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President's Message

Welcome to the first issue of Australian Military Medicine for 1996. Although the year has only just started to 'kick on' from the holiday season, it already appears to be one which has the potential for changes in Military Medicine in Australia. It is to be hoped that with the change in government, the bipartisan approach to maintaining the profile of all aspects of health support in local and international military and humanitarian projects continues. As discussed in the 50th anniversary year of the end of the Second World War, Australia's contribution has been greater than one would expect from a country of our population and resources.

To assist in ongoing research in the areas of military medicine, I am pleased to announce the proposed establishment of a database of Australian research in military medicine. The cost of establishing the database and the cataloguing software is to come from the prize money donated to AMMA at last year's conference by Steve Rudzki. Once established this resource will be available for the use of all members. On the subject of research, just a quick reminder to those who have a project but are seeking funding assistance, the deadline for this year's AMMA Grant applications is fast approaching. AMMA will endeavour to assist members in worthwhile research projects as stated in the aims of the organisation. Details concerning applications will be found elsewhere in this issue.

The AMMA Council has recently farewelled Chris Maron from Council as he has been posted to the UK. Chris was one of three councillors who had been members since AMMA was founded, holding the positions of inaugural Treasurer and later Member. His contributions, diligence and sense of humour will be missed. I take this opportunity to publicly thank him for his efforts in the establishment of AMMA.

As the call for nominations for Council membership are included in this issue of the journal and the constitution only specifies the membership of Council being between five and eight members, Council have elected not to declare a casual vacancy at this time because of the proximity to Council elections. If, however, any member wishes to assist Council in any capacity please do not hesitate to contact either myself or the Secretary. I encourage all members who wish to contribute to the organisation of the association to consider nomination to Council. I intend to nominate for one further term as President in order to consolidate some of the administrative changes Council have brought about during this term of office. I hope that the association will allow me to do so and to further develop the association to meet the needs of it's membership.

Once again I encourage you all to allow Council to know how we may best meet your needs. Any suggestions on how to improve the association or further develop it are always appreciated.

Nader Alou-Seif
Editorial

On the High Price of Health Care

It's on again. We spend too much on health care in the ADF. Finances are tight, budgets need to be contained.

Unfortunately, when the 'bean counters' get hold of health care costs and try to contain them, they do so with little or no understanding of the issues involved. Health care costs in the ADF are perhaps a little easier to manage than in the wider community because we have a fixed population whose members are 'fit' when they first join it, we have more 'control' over the service providers, and we have a fairly well defined charter to guide the kind of health care we deliver.

When they join the ADF, individuals are likely to be free of significant disease. However rates of illness and injury are probably no less than in a comparable civilian population (matched for age and sex). In some areas, such as sporting injuries, rates are probably higher than the general community. Service personnel are also not immune to serious diseases - there is at least one heart and one kidney transplant patient in the ADF, and quite a number of our senior personnel have had coronary artery by-pass surgery.

Because of the 'managed' nature of ADF health care, the problem of supplier induced demand is probably less than in the outside community. The ADF has a system of pharmaceutical supply that not only provides medications at a lower cost than are available to the general public, but places limits on the provision of certain more expensive items. The use of 'alternative' health practitioners is strictly controlled. There is a process of review (generally not onerous) of the activities of health care centres.

The provision of health care in the ADF is governed by instructions that guide us towards the maintenance of a force that is 'fit to fight': that is, the ADF's commitment to health care provision is theoretically limited to that which is required to bring an individual to a level of health that is commensurate with fitness to operationally deploy. More expensive procedures, particularly in the cosmetic field, are generally not available through the system.

There is no doubt that there has in recent years been a significant increase in health care costs in the ADF. Although there are no published data on which to base such an assertion, it is probable that this increase is due to increased costs rather than increased illness rates. These increased costs are mainly due to the higher levels of technology available in the diagnostic and treatment areas, and the consequent change in case management.

The multitude of diagnostic procedures now available to us has dramatically increased costs. Where before a closed head injury was managed with an x-ray and MICO therapy (Masterly Inactivity, Cat-like Observation), we are now obliged (probably with some clinical justification) to do a CT scan early to exclude an intracranial bleed. The work up procedures for epilepsy and ischaemic heart disease are now much more technologically based than in the past.

Treatment modalities have changed dramatically as well. CABG's are now routine, and coronary angioplasties are becoming more frequent as a first step management procedure. Orthopaedic and general surgery is becoming more technologically based with arthroscopic and laparoscopic procedures. Medications are becoming more expensive.

Of course, there is a positive side to all this. Recovery times are reduced, and more people are able to return to full duties. Remember the days when a patient took six weeks or more to fully recover from a meniscectomy or herniorrhaphy? In the pre-CABG days, what became of the senior officer with severe ischaemic heart disease - what chance the ability to return to a full, active and productive life? Unfortunately (for us health care providers) these intangible costs are not visible, and are generally left out of cost-benefit analyses. For a fighting force, of course, these costs can be critical.

