to chemical, biological and radiological (CBR) emergencies was identified and developed in preparation for the Sydney 2000 Olympic Games and beyond. The events of September 2001 have thrown this continuing need into relief and highlighted the significant work still required to improve the capabilities and response for civil protection.

This paper highlights the key developments leading up to the Olympic Games, the key lessons learned from the aftermath of the US terrorism attacks and the ongoing development underway. A particular focus will be the significant progress made in improving inter-agency work at the regional, state and national levels, not just for CBR emergencies, but also for emergency management in general and the benefits this has led to. Cooperation between the civilian sector and Defence agencies highlighted includes training, capability development and mutual understanding of each other's role. International aspects of similar developments will be described as part of the global review of the subject.

THE NEED FOR A RESPONSE

As, is often stated, mankind has a long history of using chemical and biological materials as weapons, why did the late 20th Century see a dramatic rise in concern over this issue? Were our systems not resilient enough to cope? After all, even in the last century, countries have had to cope with epidemics and pandemics of devastating proportions and still do. Chemical industry accidents and warfare have thrown up examples where thousands have been affected. Nuclear industries have had to cope with transnational accidents and effects. So what changed?

CONVENTIONS AND THREATS

The development of treaties and conventions covering biological (BWTC)¹ and chemical weapons (CWC)² seemed effectively to lessen the likelihood of deliberate use of these materials both in a military and civilian context. Perhaps, and this is somewhat speculative, the hope was that it would go away and the necessary investment could be scaled back. Then a sequence of events in the 1990s rekindled the concerns of the earlier generations. The Gulf War (1990-91), the subsequent UNSCOM missions to Iraq, the use of sarin by

the Aum Shinrikyo cult³ and (in the United States) domestic threats from chemical and biological materials in the mid to late 1990s heightened awareness. By the time of the Atlanta Centennial Olympic Games in 1996, the United States (US) was embarked on a domestic preparedness program later enshrined in legislation that year⁴ to combat the threatened potential use of CBR material. Other countries followed to lesser degrees.

WHY THE OLYMPIC GAMES?

From the post-Games report of Atlanta,^{5,6} it became clear that, at least in the continental United States, the authorities perceived a risk from the use of CBR materials in conjunction with this highly focussed international event. The combination of worldwide television and the recent events in Tokyo raised the spectre of a terrorist attack beyond hostage taking or a conventional bomb. In the end, the tragedy of the Centennial Olympic Park bombing⁷ involved a backpack with explosives. Federal initiatives following the Nunn-Lugar-Domenici Act continued to progress the development of the response. Intriguingly, the need for a strong public health infrastructure was identified as a critical gap.

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WHERE WAS PUBLIC HEALTH?

Looking back to before the Second World War, the United Kingdom had established the Public Health Laboratory Service (PHLS)⁸ to cope with epidemics arising during civil disruption from wartime and deliberate use of biological agents by the enemy. Similarly, the Epidemic Intelligence Service (EIS) was established in 1951 by Langmuir, a Centre for Disease Control epidemiologist who identified the need to train physicians and other scientists to be prepared to deal with biological warfare.

By the 1990's, however, the purpose and linkages to the deliberate use of "germ warfare" had been all but lost. Indeed, the current generations of epidemiologists and public health staff had little engagement in the subject matter and were sceptical of the need. Even the revelations of one of the former Soviet Union's program's directors^{9,10} were not necessarily viewed as indicative of an imminent threat.

WHAT WAS DONE FOR THE SYDNEY 2000 OLYMPIC GAMES?

In the context of the Olympic Games, however, risk management approach demonstrated the need to develop some capacity to manage such events. This saw a review through 1997 and 1998 of the baseline capacity and gaps across all agencies. Focussing on health services, the pertinent issues, in the context of a massive world event (with intense outside scrutiny), led to development of systems for decontamination, acquisition of personal protective equipment, use of a baseline surveillance system to track disease incidence, acquisition of pharmaceuticals, training and awareness raising and, of course, numerous meetings.

The health service development, however, is only one part of the process and it took place in the context of well-developed emergency response structures and concurrent development with other agencies (including fire, police, ambulance and Defence). This has been the key because the inter-action (not the specific technical aspects) to make it work is what is required for any disaster response and the New South Wales bushfires of 2001/2002 more than demonstrated that the familiarity with each other greatly assists any response.

WHAT TO PLAN FOR?

The one nagging problem remained however – how big an event should be planned for and what arbitrary

number do you pick? This is, in part, based on a projected feasibility of an attack in terms of magnitude but also ranking this threat against other more likely demands on agencies. The often quoted WHO 1970 report describing ideal spread by aircraft over a major city concluded that the release of aerosolised anthrax, upwind of a population of 500,000, could lead to an estimated 125,000 casualties, of whom as many as 95,000 could be expected to die¹¹. Dramatisations on television outlining hypothetical releases on a subway system projected tolls that stop registering in the mind¹² and the Office of Technology Assessment (OTA) computed examples of projected death tolls between 300,000 and 3 million¹³. These numbers are difficult to comprehend and to plan for. Even planning for 1,000 casualties is far outside "normal business". Nevertheless, in 2000, a capacity existed to manage an event of this magnitude during and after the Games.

So, in early 2001, New South Wales, like others, had (and still does) a good system of a multi-agency response to all hazards emergencies and a capability to respond to specific CBR events at a low order of magnitude.

WHAT CHANGED IN 2001?

The attacks on New York and Washington suddenly crystallised for some the "threat" of terrorism. Not that this was new, with numerous preceding examples such as the 30 years of Northern Ireland conflicts, the US Embassy bombings in Africa, and groups such as ETA in Spain and others, which had all demonstrated the use of conventional means of terror. It was as if the next step to move to a CBR event was just a question of waiting.

Prior to the October anthrax releases, two events that perhaps gave credence to the "not if... but when" lobby were the publication of some details of the US study on manufacturing feasibility outlined in an NBC television program and the New York Times^{14,15}. The program was named Biotechnology Activity Characterisation by Unconventional Signatures, or Project BACHUS. This demonstrated the feasibility of production, at relatively low cost, of biological agents. Canadian experiments¹⁶ on powder dispersal from envelopes found that the correct powder would spread very rapidly from routine mail opening. These experiments demonstrated (if the intent

was present) both feasible methods of manufacture and dispersal that were not generally understood previously in emergency response agencies.

This leads us to the pattern of discovery and response to the anthrax cases in Florida, Washington and New York in 2001. Descriptions are found at the CDC website but this event affected 22 people with 11 inhalational cases and five deaths¹⁷. The staggering statistic, however, is the 10,000 or more put on prophylaxis¹⁸.

Subsequently, the mistaken attribution of powders in envelopes after the events of October 2001 have thrown the continuing need for a response capability into relief and highlighted the significant work still required to improve the capabilities and response for civil protection.

KEY LESSONS LEARNED

From the aftermath of the US terrorism attacks, there was a worldwide surge in items found, or attributed, with suspicious features. In Australia, none of the items turned out to be contaminated but it would be complacent to assume that future contamination could not occur. The challenge is for a sufficient understanding to develop that does not require responses to "Ajax" or sugar powder but will respond to the finely milled easily dispersed powder that may not be visible after opening.

Above all, the first cases of anthrax identified in the US were done by clinicians treating a clinical case and not by some elaborate surveillance system. Once recognised then surveillance could be initiated and cases sought. However, it is still a matter of time, place and person. Furthermore, the pattern of clinical disease was mixed with both cutaneous and inhalational presentations occurring. Lastly, some patients with inhalational anthrax were successfully treated.

FUTURE DEVELOPMENTS

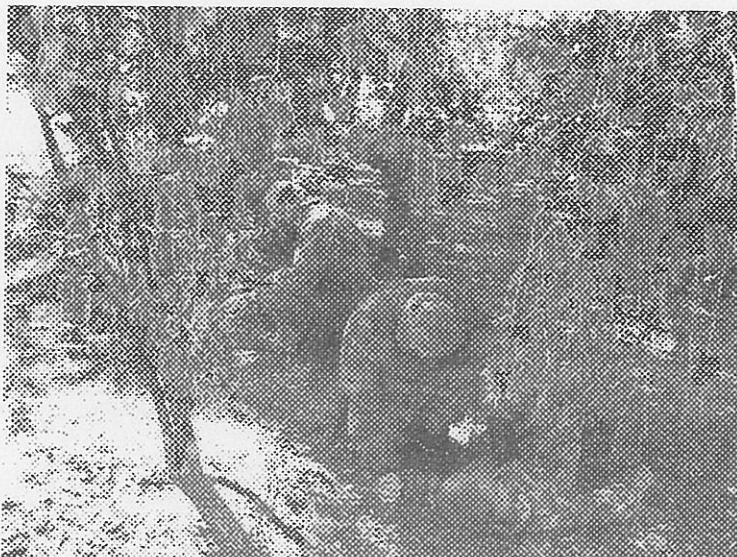
Work continues on improving and refining the response capability in Australia. Particularly important is the significant progress made in improving inter-agency work at the regional, state and national levels, not just for CBR emergencies, but also for emergency management in general and the benefits this has led to. Cooperation between the civilian sector and Defence agencies is also crucial, both in recognising boundaries but also sharing knowledge and expertise.

The World Health Organisation has now revised its guidelines¹⁹ and is developing regional tools to assist developing countries manage local incidents and those that cross into their jurisdictions²⁰. At the core of this, however, is the need to balance this against other public health priorities and the challenge ahead is to make the investment count on many fronts, as it has to date.

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Students involved in an NBC triage exercise at the last Medical Officers' Nuclear, Biological and Chemical Defence Course— April 2002

Photo courtesy of CAPT Andy Robertson

REVIEW ARTICLES

Most Recent Developments in Japanese Encephalitis Vaccines

Scott Kitchener¹

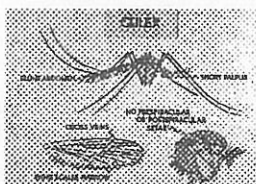
ABSTRACT

ONLY ONE VACCINE AGAINST JAPANESE ENCEPHALITIS is available for use in Australia. Other vaccines in Asia have supplanted this vaccine. Some vaccines used in Asia, however, would not be acceptable in Australia. A number of candidates are in clinical development based on more efficient platforms and cleaner production lines. The ADF is involved in clinical trials to ensure earliest availability and applicability to Australian Service personnel.

MAP 1: Distribution of Japanese encephalitis in Asia 1970-1998¹

INTRODUCTION

FIGURE 1: The vector for Japanese encephalitis virus (Image: *Culex* mosquitoes, *Arboviral Encephalitides*, www.cdc.gov, last updated 13 July 2001).

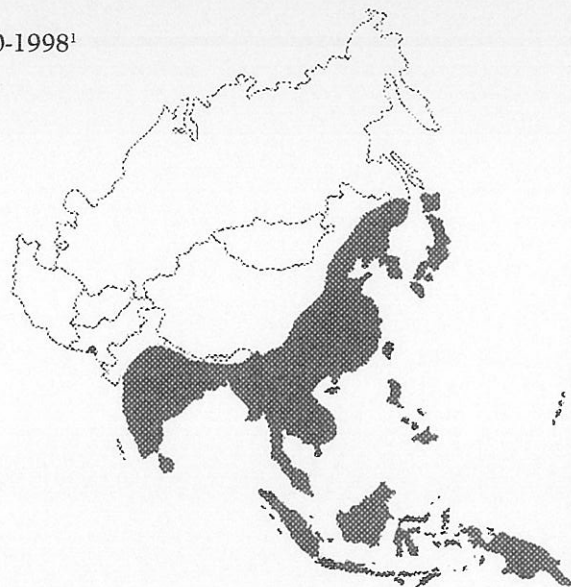


Japanese encephalitis (JE) is the leading cause of viral encephalitis in Asia with WHO estimates exceeding 70,000 cases annually despite reporting being incomplete.