A simple solution to the cost of ADF health care that is often touted is the use of Medicare cards. Why, ask the bean counters, should our people be entitled to use the private system? Leaving aside the issue of benefits of Service (of which free health care seems to be one of the few remaining!), the most cogent argument in favour of the use of the private health care sector is the 'control' over service provision such use affords us. Those who live in New South Wales will surely remember the debate over public hospital waiting lists that occurred during the last State election campaign. Would our commanders be happy to accept prolonged levels of reduced operational availability in (possibly key) personnel while they wait six months or more for elective surgery to allow them to regain fitness for full activities? Would these same commanders be prepared to accept such delay when they need elective surgery themselves?

There is an interesting example of the possible effects of the use of a public health system. In 1994, as part of wider Defence cost savings, the UK Defence Forces closed all of their Service hospitals apart from the Royal Naval Hospital, Haslar (at least they got that part right!). The solution for the provision of inpatient services in other areas with significant Service populations was to integrate military medical units into National Health Service hospitals. Two years later, the experience in these hospitals has been one of poor Service-civilian interrelationships and an inability of the military units to control elective admissions. This latter
has resulted in a very large number of personnel being sent South to Portsmouth so that they can have elective surgery provided in the military hospital in a timely manner.

The impact of all these issues is also modified by individual demands and expectations. Service personnel believe they have certain 'rights' to a particular standard of health care; often these perceptions are misguided, but if the ADF restricts access below certain levels of care that can reasonably be expected in the civilian sector we leave ourselves open to criticism and complaint. A useful benchmark that is often taken is Medicare services, and yet the ready provision of services to private health care standards (such as spectacles) will make contraction in such service provision in the future very difficult, if not impossible. Perhaps now the Service benefit of 'free' health care is seen by many to equate to a non requirement to pay both the Medicare levy and private health insurance.

When the debate begins, as it surely will, we must ensure that all intangible costs (travel times, waiting times etc) are included in terms that our bean counter friends can readily understand.

Russ Scholich

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DISCLAIMER
The views expressed in this journal are those of the authors and do not reflect in any way official Defence Force policy or the views of the Surgeon General, Australian Defence Force or any military authority.

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4th ANNUAL SCIENTIFIC MEETING OF HYPERBARIC AND DIVING MEDICINE

Date: 29th to 31 August 1996
Venue: Hotel Grand Chancellor
Hobart, Tasmania, Australia

This international scientific conference is being held by the Australian Hyperbaric Technicians & Nurses Association in conjunction with the Australian and New Zealand Hyperbaric Medicine Group. The main conference will cover hyperbaric medicine on the Friday and diving related issues on the Saturday.

Keynote speakers will be Professor Dirk Bakker and Mr Dick Clarke. Professor Bakker, medical director of the Amsterdam Academic Medical Centre, Chief Department of Hyperbaric Medicine and past president of the International Congress on Hyperbaric Medicine has published extensively on related subjects. Mr Dick Clarke Administrative and Clinical Director of Hyperbaric Medicine at the Richland Memorial Hospital, Columbia, USA and President of National Baromedical Services has extensive experience in saturation diving and hyperbaric systems.

This conference first held in 1992 is rapidly becoming the most important scientific forum for diving and hyperbaric medicine in the Southern Hemisphere.

Conference Arrangements:
Sean Rubidge, Royal Hobart Hospital, Hyperbaric and Diving Medicine
Unit G.P.O. Box 1061L, Hobart 7001, Tasmania, Australia,
Phone 002 388322, Fax 002 388322 or 002 347 684.
Alpha viruses
S.C. Sharpe

Aetiology
Alphaviruses are single-stranded RNA viruses, spherical in shape, and with a diameter of around 60-70nm. They have a lipoprotein envelope, and have glycoprotein surface spikes containing major antigens. They belong to the family Togaviridae, which also contains the Flaviviruses (including Dengue fever virus, yellow fever virus, West Nile virus, St Louis encephalitis virus, Japanese encephalitis virus), Rubiviruses (Rubella) and Pestiviruses. Other medically important alphaviruses include O'nyong-nyong virus, Ross River virus, and Sindbis virus.1

Eastern equine encephalitis (EEE) virus has high persistence in the wet, and fair persistence on dry surfaces.

Venezuelan equine encephalitis (VEE) virus has a very high persistence in the wet, and a fair persistence on dry surfaces. It can be readily cultured in embryonated eggs, dried, and delivered in a powered form.

Chikungunya virus has fair persistence in both wet and dry environments.

Epidemiology
Alphaviruses have a wide host range, and are able to multiply in both arthropods and vertebrates. In nature, vertebrate hosts include birds, monkeys, rodents, and horses (especially with VEE virus). The mosquitoes *Culex*, *Anopheles* and *Mansonia* are the natural arthropod hosts.2 All known alphaviruses are mosquito-borne.3

Spread of the virus to man is accidental.