Approximately a third of clinical cases will die and about one half will have residual neurological sequelae². Nevertheless, the chance of contracting JE travelling in Asia is around 1 in a million³. The distribution of the virus has extended to include Australia, where it is now identified by the US Centers for Disease Control as seasonally endemic.

THE HISTORY OF EXISTING VACCINES

With the rising problem of Japanese encephalitis causing non-battle casualties in the Pacific Theatre after 1941, Major Albert Sabin prepared an inactivated JE vaccine in mouse brains for use by US Service personnel. In the post-War reconstruction of Japanese industry, several JE vaccine candidates were produced by various agencies. These were generally derived from two main strain groups isolated 30 years before, the Nakayama strain and the JaGAR group. The immuno-



genicity derived from the latter was inadequate despite various growth media, including mouse brains and cell cultures from hamster and monkey kidney cells⁵. By 1965, the Japanese were prepared to undertake large-scale Phase III trials of the lead candidate Nakayama strain vaccine. During the JE transmission season of that year, a collaborative group including the Taiwanese Department of Health, National University College of Medicine and Serum and Vaccine Research Laboratory; and the Japanese National Institute of Health and Nagoya University Medical College, conducted an Herculean study recruiting 110 166 children across four provinces of Taiwan⁶. One or two doses of Nakayama strain inactivated vaccine or tetanus toxoid placebo were administered prior to the peak transmission season and 62 cases of JE were detected among the

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volunteers in the following season. The efficacy in preventing JE was determined to be 80%. This initial vaccine was subsequently used in Taiwan⁷ and Japan⁸ to great effect.

In China, Dr. Yu Yong Xin of the National Institute for Control of Pharmaceutical and Biological Products, Temple of Heaven, Beijing, developed the SA14 JE strain into an attenuated vaccine and the virus was adapted for growth in a canine cell line⁹, and then tested by the Eckels and Trent at CDC to be stable and clean for human studies¹⁰. Xin then demonstrated the SA14-14-2 vaccine to be safe and immunogenic in a population of 1026 children and it was incorporated into the Chinese paediatric schedule of vaccinations in 1988. A case control study conducted after an outbreak of JE in Sichuan Province (China), involving 56 confirmed cases of JE and 1299 controls, in which one dose previously administered was 80% and two doses approximately 97% effective¹¹. After 100 million doses of the vaccine were used in China, Korean researchers conducted further studies to confirm safety and immunogenicity in their children ahead of licensure¹². The SA14-14-2 vaccine is used extensively in China, being manufactured by four agencies; in Korea by one private company and is under consideration by Health Departments in Thailand and Nepal.

By 1985, two groups of JE viruses were thought to exist. At this time, Dr. Charles Hoke and colleagues at the US Armed Forces Research Institute for Medical Sciences (AFRIMS) in Bangkok were preparing for a JE vaccine field efficacy trial in Thailand. On the advice of Konosuke Fukai of the Research Foundation for Microbial diseases of Osaka University, Japan, Biken, a bivalent vaccine with the mouse brain derived inactivated Beijing-1 JE vaccine strain, was used in the trial¹³.

The landmark Thai study by AFRIMS, the Ministry of Public Health and Biken, forms the cornerstone of guidelines¹⁴ for the only internationally registered vaccine, the Biken Nakayama strain mouse brain derived vaccine, JE-VAX[®], distributed in Australia currently by CSL. The efficacy found by Hoke and colleagues in this study was 91% following two doses¹³. Including the placebo group, 65,224 children were vaccinated; however, only 21,628 received the Nakayama strain vaccine alone with only one case of JE found in this group while 11 presented from the placebo group. Confidence intervals (95%) are high, ranging from an

efficacy of 70% to 97% as the foundation for efficacy of this vaccine is based on 13 cases of Thai children in an endemic area. A third group (n=22 080) received the bivalent vaccine and the efficacy figure quoted in Australia is actually that derived from the combination of the two JE vaccine recipient groups¹³.

The Beijing-1 strain of JE was isolated in 1949. As 21 of the 162 cases of JE in Taiwan between 1986 and 1991 had been previously vaccinated with the Nakayama strain vaccine, the heterologous neutralising antibody response in children was reviewed to illustrate that the Beijing-1 strain vaccine was more immunogenic against wild strains circulating in Taiwan (CC-27 and CH-1392)¹⁵. As the Nakayama strain JE was isolated in 1935, this may reflect a slow antigenic drift in the wild virus since, resulting in reduced immunogenicity of this strain. Today in Japan, Korea and Thailand, children are vaccinated with Beijing-1 strain mouse brain derived vaccine.

The evidence for when to boost the Nakayama strain vaccine is based on less robust evidence. In the Mae Hong Son Province of Thailand, an area of low JE transmission, 199 children vaccinated were found to respond well (94% developed neutralising antibodies); however, their immunity decayed rapidly, so that more than half were susceptible after one year and a booster was given¹⁶. Nevertheless, the Australian guidelines (Immunisation Guideline, 7th edition)¹⁴ are based on the opportunity review of 39 US soldiers originally involved in the US licensure studies of the vaccine approximately three years earlier¹⁷. Only 17 soldiers could be adequately investigated to reach the conclusion that 16 (94%) had detectable antibodies persisting to three years. Australian Defence studies found 51-65% of soldiers retained detectable JE antibodies one year after vaccination¹⁸.

DESIRABLE ATTRIBUTES IN FUTURE VACCINES

Though the JE virus is not known to mutate at a high rate, the immunogenicity of older vaccine strains has recently been called into question¹⁹. There are four genotypes (classes of genetic variation) of JE²⁰. These tend to follow loose geographic boundaries. All available vaccines are derived from genotype III strains. Notably, in January 2000, a second genotype (I), typically found in continental South East Asia and

the Korean Peninsula, entered the Australian region²¹ to accompany the earlier incursion of a genotype (II) typical of Indonesia and Malaysia²².

The other problems with the existing inactivated mouse-brain derived vaccines are that they are quite reactogenic (cause reactions when given), require numerous doses, are expensive and ultimately are relying on mammalian neural tissue²³. Therefore, an ideal prototype for second-generation JE vaccines would be grown in a pure cell line capable of up-scale for inexpensive production, have low reactogenicity and, after one dose, be immunogenic across all four genotypes or, at least, be comparable to the most recent vaccine strain (SA14-14-2).

THE VACCINES IN DEVELOPMENT

Japan

The Kanonji Institute (Osaka University) has begun moving their inactivated Beijing-1 strain from mouse brain production lines to that of micro-carrier-attached Vero cells. This vaccine will move into Phase III trials late in 2002. In competition in Japan is the Chemo-Sero Therapeutic Research Institute (Kaketsuken) that has a similar Vero derived inactivated JE vaccine from the Beijing-1 strain approaching Phase II trials.

While the Vero cell line was originally from an African Monkey renal cell line, most of the commercially available Vero lines are considered highly purified of adventitious agents. It is also a favoured system for inexpensive up-scaling of production.

For final approval of these vaccines, the Japanese regulatory authorities are likely to accept serological outcomes (development of antibodies from the vaccine) rather than requiring the vaccine be tested and to protect in the face of wild virus. The issue then becomes which antibodies to accept as an outcome. Testing against the homologous vaccine strain (looking for antibodies to Beijing-1 grown in Vero cells) will probably provide a false positive to some degree when extrapolated to field efficacy of the vaccine, particularly against various genotypes.

Continental Asia

The Chinese SA14-14-2 strain live attenuated vaccine has been overwhelmingly effective as a public health intervention, reducing Japanese encephalitis in many areas of China. However, this vaccine has been pro-

duced in hamster kidney cell lines that have apparently met WHO/OMS standards of purity, though the national Vaccine and Serum Institute is moving the strain into Vero cells. The potential of this vaccine for the Developing World has not been missed with the WHO/OMS Western Pacific and South East Asian Regional offices, in association with the Global Alliance for Vaccines and Immunisation (GAVI), producing a statement to accelerate international regulatory approval.

Similarly, the Glovax Corporation of Seoul, Korea has been collaborating with the Chengdu Institute of Biological Products in China for validation of manufacture scale Vero cell vaccine production. The Republic of Korea has also managed to control epidemic JE using vaccination and is moving to introduce this live attenuated vaccine into the childhood immunisation schedule to maintain control. Nevertheless, this vaccine is a live attenuated strain of a wild virus and is unlikely to be accepted for use in Australia while an inactivated and reasonably effective vaccine is licensed.

United States

The US Army at the Walter Reed Army Institute of Research (WRAIR) has been developing the SA14-14-2 strain as an inactivated vaccine. This program has completed initial human testing, including dose ranging. The preliminary results are promising for a multi-dose schedule. Phase II trials are due for 2003; however, producing an inactivated vaccine in Vero cells will have low yield so that the vaccine will be expensive. While Barr Pharmaceuticals is collaborating in this project, the vaccine is primarily for the US military. The ADF is involved in negotiations to conduct further phase II trials; however, production of the vaccine has been delayed.

Europe

The chimeric virus approach to vaccine production has advanced most with JE. This technique inserts part of the JE genome into another virus used as a vector. The antigens expressed engender antibodies specific to JE. Recombinant vaccinia viruses were first synthesised in this manner²⁴, although now the 17D Yellow Fever vaccine strain is used as a backbone for the technology in a series of flavivirus vaccines²⁵. The chimeric JE/17DYF vaccine successfully passed

through Phase I studies recently²⁶. Despite the backbone, the vaccine does not stimulate immunity specific to Yellow Fever. An expanded Phase II trial, yet to be published in scientific literature, has confirmed the findings that the vaccine is safe and immunogenic (Acambis Press Release, January 2002). The Australian Defence Force will take this vaccine into further phase II trials shortly.

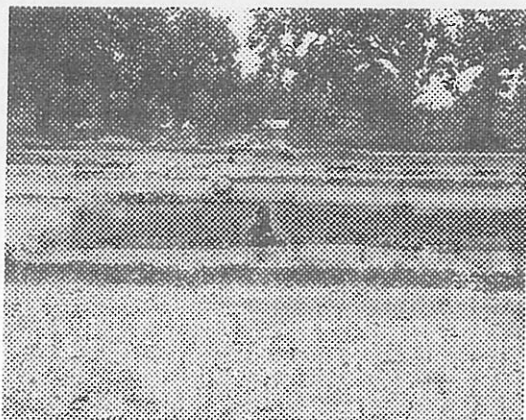


FIGURE 2: Typical breeding site for *Culex* mosquitoes, in East Timor.

FURTHER HURDLES TO BE OVERCOME

With the incidence of JE, the total sample size for each of three groups of in excess of 20,000 Thai children in the Thai efficacy trial¹³ barely demonstrated efficacy of the JE vaccine over tetanus toxoid in prevention of JE. For registration of future vaccines,

"non-inferiority" Phase III efficacy trial would need to be larger again, proving preclusive in logistics and cost, particularly with a placebo group which would now be unethical to use.

At the last WHO/OMS Steering Committee on JE/Dengue vaccine development in Geneva in April 2002, Japanese manufacturers indicated local regulatory authorities might provide second-generation vaccines with the opportunity to complete phase III trials based on serological outcomes – antibodies being a surrogate of protection against the wild virus. This approach has been suggested for US regulatory approval²⁷, though this is yet to be confirmed. With similar issues, the approach taken by the Australian Therapeutics Goods Administration is likely to be comparable to that of the US Food and Drug Administration.

CONCLUSION

In the next five years, several second-generation JE vaccines will be available. These will be less expensive, not produced in neurological tissue of rodents and immunogenic after fewer doses. The latter will particularly reduce the logistic cost of vaccine delivery. Such vaccines will change the public health response to JE, allowing vaccine disease prevention to be more readily available to endemic populations. The ADF is well placed in the development of both the existing and second-generation JE vaccines to ensure personnel have the most efficient and effective protection against the "plague of the orient".

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REVIEW ARTICLES

The Hazards of Surgical Smoke/Plume

Rick Loveridge¹

ABSTRACT

DURING SURGICAL PROCEDURES using laser or electrosurgical units, the thermal destruction of tissue creates a smoke byproduct. Research study has indicated that this smoke plume contains toxic gases and vapours. At high concentrations, the smoke causes ocular and upper respiratory irritation in healthcare workers and creates visual problems for the surgeon. The smoke has unpleasant odour and has been shown to have mutagenic pathogens.

A study was undertaken in 1999 aimed to evaluate the surgical smoke produced in laser surgery. It showed that the particulate matter of laser smoke originating from biological tissues should be classified as cytotoxic, genotoxic and mutagenic.¹

INTRODUCTION

During surgical procedures using laser or electrosurgical units, the thermal destruction of tissue creates a smoke byproduct. Research study has indicated that this smoke plume contains toxic gases and vapours. At high concentrations, the smoke causes ocular and upper respiratory irritation in healthcare workers and creates visual problems for the surgeon. The smoke has unpleasant odour and has been shown to have mutagenic pathogens¹.

The aim of this paper is to review the evidence of toxicity from surgical smoke by-products and to outline the importance of Defence health facilities using surgical smoke evacuation devices to effectively control toxic smoke and gasses.

HISTORY

In the late 1980s and early 1990s², laser clinicians and researchers became concerned about the potential dangers of breathing smoke or "plume" generated by laser surgery. Numerous study results began to appear that described the contents of laser smoke. These studies addressed the transmission of dangerous chemical contaminants, viruses, bacteria and viable cells in laser smoke. As the research reached the market place, concern grew and hospitals working with laser surgery began to purchase smoke evacuators to remove the surgical plume generated during laser surgery. There was, however, little investigation and evidence produced to support the use of smoke evacuators during electrosurgery (ES).

In 1987, Baggish published research results on surgical smoke hazards³. He demonstrated that fine particulate matter produced by carbon dioxide laser use caused pathological changes in the lungs of rats³. In 1991, Baggish found Human Immunodeficient Virus (HIV) cells in the smoke⁴. He had collected smoke through sterile silastic tubing, cultured it and revealed that the HIV survived for as long as two weeks. He concluded that smoke evacuation collection tubing was hazardous⁴. In further studying the smoke, he concluded that efficient smoke evacuation must be maintained close to the operative field in order to remove the smoke before the operating room staff inhales it and that universal precautions must be observed with smoke by-products in all patients⁴.

Another study by the Hazard Evaluation and Technical Assistance branch of the National Institute for Occupational Safety and Health in the USA revealed that electrosurgical unit (ESU) smoke was mutagenic. Further research also found that the mutagenic particles found in ESU smoke were unstable and they showed mutagenic potential for up to two hours.⁴

ANALYSIS OF SURGICAL SMOKE/PLUME

Various research studies have confirmed that the contents of surgical smoke may contain⁵:

1. Biological Agents.

These may include:

- Viruses – HIV, Hepatitis B and C;

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- Bacteria – Staphylococcus aureus, Mycobacterium tuberculosis, E. coli; and
- Fungus -Fungal spores.

2. Cellular tissue.

May include carbonized tissue and aerosolized blood.

3. Chemicals.

These may include:

- Mutagens, carcinogens, allergens, irritants to respiratory tract and toxic gases; and
- Other chemical byproducts, including acetonitrile, acrolein, free radicals, hydrogen cyanide, acrylonitrile, alkyl benzenes, benzene, butene, carbon monoxide, creols, ethane, thylene, formaldehyde, methane, propene, propylene, pyridine, pyrrole, styrene, toluene, and zylene.

A study, undertaken in 1999 to evaluate the surgical smoke produced in laser surgery, has shown that the particulate matter of laser smoke originating from biological tissues should be classified as cytotoxic, genotoxic and mutagenic.¹ It is now believed that the smoke produced in electrosurgery is as toxic as that produced in laser smoke⁴.

Patients, healthcare workers and observers in the Operating Room (OR) are exposed to toxic smoke in a surgical procedure in which smoke from tissue interaction with an ESU or laser is not evacuated. As outlined above, the aerosols produced when lasers or ESU are used may contain particulate matter, gases, mutagens, carcinogens and sometimes DNA components. In one study, when smoke evacuators were not used, the OR filled rapidly (within five minutes) with particulates and the surgical smoke did not dissipate through the ventilation system until 20 minutes after the ESU ceased⁵.

RECOMMENDED PRACTICES

The current recommended practice for surgical smoke in the OR was amended in December 2000. The amendment states that Australian Council of Operating Room Nurses (ACORN) believe that evacuation of surgical smoke in the operating room creates a safer environment for the patients and the healthcare workers.

ACORN STANDARDS

This standard (Table 1) is to be used in conjunction with Standard A11 – Laser Safety in the Operating Suite⁶.

TABLE 1: ACORN Standards⁶

Standard	Criteria
The healthcare facility shall provide protection from potential hazards of smoke for peri-operative personnel.	<p>The peri-operative nurse:</p> <ul style="list-style-type: none"> • Provides protection by utilising smoke evacuation and ultra low penetration air (ULPA) filtration systems. <p>High filtration masks may be used as a further protection from the occupational exposure to surgical smoke.</p>
Activities shall be directed to confine and contain contaminants generated by surgical smoke during the surgical procedure.	<p>The peri-operative nurse:</p> <ul style="list-style-type: none"> • Positions suction collection devices at the source of the smoke; • vents laparoscopic smoke by means of a filtered system; • utilises evacuation systems according to the manufacturers instruction; and • disposes of all smoke evacuation supplies according to the Infection Control policy for biohazard.
Peri-operative personnel shall demonstrate competency in the use of equipment used to evacuate surgical smoke.	<p>The peri-operative nurse;</p> <ul style="list-style-type: none"> • ensure primary education in the use of the equipment; and • attends continuing education programs
The healthcare facility ensures that selection criterion for equipment used for surgical smoke extraction reflects new technological advances as they become available.	

CONCLUSION

There are two issues to be considered when operating room personnel are exposed to surgical smoke. The first is biohazard. The possibility of contracting viral diseases and/or inhaling fine particulates that affect the lungs makes smoke inhalation potentially very harmful. Therefore, surgical smoke must be considered with other bodily fluids. It must be disposed of correctly and the consumables used to dispose of the surgical smoke must be considered as biohazards and also disposed of as such.

The second issue is the adoption of safe work practices whenever surgical smoke is generated. This should include the implementation of guidelines that include the use of appropriate protection equipment. The ACORN standards address the use of surgical smoke evacuators, in-line suction filters, the routine

suctioning of diathermy smoke and the recommended method, appropriate masks, patient protection and the disposal of items used in the control of surgical smoke.

It is plausible that operating room staff, including managers, will be cautious in adopting new standards and procedures concerning diathermy smoke whilst the viability or otherwise of DNA and matter isolated from ES filtrate is still under discussion.⁶ Operating Room personnel and supervisors in the OR have a duty of care if they consider that an identified risk exists. While this risk is ill-defined, there appears to be the potential for contamination and mutagenic effects from repeated exposure to the toxic and gaseous byproducts of ESUs and Laser smoke.⁵ OR supervisors must consider ways to overcome surgical smoke exposure to their patients, staff and visitors⁷.

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Students preparing for the Mask testing Facility at the last Medical Officers' Nuclear, Biological and Chemical Defence Course— April 2002

Photo courtesy of CAPT Andy Robertson

TEN YEARS ON

Should Defence Force personnel receive Influenza Vaccine?

James Ross¹

THE ATTITUDE TOWARDS INFLUENZA in Australia appears quite different to that of many other countries. Whereas mass immunisations have been conducted in the United States in response to threats of major epidemics, and there is widespread use of the influenza vaccine in the Defence Forces in Europe and North America, there is little call for it in Australia. There are potential benefits to the Defence Force from mass immunisation of personnel, both financial and medical. What is needed is a realistic scrutiny of the costs involved and the benefits accruing from an influenza vaccination program.

The National Health and Medical Research recommendations for influenza vaccination in 1991 were:

- a) Individuals at greater risk of complications:
 1. Adults and children with chronic debilitating disease, especially those with chronic cardiac, pulmonary, renal and metabolic disorders
 2. Persons over 65 years
 3. Residents of nursing homes and other chronic care facilities
 4. Persons receiving immunosuppressive therapy.

b) Persons engaged in medical and health services, and essential public utilities if these individuals are at increased risk owing to medical disorders such as those above. In the event of a pandemic or other major outbreak, advice should be given about vaccination of staff particularly liable to exposure.

I suppose the Defence Force could be considered a public utility, but this reactive policy is at the mercy of the speed of transmission of the virus through the population and the supply of the vaccine. Even in response to the threat of a pandemic, mass immunisation is not recommended. Mr. Brian Howe, the Minister for Health and Community Services, stated on 7 December, 1990..." The shortage of influenza vaccine experienced earlier this year gives some indi-

cation of the extent of public concern about influenza and the awareness of the existence of a safe and effective vaccine. It is therefore important that, in implementing a vaccination strategy, the public health professionals, vaccine manufacturers and vaccine recipients understand the aims and objectives of the strategy in reducing the potential for serious morbidity in at risk groups, in promoting the role of natural immunity in the remaining population and in monitoring the efficacy of the vaccine and its potential for side-effects..."

When the demand for the vaccine went up, then, the response was not to reassess the recommendations, but to suppress the demand. This is fair enough, if there is a strong argument for the policy as is. The argument alluded to by Mr. Howe was that, despite the existence of a "safe and effective vaccine, natural, herd immunity should be relied on by the general population." Unfortunately, the vaccine is not wonderfully effective; the only epidemics of influenza experienced at United States Air Force Base Lowry were when there was an antigenic shift in the influenza virus, resulting in widespread diseases in the vaccinated and unvaccinated population. Theory goes that exposure to influenza virus provides a stronger antibody response and better resistance to influenza in the future for the individual, and also provides a pool of relatively protected people who should limit the spread of the virus through the community.

I consider that the arguments for vaccinating the Defence Force, and other working populations as well, are good. Firstly, it is not proposed to vaccinate the entire population; natural immunity would still be present. The extent of natural immunity for it to be effective on a population basis is not really known. The great advantage of reduced morbidity and mortality is the economic benefit; a cost-benefit analysis for employers shows a cost saving, given certain assumptions. As this

¹ GPCAPT James Ross is currently the Director Health Projects in the Defence Health Service Branch. He was the inaugural President and this was one of the first articles published in Australian Military Medicine.

would be wholly employer funded, there would be a saving for the health care system, and improved productivity would improve the country as a whole.

A cost-benefit model requires the calculation, in dollar terms, of both expenses due to, and gains from, intervention. Calculating human suffering is difficult. The effects are not only to the victim, but also to the family and others directly and indirectly affected by the illness. As such, the benefits in avoided suffering tend to be ignored, and gains underestimated. Attempts to produce a cost-benefit analysis have been conducted, with varying conclusions. Many assumptions had to be made based on inadequate data.

The incidence of influenza varies among populations and across years. It is only once every few years that an influenza epidemic occurs in Australia. If a group is to be vaccinated, the costs may outweigh the benefits three times out of four, but the year of an epidemic could very well tip the balance in favour of the intervention.

At the heart of this influenza vaccine cost-benefit analysis is an estimation to be soundly based. This is an area of research that is crying out for study. A major problem with such research is that it has to continue until an epidemic occurs to be able to get a meaningful assessment of the difference between vac-

inated and unvaccinated individuals. Studies estimating reduction in sickness absence among workers have had to base their estimates on less than optimal information. To give you an idea of the sort of figures that we may be dealing with, I will outline a possible scenario. A mass vaccination campaign in the Defence Force may cost in the vicinity of \$15 per patient, including vaccine, materials, facilities, medical staff costs and time lost from work by the employee. If a vaccinated individual had a 0.5 days less in sick leave on average over the influenza season than an unvaccinated individual, then using pay as a proxy for productivity in Defence Force, there is a saving of around \$75 per person. This level of saving need only be achieved every five years to make it viable, excluding savings to the health system and to human suffering.

The case for vaccination is not watertight by any means. There are problems of adverse reactions, resistance to vaccination by some personnel, and possible loss of herd immunity. However, if there is a desire to lessen the possibility of a marked reduction in the responsiveness of the Australian Defence Force due to an influenza epidemic, and to reduce the excess morbidity and mortality due to the infection, while actually saving money, then the idea needs to be taken seriously and further investigated.



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HISTORY

Tudor Naval Medicine 1485 – 1603: Part One

Neil Westphalen ²

INTRODUCTION

THIS IS THE FIRST OF A TWO-PART ARTICLE on English naval medicine during the Tudor period, from the end of the Wars of the Roses in 1485 until the death of Elizabeth I in 1603. Both parts follow an article on medieval naval medicine and have the same aim of making comparisons with contemporary ADF practice, in order to identify common issues.¹

Like the previous article, they are based on the first of a four-volume history of naval medicine, written by Surgeon Commander J.J. Keevil RN (Rtd) in the late 1950s.² However, it has been possible to update Keevil's work, following the salvage of the 600 ton Tudor warship *Mary Rose*. The *Mary Rose* sank off Portsmouth on 19 July 1545, after she flooded through her gun ports whilst in action against a French fleet. There were only about 35 survivors out of 700 men, compared to her normal complement of 400, suggesting the *Mary Rose* was overloaded when she sank. The wreck was rediscovered in 1971 and raised in 1982.

This part describes Tudor medicine from a naval viewpoint and Tudor ships from a medical viewpoint. The second part will discuss the medical aspects of Tudor naval operations.

BACKGROUND

Early 16th century England had about 2.5 million people, suggesting a small population increase for the first time since the 1345-1348 Black Death and the Wars of the Roses. Most were rural dwellers, with London having only about 60,000 people. As it is estimated that there were only about 5,000 English mariners at this time, the English lacked the need and the resources to make any special provision for the health care of seamen, apart from the Laws of Oléron.³

After 1450, the sons of English noblemen began to join merchant-adventurer companies instead of the religious orders. The ensuing fall in the number of novices, combined with the reduced endowments by those who were becoming more concerned with material rather than spiritual gain, led to the decline of the charitable 'houses of pity' that provided health care for the masses during the Middle Ages.²

The end of the Middle Ages was a time of considerable economic disruption and unemployment, such that from 1493, begging licenses were issued to scholars, soldiers and seamen in order to control vagrancy. Municipalities and parishes were made responsible for dealing with the poor, while the drift to the cities was

addressed firstly by forced return to the parishes and later by punishing unlicensed beggars.²

Although Henry VIII's war with France and Scotland in 1512-13 temporarily solved the unemployment problem, it rebounded thereafter and was further exacerbated by his dissolution of the religious orders after 1537. In the 1530s, it was estimated that England had about 800 religious communities totalling about 10,000 people.³ Henry's dissolution of these communities was based on political expediency, the lure of material gain, and abuses by the religious orders themselves. His takeover of their revenues led to the closure of nearly all the charitable institutions, including the seamen's hospitals or 'masyndews'. It is estimated this left England with only about 5,000 hospital beds for the entire population³. Although his father, Henry VII, had left £6666 in his will for the first English military hospital at the Savoy in London, it was not completed until 1517 and, in any case, only had 100 beds. After Edward VI appointed some of the Savoy Hospital's revenue for other hospitals, it was always in financial difficulty and its dissolution in 1702 ended the religious medical outlook of the Middle Ages.⁴

1. CMDR Neil Westphalen is the Senior Medical Officer at HMAS STIRLING.

After the 1550s, the parishes began funding their own hospitals, with supplementation from lay benefactors, the privy purse, and levies, such as those on ships entering Bristol for the local mariner's hospital. One benefactor was Sir John Hawkins, who received a licence in 1594 for England's first naval hospital, a ten bed facility at Chatham. However, it was only after a 1597 Act allowed benefactors such as Hawkins to make donations without royal approval, that English hospitals could provide even the basic medical care that was previously offered by the medieval religious orders.⁴

The Tudor wars were therefore fought with minimal provision for medical care for anyone, let alone soldiers and sailors. One effect was to lay the whole English population open to epidemics of plague, typhus and intestinal infections⁵. Evidence from human remains recovered from the Mary Rose certainly suggests that the standard of Tudor health care was poor. Excavating the wreck showed that her crew had been trapped at all levels throughout the ship but, not surprisingly, had tended to congregate near the companionways. Although they were completely mixed together, over 90 skeletons were partly reconstructed, by matching paired lower limb bones with pelves and spines and using forensic dentistry to match skulls with mandibles. It was estimated the remains represented between 100 and 300 individuals.³

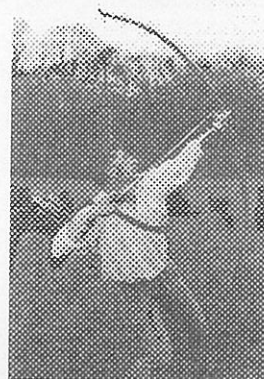
As might be expected, no women were identified and most of the crew were in their late teens and early twenties, although there was at least one child aged only ten. Their average height was about 171 cm and they had similar facial characteristics to 21st century males. Their dentition was fairly good, with modern patterns of tooth decay, but with better occlusion and less crowding. It was noted that many adult teeth had enamel hypoplasia suggestive of previous malnutrition, consistent with a severe famine during the English winter of 1527-1528. Other evidence of dietary deficiencies suggested childhood rickets and adult osteomalacia, and possibly healed scurvy.

Evidence of trauma included several healed lower limb, nasal, rib and skull fractures. There were also several avulsion injuries, particularly of the tibial tubercle, and several fracture-dislocations of the hip. One case of Perthe's disease was found. Osteoarthritis was present in several spines and one set of elbows, and appeared to be age-related. However, evidence of infectious disease was limited

to possible TB, with no evidence of leprosy or syphilis.

A separate finding was a 12.5% incidence of os acromiale (non-union of the acromial epiphysis), mostly on the left side, compared with a modern incidence of only 3%. One possible reason for the higher incidence in the Mary Rose crew relates to the use of longbows from childhood by dedicated archers. Henry VIII enforced a 14th century law that all fit males from seven to 60 had to practice with the longbow. Tests of longbows recovered from the Mary Rose indicate that they required a draw force of up to 75kg, compared to modern competition bows which only require about 20kg. As longbows are drawn differently to competition bows (for a right-handed man, by extending the left arm and shoulder instead of flexing the right), it may have been this technique, as well as the forces involved, that is responsible for the high incidence of os acromiale.³

The overall conclusion was of a relatively fit population, but with a high incidence of childhood dietary deficiency, and several old lower limb injuries that could be consistent with unstable seagoing conditions.

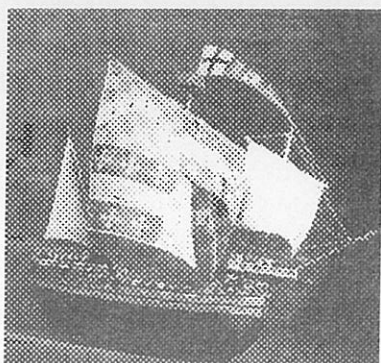


Above: Mary Rose specimen showing bilateral os acromiale³
Left: Contemporary bowman with replica Tudor longbow at full draw weight (75kg)³

TUDOR NAVAL AND MEDICAL DEVELOPMENTS

After several false starts, the Royal Navy was established by Henry VII, who built five ships and the first English dry dock (at Portsmouth). In so doing, his fleet developed from a mere armed transport service into a fighting force in its own right. Even so, Henry VII continued to hire his ships out in peace and to hire or impress merchantmen for war, a pattern that was followed into the next century. In the event, his ships were only used for anti-piracy patrols and they only fought one minor action, off Sluys in Holland, in 1492.²

Henry VII also contracted with his noblemen to provide him with soldiers, but left it to them to decide whether to take surgeons as well. Those who did either brought one with their retinue or had one indentured for the job by the London Barber-Surgeons Company. Although English surgeons first went to sea in this way, they were only taken to treat wounded soldiers, who ostensibly still did all the fighting. This meant no formal medical arrangements were made for Henry VII's sailors.²



Left: Model of an English carrack from the reign of Henry VII, from the Science Museum, London. Note the clinker hull construction and lack of gunports.⁵

Henry VIII ascended the throne in 1509 at a time of escalating tension with Scotland and France. Recognising the need for a strong navy, he initiated a maritime revolution when he commissioned the Mary Rose in 1511. Rather than carrying many small antipersonnel guns in the fore and aft castles and upper decks, she had 15 large 'antiship' guns below deck, firing through gun ports in the hull.⁶ These gun ports also led to carvel (edge-to-edge) replacing clinker (overlapping) hull construction. Three years later the Mary Rose was joined by the 1000 ton Henry Grace à Dieu, with a crew of 500 sailors and 500 soldiers.² The Mary Rose was rebuilt at least twice before her loss in 1545.

Mary Rose c15456
 Length: 105ft (32m)
 Beam: 38ft 3in (11.6m)
 Depth: 15ft 1in (4.6m)
 Displacement: 600t
 Rigging: four masted square rig with lateen mizzens
 Armament: 78 guns (91 after 1536)
 Complement: 415



Note the carvel hull construction and gun ports.

The surviving hull structure consists of a half section from bow to stern, with the whole port side missing. The lowermost level is the hold, containing ballast, stores and a brick galley. Two skeletons were found in the hold with remnants of straw nearby, suggesting they were sick or wounded. The level above the hold is the orlop, which contained more stores and equipment, as well as longbows and other hand weapons. Above the orlop is the main gun deck, with six large guns per side and four surviving cabins, including one for the surgeon. The upper deck had more guns and hand weapons, with archers shooting from behind protective blinds. It was also covered in anti-boarding netting, which meant that only those in the masthead fighting tops had a chance to escape when she sank.³

Large below-deck guns eventually eliminated the need for soldiers at sea, by allowing ships to stand off and batter each other, instead of having to grapple and board to fight hand-to-hand. Fewer soldiers allowed more seamen to be carried, thereby enhancing ship handling efficiency⁷. As a height advantage was no longer required for boarding, the fore and aft castles were reduced in height, while the ships' length-to-beam ratio was increased to improve seaworthiness. Henry VIII's 'high-charged' carracks became Elizabeth I's 'race-built' galleons, which in turn evolved into the line-of-battle sailing ships that dominated maritime power until the 1850s⁸. These developments led to distinctly different warships and merchantmen, and allowed the former to fight offensively rather than wait to be attacked⁷. Further improvements to the warfighting capability of English ships came when the 22 different types of gun in naval service under Henry VIII was reduced to five under Elizabeth I.

Other technical improvements led to incidental health benefits. For example, better bilge pumps allowed for drier and hence healthier ships². In 1578, Sir William Wynter recommended replacing gravel ballast with large stone ballast to allow ship's holds to be kept clean,² but this took time to be accepted, with the French continuing to bury their dead in the ballast until the 18th century.⁹ The French also suggested hammocks as early as the 1550s as they were easier to clean than lice-ridden straw beds, but their introduction aboard English ships after 1597 was driven by Sir Walter Raleigh's dislike of cabins, as dens of sickness and fire and splinter hazards in action². In 1590, Sir

John Hawkins followed Wynter's suggestion to move the 'cookroom' or galley from the hold (as in the Mary Rose) to the upper deck, thereby reducing contamination, improving ventilation, and allowing better stowage.²

Sanitary arrangements, however, remained basic, with a 'necessary seat' in an exposed and sometimes dangerous location forward, while tubs of water were kept between decks for use as combined urinals and fire buckets³. Meanwhile, the Laws of Oléron still did not permit sailors to undress at sea, resulting in hygiene problems.

As his sailors began to fight their ships themselves without soldiers, Henry VIII formalised his father's ad hoc medical efforts by instituting the first English naval medical service. The Exchequer accounts for his 1513 expedition to France lists 19 ships with no less than 32 surgeons serving under four master surgeons, led by a chief surgeon named John Veyrier. As a major fleet unit, Mary Rose had Robert Sympson as one of the master surgeons and Henry Yonge as his 'mate' or assistant. These surgeons received the same non-combatant status that English military surgeons had had since 1491. The same organisation was probably also used for the war with France in 1545 and the Spanish Armada in 1588.¹⁰

However, although a few disabled mariners received gratuities, the care of temporarily disabled seamen ashore still relied on the Laws of Oléron. A 1513 account had 'Andrew Fysche, one of the gunners of the Mary Rose to heal him of his hurts, 13s. 14d'. In the absence of pensions, most permanently disabled seamen relied on begging licences or competed with the other sick and poor for what little charitable accommodation remained after the Dissolution, until Lord Howard, Sir Francis Drake and Sir John Hawkins organised the Chatham Chest in 1590. This was an independent mutual benevolent fund, to which every seaman in the royal ships contributed sixpence a month. Despite abuses, the Chatham Chest lasted until 1829.²

In 1546, Henry VIII replaced the office of Keeper of the King's Ships that had existed since 1209 with a Naval Board of five officials, who were responsible for the building, maintenance, victualling and manning of his ships. Despite considerable nepotism and corruption, the Naval Board generally did a responsible job until the Admiralty was completely reorganised in



Begging licence of William Browne of London, issued by Lord Howard of Effingham in 1590. This allowed him to beg in all churches for one year, after he had been wounded in action during the 1588 Armada campaign.

(Landsdowne MSS, 144 f 53. British Museum.

Taken from Keevil JJ.

Medicine and the Navy

1200 - 1900. Vol 1

(1200-1649). London:

E&S Livingstone; 1957,

pp 56.)

18325. However, the first shore-based naval medical commission was not established until 1653 and it was not until 1702 that the Royal Navy established a permanent medical department.¹¹

TUDOR BARBER-SURGEON TRAINING

The Tudor period had four types of medical practitioner. The most prestigious were physicians with university degrees, albeit in humoral medicine. These were followed by members of the Fellowship of Surgeons, who were also university trained, highly skilled and often qualified in both medicine and surgery. Next were the barber-surgeons, who qualified by apprenticeship to a master surgeon, followed by the apothecaries, who sold medicines from their shops with free advice and were regulated by the Grocer's Company. These practitioners also competed with traditional non-qualified herbalists, quacks and astrologers.¹⁰

Henry VIII's 1511 Medical Act made the London bishops responsible for examining London's barber-surgeons and a similar act was passed for physicians in 1518. In 1540, Henry VIII made the Fellowship of Surgeons responsible for regulating the London Barber-Surgeons Company, and he also established a similar relationship between the physicians and the apothecaries². This exacerbated the divide between surgeons and physicians, with disastrous consequences

for sea-surgeons because they had to practice both. The 1511 Act also tried to define the medical profession, thereby arousing opposition from the unqualified practitioners. This led to the 1542 'Quack's Charter', which also made them liable for sea service.²

By 1563, apprentice surgeons had to be less than 21 years of age on entry. They had to serve a seven year apprenticeship, during which their lives were closely regulated down to dress and hairstyle and they were not allowed to marry. Their apprenticeship was practically oriented, although their use as servants led to difficulties from those fathers who felt they were not getting value for their indenture money.²

Although Barber-Surgeons were allowed to dissect four executed criminals per year after 1540, most of their anatomical and other training came from books. The leading authors included Thomas Vicary (d 1561), John Read, Thomas Gale (1507-1587) and William Clowes (1544-1604), all of whom wrote in English rather than Latin for the first time. Vicary produced a compilation of previous authors as *A Profitable Treatise of the Anatomie of Man's Bodie* in 1548. Read translated passages from Franciscus Arceus and John Arderne into *A most Excellent and Compendious Method of curing Woundes in the Head and in other Partes of the Body* in 1588, and was noteworthy for attacking quackery. Although he never served at sea, Gale had considerable interest in young military surgeons and wrote *An Excellent Treatise of Wounds made with Gunshot and An Enchiridon of Chirurgie* in 1563.²

However, the father of English naval medicine is William Clowes. He qualified at 19 years of age and served for several years at sea as well as ashore. In 1570 aboard the Queen's ship *Aid*, he treated a boatswain who sustained two fractured ribs from a capstan bar, by incising the fracture site to remove a sliver of bone which was abrading the pleura. The wound was redressed on day five and had healed by day ten; a creditable effort aboard a 200 ton Elizabethan warship. On leaving the navy, Clowes worked at St Bartholomew's in London, but returned to military service in the Netherlands in 1586-7, where he later stressed the importance of improvisation, using fingers as instruments and scabbards as splints. He was appointed to the fleet again in 1588 for the Armada, but was soon released.²

Like Gale, Clowes also tried to improve the status

of military surgeons, vehemently attacking quacks despite their protection by the 1542 Act. In 1588, he wrote *A Prooved Practice for all Young Chirurgeons*, which he updated in 1596 into *A profitable and Necessary Booke of Observations for all Those that are Burned with the Flame of Gun Powder, and also for Curing of Wounds made with Musket and Caliver shot, etc.*² For amputations, Clowes had a strong operating table on which an assistant could sit astride the patient, holding both arms down. For below knee amputations he had another assistant astride to hold down and steady the thigh and a third to hold the distal limb. He used a tourniquet for both haemorrhage control and analgesia. The amputation was performed circumferentially and, as the tourniquet was released, he found and stopped each bleeder. With the addition of four cross sutures to cover the stump, this technique was used at sea for the next three centuries.²

Although recognising the need for naval surgeons to also practice medicine, Clowes cautiously stated that he used all honest and lawful measures to practice both medicine and surgery, if no physician was available. He recognised the primary and secondary stages of syphilis as the only time it could be treated by external application of mercury and gave a full account of scurvy, even associating it with the seamen's diet.²

Although the College of Physicians often tried to prevent lectures to the Barber-Surgeons on medical issues, Clowes did so until he handed over to John Banester (1540-1610) in 1600. Banester had served ashore with Clowes in 1563 and 1586 and lost 45 patients (one third of his crew) during a failed expedition to the East Indies in 1582, of whom only three were surgical cases.²

After seven years training, the apprentice was examined in anatomy, surgery, pathology (such as was known), the significance of certain signs and managing emergencies. He then received a restricted licence allowing him to receive wages while working as an assistant. To receive an unrestricted license, he waited another year and then either underwent further oral examinations, or gave a lecture every six months until the Company was satisfied. He then paid £4 and was presented to the London bishops, after which he was licensed to set up his own practice as a Company freeman². Country surgeons either made do with the local bishop (with resulting problems if he failed to consult



*John Banester
lecturing at
Barber-Surgeon's
Hall in 1581²*

the local barber-surgeon's guild) or underwent a modified examination by the Company before being licensed by the London bishops².

However, as sea-surgeon apprentices were typically impressed from the country, they had not contributed previously to the Company and were therefore excused the period of restricted practice. This meant that they only had to pay seven guineas to the Company to be admitted as a freeman. Although apprentices could complete their training as mates to qualified sea-surgeons, a problem lay in the fact that ship's captains could employ anyone in any job. This meant apprentices frequently bypassed the examination altogether if their mentors died, such that this almost became a normal naval promotion, without reference to the actual responsibilities or qualifications involved.²

THE MARY ROSE MEDICINE CHEST

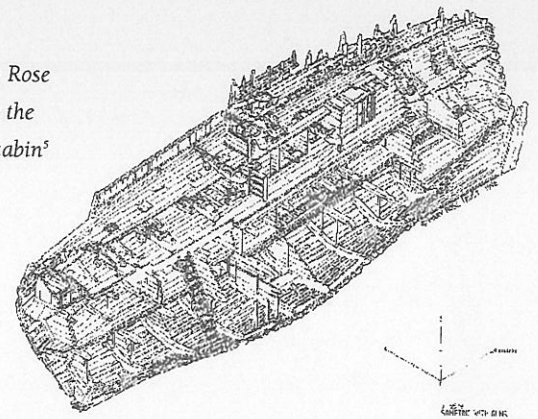
Clowes advised his students on what a military medicine chest should contain, using his own 1563 chest as a model. Given the alchemic approach to therapeutics at the time, apart from the usual purgatives the drugs were often rare and costly but often did little more than sweeten the air or hide the taste of rotting food.

Clowes' medical chest was probably similar to one retrieved from the Mary Rose in 1980. It was found in one of the cabins on the starboard side of the main gun deck. Almost empty of silt and undisturbed, it measured 1330 x 485 x 460mm¹² and was made of walnut with dovetailed joints on the corners, with a solid bar at each end pierced for rope handles. There were no internal partitions, except for a shallow lidded shelf on one side.

The 64 objects within included nine wooden containers with lids, eight containing ointments and one

containing peppercorns. One ointment had a resinous substance which may have been frankincense, complete with scoop marks from the surgeon's fingers. There were also five carefully corked ceramic jars from Siegburg in the Rhineland, with contents that may have included linseed oil, resins, henbane, quince or belladonna. Also found were several sausage-like rolls of unguents, made with a 2:1 ratio of fuller's earth and frankincense, which may have been used as plasters.³

*Drawing of Mary Rose
remains, showing the
barber-surgeon's cabin⁵*

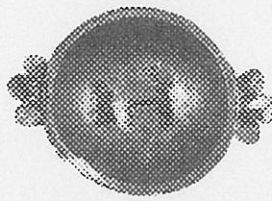


The chest had one brass and one pewter syringe, their needles having small rounded nipples at the tips. Ambrose Paré (1510-90) referred to the use of the small syringe for urethral syringes for bladder stones and strictures from gonorrhoea and to the use of the glister or large syringe to treat the 'flux' (diarrhoea) and constipation.

Although the steel had corroded away, the chest also had had a collection of surgical instruments, with eight handles similar to 17th century cauteries and a larger handle that may have been part of an amputation saw or large knife. There was a wooden mallet, eight cut-throat razors (indicating the surgeon was also the ship's barber) and a whetstone. Other items included a large brass shaving bowl, a small pewter bleeding bowl with the initials 'WE' on one handle, a small brazier for warming a chafing dish, and a heavy mortar for grinding drugs.

*Syringe from the Mary Rose
barber-surgeon's chest¹³*





*Bleeding bowl from
the Mary Rose
barber-surgeon's chest¹³*

*Urine bottle from the Mary Rose
barber-surgeon's chest¹³*



Apart from the chest, the barber-surgeon's cabin had more wooden and glass drug containers, as well as personal possessions including pewter plates, wooden bowls, shoes, combs and a purse of silver coins. There was also a low wooden bench that may have been used for applying plasters. A highlight was the surgeon's coif or hat, made of fine silk velvet and similar to those seen in a portrait of Henry VII, painted in 1540 by Hans Holbein The Younger (1497-1543) during a visit to the Guild of Barber-Surgeons.



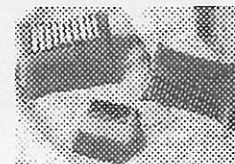
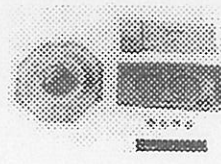
Left: Portrait by Hans Holbein the Younger (1497-1543) of Henry VIII granting his Charter to the Barber-Surgeon's Company in 1540. Thomas Vicary is next to Henry on his left. Note the coifs.³

Right: Barber-surgeon's coif from Mary Rose, worn by a reluctant volunteer before restoration¹⁴



As one of Henry's major fleet units, it seems likely that the Mary Rose had a master surgeon and an assistant on board. It was odd that, despite the preparations for action, the chest was intact (but ready for use), yet the surgeon was not in his cabin when she sank. A further mystery was revealed when a set of apothecary's scales was found on the after portion of the upper deck.⁵ A clue may be two letters from Henry's commanders referring to an outbreak of the

'bloody flux', which prostrated entire ship's crews. It is possible that, when the Mary Rose sank, her surgeon was treating patients in the hold, while his assistant was weighing out ingredients for medicines on the only part of the ship with enough light to see what he was doing. It is therefore possible that the Mary Rose sank, not through overloading or incompetent handling, but by a crew that was too ill to act in an emergency.⁵



*Apothecary
scales and
combs from
Mary Rose¹⁵*

Although not directly related to medical issues at sea, the 81 combs recovered from the wreck may be indicative of shipboard hygiene standards. All except two were double-sided and made of boxwood¹⁵. Of note are the fine teeth of many combs, suggesting that they were used for delousing, rather than mere tonorial elegance. In the likely absence of any other means of controlling fleas and the restrictions on removing clothing at sea, the number of combs found suggests that the standard of hygiene was less than ideal. The fact that the barber-surgeon had two combs (one found within the chest) suggests he was not immune from acquiring his own dermatological livestock.

SEA SURGEON'S CONDITIONS OF SERVICE

The first English sea-surgeons had significant problems with their status. Apart from the gentry, who acted as commanders in English ships until Francis Drake hanged one for mutiny, the most important seagoing officers were the gunner, the boatswain and the carpenter. Although a few master-surgeons served at sea with the gentry, most were ranked with the cook, smith, tailor, shoemaker, trumpeter and musician, which meant they lacked a meaningful place in the seagoing command hierarchy.³

The fact that surgeons started their careers as apprentices also created ambiguity, especially while the Barber-Surgeons Company had more barbers than surgeons. Although barbers and surgeons were separated as far back as 1376, barbers were still permitted to perform 'procedures' such as trimming corns, while the

Mary Rose chest confirmed that naval commanders used their surgeons as barbers. This meant apprentice sea surgeons had to acquire barber's tools and learn how to use them before joining their first ship.²

The impressment (compulsory service) of surgeons also contributed to their low status, especially as those liable ranged from fully qualified practitioners to midwives, oculists, dentists and bonesetters, who often used 'real' surgeons to perform procedures that were outside their expertise. Often their deficiencies were not revealed until it was too late and it was the ensuing clinical disasters that gave all sea-surgeons a poor reputation. Martin Frobisher's death through mismanagement, despite a slight wound in the thigh by a bullet at Brest in 1594, probably did little for their credibility.

Social barriers within the profession militated against sea-surgeons, as they were held in low esteem not only by the physicians, but also by their land-based brethren. The lack of legal authority to give internal medicines meant that they were often put on trial by physicians on returning home². Yet at least some Tudor sea-surgeons must have given some confidence to their ship's company, because sailors often refused to go to sea without one and when carried he was usually placed out of harm's way in the hold during action.²

As in the past, noblemen continued to make their own arrangements with either the Fellowship of Surgeons or the London Barber-Surgeons Company. William Gooderus, John Banester and William Clowes were all engaged on these terms, with Gooderus becoming serjeant surgeon of the Company, while Clowes and Banester passed on their military medical experience to young apprentices². However, because neither the physician's nor the surgeon's guilds had any specific responsibility for seamen's health care, it was only via these indirect means that any naval health knowledge was passed on at all. The lack of a shared pool of expertise in naval medicine therefore meant that the same mistakes were repeated again and again.

Furthermore, as neither the first Fleet Instructions dated 1530 or those of 1545 had any medical instructions, the royal ships at first failed to benefit from the medical lessons learned by the merchant adventurers during their overseas raids. It not until 1596 that the Instructions Issued to the Royal Navy included 'you shall give orders that your ship may be kept clean daily and sometimes washed; what with God's favour, shall preserve from sickness and avoid many inconveniences'².

Part of the problem lay in confusing 'comfort' for 'hygiene', with a 'school of toughness' deriding the health benefits of liberal diets, dry clothes, warmth, and bed sheets. Yet it was these informal contacts between the royal ships and privateers that led to the unwritten rules that became the foundations of naval hygiene².

Access to exotic overseas flora could have allowed sea-surgeons to import therapeutic drugs, including aloe, senna and ipecacuanha. However, as most surgeons lacked the authority and/or necessary training in internal medicine, it was often their captains who brought back reports of maladies and treatments². One example was John Lock, who wrote the first description of trachoma, during a visit to Cyprus in 1553. In 1572, a merchant named Henry Hawks first linked illness to 'mosquitos', but its loss meant that mosquito-borne disease continued to be ascribed to 'night air' for another 300 years².

A divided medical profession and their low status afloat meant living conditions aboard were largely controlled by ship's captains. As health care ashore extended beyond the medical professionals, the captains' involvement in treating 'sea-diseases' fell within this pattern. With the physicians trapped by their humoral theories of disease, the captains' efforts often met with some success. This stemmed from their authority and practical experience, although they were just as prone as physicians to theorising as to why things worked, without any attempt at scientific validation². From there, it was only a small step to captains taking over all non-surgical health issues, leaving the surgeons with only the actual hands-on application of their skills. London surgeon Thomas Roos wrote in 1519 that this included controlling haemorrhage, trephining, couching for cataract, removing sequestra, suturing wounds, lancing abscesses, reducing fractures and dislocations, dental extractions and bloodletting.²

It is therefore not surprising that the first book on tropical diseases was actually written by a non-medical adventurer. In 1598, George Wateson's *The Cures of the Diseased in Remote Regions preventing Mortality Incident in Forraine Attempts by the English Nation* presented a confused mix of typhus, yellow fever, dysentery, erysipelas and prickly heat. Wateson recorded some useful elements, although he avoided mentioning any conditions of which physicians at home were already aware, while dressing up simple

conditions with expansive Spanish names (such as 'cameras de flux' for the bloody flux) to make them seem more exotic².

The second part of this article will discuss the medical aspects of Tudor naval operations.

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REMINDER

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ABSTRACTS FROM THE LITERATURE

Contributed by James Ross

Staub D, et al. Effectiveness of a repellent containing DEET and EBAAP for preventing tick bites. *Wild Environ Med* 2002; 13(1): 12-20.

OBJECTIVE.

TOPICAL REPELLENTS can provide effective personal protection from tick-borne diseases by preventing the attachment of ticks. The goal of this study was to assess the effectiveness of a commercially available repellent spray containing both N,N diethyl 3 methylbenzamide, previously known as N,N diethyl m toluamide (DEET) and ethyl butylacetylaminopropionate (EBAAP) against tick bites in a population at risk in Switzerland under real life conditions.

METHODS

The effectiveness of an insect repellent spray containing both DEET and EBAAP was evaluated in a randomised double blind placebo controlled study. The study requiring simple application of the repellent to exposed skin, was carried out on 276 forestry workers and orienteers under everyday conditions in Switzerland from May to September 1999. We measured total effectiveness of the repellent by the following formula: percentage effectiveness + 100 x (Tp - Tr) / Tp where Tp and Tr were the average number of tick bites per hour spent in the wooded areas for the repellent and placebo groups, respectively.

RESULTS

The average number of tick bites per hour of exposure to wooded areas differed significantly between the placebo (n=138) and repellent (n=138) groups, 0.17 v 0.10 (P< 0.05). Total repellent effectiveness against tick attachment was 41.1% (95% CI, 2.5 - 79.6). On the arms an effectiveness of 66% (95% CI 17.3-114.7) was observed. No significant difference in the average number of unattached ticks could be found.

CONCLUSIONS

This study found that an easily applied repellent is moderately effective in reducing the risk of tick bites.

COMMENT

Only moderately effective. The subjects were told to apply repellent twice a day, but not how extensively to apply it. As part of a study they are likely to be far more rigorous in application: both in remembering and in amount used. Thus, the practical effectiveness is likely to be considerably less than stated in this study. So, and this applies to protection from any vector, such protection is only partly successful and must be part of a range of protective measures.

Military Medicine 2002; Volume 167(2)

Supplement 1: Proceedings of the international conference on low level radiation injury and medical countermeasures.

This supplement provides some very useful articles on the current state of knowledge and areas of research in this field. The following are a couple of the offerings

Blakely WF *et al.* Overview of low-level radiation exposure assessment: Biodosimetry. *Mil Med* 2002;167(2 Suppl): 20-24.

The capability to make diagnostic assessments of radiation exposure is needed to support triage of radiation casualties and medical treatment decisions in military operations. At the International Conference on low-level radiation injury and medical countermeasures session on biodosimetry in the military, participants reviewed the field of biomarkers, covering a wide range of biological endpoints. Participants evaluated early changes associated with exposure to ionising radiation, including chromosomal and DNA damage, gene expression and associated proteins and DNA mutations. The use and development of advanced monitoring and diagnostic technologies compatible with military operations was emphasised. Conventional radiation bioassays required a substantial amount of time between when the sample is taken and when the data can be provided for decision making. These "reach back" bioassays are evaluated in laboratories that are not in the field: these

laboratories routinely measure exposures of 25 cGy (photon equivalent levels). Detection thresholds can be reduced approximately fivefold by the addition of significant and tiresome scoring efforts. Alternative real-time biomarkers that can be measured in field laboratories or with handheld detection devices show promise as screening and clinical diagnostic tools, but they require further development and validation studies.

Kumar KS, *et al.* Nutritional approaches to radioprotection: Vitamin E. *Mil Med* 2002;167 (2 Suppl): 57-59.

Low-level radiation injury is dependent on the radiation dose and dose rate. The major military use of any potential radioprotectant is to prevent the short-term effects of lethality and the long-term effects of cancer and other pathologies from radiation exposure that may occur in a nuclear battlefield or in a nuclear material contaminated field of operation. Therefore, a radioprotectant should not affect the ability of military personnel to perform tasks. Because exposure to ionising radiation induces free radical species, effective antioxidants either alone or in combination with other agents, can be used as potential bioprotectors. To test this hypothesis, we studied vitamin E for its radioprotective efficacy. Using CD2F₁ male mice as the model system, we observed that vitamin E at a dose of 400 IU/kg acts as a good radioprotectant against lethal doses of cobalt 60 radiation. Vitamin E was more efficacious when given subcutaneously than when given orally.

COMMENT

Vitamin E is advantageous as it is non-toxic and thus will not interfere with primary duties. Just what is the mechanism is still speculation: a 'sink' for free radicals is the most likely.

McDiarmid M *et al.* Health Effects and Biological Monitoring Results of Gulf War Veterans Exposed to Depleted Uranium. *Mil Med* 2002;167(2 Suppl): 123-124.

A small group of gulf-war veterans have retained fragments of depleted uranium (DU) shrapnel, the long term health consequences of which are undetermined.

We evaluated the clinical health effects of DU exposure in Gulf War veterans compared with nonexposed Gulf War veterans. History and follow-up medical examinations were performed on 29 exposed veterans and 38 nonexposed veterans. Outcome measures used were urinary uranium determinations, clinical laboratory values, and psychiatric and neurocognitive assessment. Gulf War veterans with retained DU metal fragments were found to be still excreting elevated levels of urinary uranium 7 years after first exposure to DU (range for exposed individuals is 0.01-30.7 ug/g creatinine vs 0.01-0.05 ug/g creatinine in the nonexposed). The persistence of the elevated urine uranium suggests ongoing mobilisation of uranium from a storage depot resulting in chronic systemic exposure. Adverse effects in the kidney, a presumed target organ, were not seen at the time of the study; however, other subtle effects were observed in the reproductive and central nervous systems of the DU exposed veterans.

COMMENT

If any significant health effects do occur from DU, it requires a very long latency period. DU shrapnel produces no medium term health effects, so the concerns about short-term exposure can be laid to rest, unless there is a unique exposure.

International Conference on the Operational Impact of Psychological Casualties from Weapons of Mass Destruction - Proceedings. *Mil Med* 2001;166 (Suppl 2).

Another proceedings produced by Military Medicine as a complete supplementary issue.

Holmstedt-Mark B, *et al.* The psychological aspect of the Anthrax Vaccine: 'The Dover Experience'. *Mil Med* 2001;166 (Suppl 2): 36-40.

Discussion focuses on the Department of Defense (DoD) Anthrax Vaccination Implementation Program (AVIP) at Dover Air Force Base in Delaware (AFB DE). The history relates to the effects of an organised 'anthrax -no' group in using the Internet and the media to launch an intense rumour campaign on the DoD AVIP, which leads to mistrust of

and lack of confidence in senior leaders and the medical community. For many airmen, the fear of the vaccine takes precedence over the threat of the disease.

Dover Wing and Medical Group personnel combat the 'anthrax -no' campaign by providing increased education on the AVIP. Experts in the field are brought in to Dover to answer questions and to provide information to begin the process of rumour control. Policies are established by the medical group to assure the community's medical needs are expediently, thoroughly and competently met. The primary focus is to provide a safe, non-judgmental environment for members to voice their concerns and to resolve their medical issues.

COMMENT

The DoD policy on anthrax vaccine for the military in the US has just changed (end Jun 02), not because of risk profile from the vaccine but because of difficulty in obtaining sufficient stocks, the need to stockpile for possible use in civilians and the recognition that the risk of a widespread outbreak is remote. That the vaccine is 1960s technology at best, requiring 6 shots over 18 months and annual boosters and is very expensive are other relevant issues. There have been 450 US military who have been disciplined in some way as a result of refusing to have the vaccine.

Pastel R. Collective Behaviours: Mass Panic and Outbreaks of Multiple Unexplained Symptoms. *Mil Med* 2001;166 (Suppl 2):44-46.

The general public, the mass media, and many government officials believe that the use of weapons of mass destruction (WMD) will inevitably lead to mass panic and/or mass hysteria. However, studies of disasters and wars show that disorganised flight in the presence of a real or perceived danger (ie mass panic) is rare. On the other hand, in a real or perceived WMD scenario, outbreaks of multiple unexplained symptoms (ie mass psychogenic illness, mass sociogenic illness, mass hysteria or epidemic hysteria) may be prevalent. Many of these symptoms (fatigue, nausea, vomiting, headache, dizziness/lightheadedness, and anorexia) are common in combat and after toxic chemical exposure, chemical weapon exposure, prodromal infectious disease, and acute radiation sickness.

COMMENT

Always a fascinating subject, I feel, mass psychogenic illness. It will likely be a significant confounding factor in the assessment of possible attacks. As noted above, classic symptoms of MPI can easily mimic the poorly differentiated symptoms, particularly early in an epidemic of biological cause or anytime in a chemical cause. The more expectant of an outbreak, the more likely people are to convince themselves of its reality. Particular if other people are complaining of symptoms.

Ramalingaswami V. Psychosocial effects of the 1994 Plague Outbreak in Surat, India. *Mil Med* 2001;166 (Suppl 2): 29-30.

The plague outbreak in Surat, India in September 1994 stirred a nationwide panic and a near international isolation of India. These are aspects that need serious attention. A large amount of damage to India's image and an immense economic loss occurred. Some advice for the future is suggested.

COMMENT

This was a remarkable event, and the blind hopelessness that has marked mankind's response to the Black Death resurfaced as if we had learned nothing. I recall that the ADF sent a doctor to India to placate the members of the Australian expatriate community, particularly the diplomats. 'In one night, an avoidable exodus of 600,000 people fled Surat by whatever means available, including horse carriage, ox car, or even on foot... Doctors fled the city saying 'this plague, nothing can be done'.

Dervay JP, Powell MR, Butler B, and Fife CE. The Effect of Exercise and Rest Duration on the Generation of Venous Gas Bubbles at Altitude. *Aviat Space Environ Med* 2002; 73:22-7

BACKGROUND

Decompression, as occurs with aviators and astronauts undergoing high altitude operations or with deep-sea divers returning to surface, can cause gas bubbles to form within the organism. Pressure changes to evoke bubble formation in vivo during depressurisation are several orders of magnitude less than those required for gas phase formation in vitro in quiescent liquids. Preformed micronuclei acting as 'seeds' have been pro-

posed, dating back to the 1940's. These tissue gas micronuclei have been attributed to a minute gas phase located in hydrophobic cavities, surfactant-stabilised microbubbles, or arising from musculoskeletal activity. The lifetimes of these micronuclei have been presumed to be from a few minutes to several weeks.

HYPOTHESIS

The greatest incidence of venous gas emboli (VGE) will be detected by precordial Doppler ultrasound with depressurisation immediately following lower extremity exercise, with progressively reduced levels of VGE observed as the interval from exercise to depressurisation lengthens.

METHODS

In a blinded cross-over design, 20 individuals (15 men, 5 women) at sea level exercised by performing knee-bend squats (150 knee flexes over 10 min, 235-kcal · h⁻¹) either at the beginning, middle, or end of a 2-h chair-rest period without an oxygen prebreathe. Seated subjects were then depressurised to 6.2 psia (6706 m or 22,000 ft altitude equivalent) for 120 min with no exercise performed at altitude.

RESULTS

Of the 20 subjects with VGE in the pulmonary artery, 10 demonstrated a greater incidence of bubbles with exercise performed just prior to depressurisation, compared with decreasing bubble grades and incidence as the interval of rest increased prior to depressurisation. No decompression illness was reported.

CONCLUSIONS

There is a significant increase in decompression-induced bubble formation at 6.2 psia when lower extremity exercise is performed just prior to depressurisation as compared with longer rest intervals. Analysis indicated that micronuclei half-life is on the order of an hour under these hypobaric conditions.

COMMENT

This involved pre-depressurisation exercise, not exercise during depressurisation. And, of course, there were bubbles but not symptoms, which begs the question of what actually causes symptoms. Just because there are more bubbles does not necessarily mean the risk of DCI is increased.

Grimson JM, Schallhorn SC, and Kaupp SE. Contrast Sensitivity: Establishing Normative Data for Use in Screening Prospective Naval Pilots. *Aviat Space Environ Med* 2002; 73:28-35.

BACKGROUND

Contrast sensitivity testing can be a useful supplement to standard visual acuity tests. Currently there are no standards for contrast sensitivity in military aviation. Student naval pilots, who often have better-than-average visual acuity, could be expected to have better-than-average contrast sensitivity. Any attempt to establish contrast sensitivity standards for military aviation should begin with establishing normative data, particularly data gathered from the military aviation community.

HYPOTHESIS

Student naval pilots differ from the general military population on Small Letter Contrast Test measurements.

METHODS

Contrast sensitivity was measured in a group of student naval pilots (n = 107) and compared with results from aviation and non-aviation personnel. The Small Letter Contrast Test (SLCT) was used (19). Other subjects consisted of student naval flight officers (n = 40), experienced naval pilots and flight officers (n = 35 and 86, respectively), enlisted aircrew (n = 175), and other military personnel tested before undergoing photorefractive keratectomy (n = 185).

RESULTS

Data collected provide large-group demographic characteristics and normative values for contrast sensitivity measured with the SLCT. Of the non-aviation controls, 95% scored at least 0.62 (read at least seven lines plus two of ten letters on the eighth line of the chart), and 95% of the student pilots scored at least 0.81, (read at least nine lines plus one letter on the 10th line).

CONCLUSION

Student naval pilots scored significantly better on the SLCT than the military control population. The SLCT shows potential as a screening device during induction physical examinations of military pilots.

COMMENT

Just because someone has better than average visual acuity does not mean (with certainty) they will have better than average contrast sensitivity. They are different parameters and may not be linked. It would be useful to be able to define what is the minimum acceptable for contrast sensitivity for recruitment, and then also for post-refractive or other eye surgery. Eventually a consensus will be reached on a standard.

Smith SD Characterising the Effects of Airborne Vibration on Human Body Vibration Response. *Aviat Space Environ Med* 2002; 73:36-45.

BACKGROUND

Exposure to high intensity, low frequency noise can cause whole-body vibration. Such exposures to airborne vibration can reach the limits of human tolerance and have been associated with physiological and pathological disorders. The objective of this study was to characterise human body vibration response during exposures to operational airborne vibration.

METHODS

Triaxial body accelerations were collected at multiple anatomical sites with the subject located at selected crew positions during ground-based engine runup tests on several military tactical aircraft. The acceleration time histories were processed in one-third octave frequency bands and compared with the one-third octave band noise data.

RESULTS

The most significant finding was the occurrence of a resonance peak in the fore-and-aft (X) chest acceleration in the frequency bands between 63 and 100 Hz. Both the chest acceleration and associated noise level increased as the subject moved aft of the exhaust outlet, coinciding with the report of increasing chest vibration. A relatively linear relationship was found between the overall chest accelerations and noise levels between 5 and 250 Hz. An approach to developing combined noise and vibration exposure criteria was proposed.

CONCLUSIONS

The resonance observed in the upper torso strongly suggested that airborne vibration in the 60 to 100 Hz

frequency band may be an important contributing factor in the generation of subjective symptoms and possibly physiological and pathological disorders. Additional field and laboratory studies are required to validate the relationship between the biodynamic responses, noise levels, and physiological and pathological consequences.

COMMENT

Vibroacoustic disease is a field of continuing research and increasing concern. Infrasound can cause a huge range of problems, from interference with concentration to psychological effects to significant long term disease. The range of 60-100 hz is higher than is generally viewed to be the main culprit.

Koda E. Could foot and mouth disease be a biological warfare incident? *Mil Med* 2002;167(2): 91-92.

COMMENT

This editorial provides a postulation that the foot and mouth outbreak in the UK in 2001 could have been an act of bioterrorism. While the idea is worthwhile, the detail lacks any credibility and in the end I was left with the feeling that this should never have made it into print. All concerned should have backed off and realised it was simply not the case – at least not on this occasion. Truly a silly article.

Ohrui N, et al. Physiological Incidents During 39 Years of hypobaric Chamber Training In Japan. *Aviat Space Environ Med* 2002; 73(4): 395-398.

BACKGROUND

Hypobaric chamber training for military aircrew is very important for flight safety. Since we began hypobaric training in our laboratory in 1960, some trainees have suffered physiological incidents. This study will characterise the physiological incidents during hypobaric chamber training at the Japan Air Self-Defence Force (JASDF).

METHODS

All available training records from 1960-1998 were reviewed and the frequency of physiological incidents counted and analysed.

RESULTS

There were 29,677 trainees and 58,454 exposures. Overall frequency of physiological incidents was 6.3%. Physiological incidents included ear pain, paranasal sinus pain, abdominal pain, hypoxia, hyperventilation, joint pain, and toothache. Decompression sickness (DCS-I, simple joint pain only) was rare. In cases of DCS-I, joint pain was easily relieved with controlled descent. During the last three decades, overall prevalence of physiological incidents has gradually increased from 5.3~6.1% before 1991, to 6.8~9.9% after 1991. However, prevalence rate showed no change throughout the period when ear pain was factored out. The increase in prevalence was entirely due to an increased frequency of ear pain: 3.6~4.6% before 1991, and 5.4~7.2% after 1991.

CONCLUSIONS

DCS has not been a problem in the JASDF hypobaric chamber training experience. The majority of physiological incidents during hypobaric chamber training in JASDF have been ear pain, a minor but frequent obstacle to hypobaric training. The exact cause of the observed increase in frequency of Eustachian tube dysfunction currently remains unclear.

COMMENT

A continuing topic of discussion, and perplexity, in the Aviation medicine fraternity, is the widely differing rates of Decompression Illness as a result of seemingly analogous exposures at various training establishments around the globe. Australia is firmly in the high rate camp, to the extent that the ADF no longer has hypobaric chamber runs to above 10000 feet, with hypoxia being experienced by gas-mix to reduce the oxygen percentage. This report puts Japan firmly in the low rate camp.

Ireland R. Pharmacologic Considerations for Serotonin Reuptake Inhibitor Use by Aviators. *Aviat Space Environ Med* 2002; 73:421-9

Physicians frequently use serotonin reuptake inhibitors (SRIs) to treat a variety of psychiatric and medical conditions, many of which occur in aviators. SRIs are efficacious for treating acute conditions and may also prove useful for prophylaxis against recurrence through maintenance dosage. Aviators must meet standard safe-

ty criteria in order to use medications while performing flying duties, and must receive individual waivers as well. This article reviews the particular threats that serotonergic agents pose to aviation safety. Some SRIs may prove safer than others to use in the aviation environment, but such medications will require appropriate ground testing, and must provide aeromedically safe control of the symptoms for which they are prescribed.

COMMENT

SRIs are used for long-term control of depression, as well as other psychological/dependence conditions. In aviation, the banning of SRIs in aircrew will likely lead to the underground use or poorly treated depressives. This review strongly suggests that SRIs have the potential to be safely used by aviators, provided appropriate protocols are followed. Further studies will follow

Contributed by Darrell Duncan

Chaffin J, King JE, Fretwell LD. US Army Dental Emergencies Rates in Bosnia. *Mil Med* 2001; 166 (12).

OBJECTIVE

Our objective is to report on overall dental emergency rates by dental classification in a US Army peacekeeping operation longer than 6 months in the year 2000.

MATERIALS AND METHODS

This study was a retrospective cohort analysis of dental emergencies experienced by soldiers of the 3rd Armored Cavalry Regiment as a part of Stabilisation Force VII. Before the deployment, all soldiers received dental examinations and the necessary dental treatment to make them class 1 or 2. A dental emergency was identified from the field treatment records when a soldier presented to the clinic for a 'sick call', emergency, or trauma visit.

RESULTS

Retrospective review of the records identified 211 dental emergencies. Class 1 soldiers experienced 75 dental emergencies and class 2 soldiers experienced 136 emergencies. 3rd Armored Cavalry Regiment soldiers spent an average of 201.95 days deployed. The overall emergency rate was 156 dental emergencies per 1000 soldiers

per year. Class 1 and 2 rates were 121 and 185 dental emergencies per 1000 troops per year respectively.

CONCLUSIONS

The results tend to confirm that dental emergencies continue to be a threat to overall readiness in deployed environments. Military planners need to ensure that the dental component of future forces are sufficient to care for the expected emergencies.

COMMENT

This is one of the few studies of dental disease rates that I have seen. The authors acknowledge such studies are sparse. This study has a number of limitations, as indicated by the authors. Comparison to other results, and in particular the ADF experience,, should be done with caution, in particular noting any differences in definitions of a dental emergency. The authors rightly point out that more studies of this nature are desirable to assist in the development of predictive models of dental casualties to aid planners. For instance, it would be of interest to see studies comparing the presentation rate to sick parades for each of the ADF's dental categories. This would allow validation of our current policy with respect to dental readiness.

Pijnenburg ACM, Glas AS, de Roos MAJ, Bogaard K, Lijmer JG, Boosuyt PMM, Butzelaar RMJM, Keeman, J N. Radiography in Acute Ankle Injuries: The Ottawa Ankle Rules Versus Local Diagnostic Decision Rules. *Ann Emerg Med* 2002;39(6).

STUDY OBJECTIVES

We validate the Ottawa Ankle Rules and two Dutch ankle rules in distinguishing clinically significant fractures from insignificant fractures and other injuries in patients with a painful ankle presenting to the emergency department.

METHODS

This prospective comparison of three ankle rules was conducted in the ED of a 580-bed community teaching hospital in Amsterdam from January 1998 to April 1999.

Participants included 647 consecutive patients aged 18 years or older presenting with a painful ankle after trauma. All physicians received extensive and pictorial training on how to correctly score the respective items of the rules. The physician on call recorded these items derived from history and physical examination on a standardised data sheet. All patients subsequently underwent standard radiographic assessment. A radiologist and a trauma surgeon evaluated the radiographs blinded from the results of the data sheet form and treatment given. The diagnostic performance of the three rules was measured in terms of sensitivity, specificity and the reduction of radiographs. Receiver operating characteristics (ROC) curves were constructed and the area under the ROC curves was calculated and compared.

RESULTS

Seventy-four fractures were seen, of which 41 were clinically significant. The Ottawa Ankle Rules had a sensitivity of 98% for identifying clinically significant fractures; the local rules scored 88% and 59% respectively. The potential savings in radiographs for the 3 decision rules were 24%, 54% and 82% respectively. The area under the ROC curve was better for both the local rules (0.84 and 0.83) compared with the Ottawa Ankle Rules (0.76).

CONCLUSION

Because the identification of all relevant fractures is more important than a reduction in radiographs, the higher sensitivity of the Ottawa Ankle Rules makes these most suitable for implementation in the Netherlands.

COMMENT

This study looked to see if a clinical rule validated elsewhere (the Ottawa Ankle Rule^{1,2}) could be applied in a different environment. The age range of the patients in the study was wider than the ADF population (18- 92 with and average of 35). Despite this difference in populations, it is not unreasonable to expect that the Ottawa Ankle Rules could be used within the ADF to reduce the number of ankle radiographs ordered and to reduce the likelihood of missed fractures. If the incidence of ankle injuries and ankle radiographs is known, the potential benefit of this measure could be calculated.

REFERENCE

1. Stiell IG, Greenberg GH, McKnight RD, et al. A study to develop clinical decision rules for the use of radiography in acute ankle injuries. *Ann Emerg Med* 1992; 21: 384-390.

AMMA UPDATE

AUGUST 2002

News and Information for members of the Australian Military Medicine Association

SUCSESSES

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 MOVEMENTS

- MAJ Mike Rowell to John Hopkins University to do his MPH

RETIREMENTS

- CMDR Mark Parrish has retired to take up the CEO position at Hornsby Hospital
- LCDR Jeannette Conley has retired to take up the DCS position at Ryde Hospital.

AWARDS & GRANTS

AMMA have a number of awards and grants available to members. Deadline for all awards is 30 June 2003.

For those wishing to do a research project within Defence, the project must be approved by ADHREC (The Australian Defence Human Research Ethics Committee). Information kits for

new researchers are available from the ADHREC Executive Secretary on: Tel: (02) 6266 3818
Fax: (02) 6266 4982

Research Grant - \$1000

A grant presented towards new or ongoing research. The 2002 Prize was awarded to Caroline Rickards.

Journal Editors Prize - \$750

For best paper by an AMMA Member published each year in the AMMA Journal. The 2002 Prize was divided between Sindy Vrancic and Pam Frost.

Patron's Prize - \$250

Best article published in a peer-reviewed journal by an AMMA member – must be a health related article. The 2002 Prize was awarded to Lt Col. Beverly Wright.

Australian Military Medicine Prize - \$500

Best essay by an AMMA Member on a chosen topic. The Prize was not awarded in 2002. The topic for 2003 is: *"The Challenge for the Future. Recruiting and Retaining the Best People for Defence health Operations"*.

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

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For all general AMMA inquiries contact the Secretariat.

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AMMA WEBSITE

Visit AMMA's website at:
www.amma.asn.au

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

AMMA CONFERENCES

2003 Conference

The 12th AMMA Scientific Conference will be held in South Australia from the 17th – 19th October 2003.

The program will be posted to all AMMA members.

For more information please call Leishman & Associates on (03) 6234 7844 or visit the web site: www.amma.asn.au

JOURNAL

Journals for 2002/2003 will be published as follows:

Issue	Copy Deadline
Dec 2002	31/10/02
Apr 2003	28/02/03

All queries regarding the Journal should be directed to the editor:

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CONFERENCE AND MEETING CALENDAR

Date	Conference	Venue	Contact No.
10-15 Nov 02	AMSUS Meeting	Louisville, KY	http://www.amsus.org/meetings/current.html
6-10 May 03	World Conference on Disaster and Emergency Medicine	Melbourne	RParry@meetingplanners.com.au
11-16 May 03	Asia Pacific Military Medicine Conference	Bangkok, Thailand	
17-19 Oct 03	AMMA 12th Annual Conference	South Australia	secretariat@amma.asn.au

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/
	Navy Corpsman	http://www.corpsman.com/
	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
	Military Medical Links	http://flash.lakeheadu.ca/~cfms/links.html
Professional Colleges:	ANZCA	http://www.anzca.edu.au/
	RACGP	http://www.racgp.org.au/
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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.

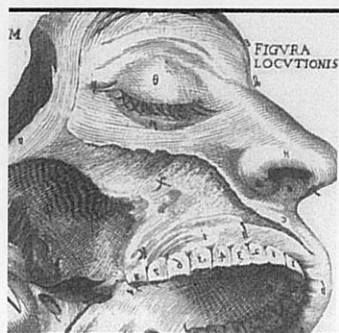
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