EEE
EEE occurs primarily in eastern United States and Canada, but has been reported in Central America and in Trinidad, Guyana, Brazil and Argentina.1 The WHO has also noted the possible isolation of the virus from Europe and Asia. The vector is still unknown, but the mosquito *Culicetia melanura* may be one. Birds and mosquitoes, which are part of the natural cycle of the disease, only develop asymptomatic infections, whereas humans and horses may become clinically ill as a result of infection.1

VEE
Western Equine Encephalitis (WEE) is found in the United States, mainly west of the Mississippi River, but has recently been detected on the eastern seaboard, Canada and South America. The vectors for WEE are *Culex tarsalis* in the central and western regions, and *Culicetia melanura* in the north. Other unidentified mosquitoes are probably also vectors for these diseases.2

The disease occurs in both sporadic outbreaks and epidemics.

VEE
VEE occurs in Florida, south-western USA, Central America, northern South America, the Amazon Valley, and southern Mexico.2 Small mammals are the natural primary host, and transmission to humans and horses occurs via the bite of an infected *Aedes* *mansonii* or *Apsorophora* mosquito.2 There are four major subtypes. Subtypes IA and IC have been associated with severe epidemics, and subtypes ID, IE, II and IIIA also cause medical problems. The other subtypes appear to be avirulent. An outbreak of the disease occurred in 1971 with subtype IB, which spread into western Texas, resulting in 84 identified serological cases, and 17 cases of encephalitis. Major epizootics occur at around ten year intervals in Peru, Venezuela and Colombia, and cause medical problems. The other subtypes appear to be avirulent.

There is also evidence that certain haematophagous mites may be able to mechanically transmit the virus to susceptible hosts (as opposed to biological transmission). The virus is unable to replicate in these mites but can be passed on to the host within a limited time after the mite has first ingested the viraemic blood meal.1

Chikungunya
Chikungunya, spread by mosquito vectors of the genera *Aedes* (particularly *Aedes aegypti* and *Anopheles*), is found in Africa, South East Asia, and India.1 There were over 20 million cases reported in Indonesia in the 1980s. Chikungunya occurs in both massive outbreaks and as a sporadic disease.

Pathology
Neutralising antibodies to the envelope glycoprotein of these viruses appear about seven days after the onset of disease, and remain in the body for many years, and confer solid immunity.2

The virus is present in the saliva of the infected mosquito vector, and is injected into the bloodstream or lymph of the host. The virus is then cleared by reticuloendothelial cells, where it multiplies, especially in the spleen and lymph nodes. Viraemia may follow, and various organs and tissues may become infected - including the central nervous system (in encephalitic diseases), bone marrow, skin, and blood vessels (in haemorrhagic fevers).

Severe alphavirus infections involve the viscera, brain, and spinal cord.
EEE
After inoculation into the skin, the virus replicates at the site of entry, and may then become viraemic. In around 4% of cases, necrotising encephalitis may follow. EEE produces lesions in the white and grey matter of the brain, especially in the basal ganglia and brain stem, and to a lesser extent in the spinal cord.\(^2\)

WEE
The virus replicates outside the central nervous system, but the CNS may become infected if viraemia occurs. WEE causes lymphocytic infiltration of the meninges, and lesions of the parenchyma, which consist of necrosis of the neurons, glial infiltration, disseminated small abscesses, demyelination, and perivascular cuffing. Small blood vessels and thrombi may become inflamed.\(^5\)

VEE
VEE is readily aerosolised, and highly infectious when inhaled. Several laboratory-acquired infections have occurred in this way.\(^4\) Additionally, the infective dose is very low: as few as 100 airborne viral particles are enough to cause disease. Person to person transmission has not been documented.

Once internalised, VEE replicates in lymphoid tissue, and other organs. Virulent strains exhibit lymphotoxic effects, and may spread to the CNS after the viraemic phase of the illness. Viral replication causes cell destruction, and induces a severe inflammatory response. The humoral response is prompt, with antibodies appearing at the end of the viraemic phase. These antibodies are protective, and will protect against a second attack.

Chikungunya
Patients experience symptoms in the systemic phase, notably fever, arthritis, and rash. In some rare cases, a haemorrhagic fever may follow.

Clinical Manifestations
Two distinct phases are seen in EEE, WEE, and VEE. The first is a systemic phase caused by the viraemia, which is characterised by fever, headache, nausea, vomiting, chills and aches. An encephalitic phase, with convulsions and coma, may then follow. Signs of neurological damage include paralysis, irregular breathing, cyanosis, and sialorrhoea.\(^1\)

EEE
EEE has a high mortality in humans (up to 50-75%), and often results in neurologic damage, such as mental retardation, paralysis, and recurrent seizures in those who survive.\(^6\)

The disease is more prevalent in children than adults.\(^1\)

The illness is characterised by an abrupt onset of fever and headache, followed by confusion, seizures, and coma. Those patients without CNS complications usually have a non-specific febrile illness with fever, headache and sore throat.

WEE
WEE is generally much less severe than EEE, but is more prevalent, and is usually restricted to children under four years and infants. The disease is usually limited to headache and fever, and is often inapparent. Mortality is seldom above 10%.\(^1\)

Children under 12 months may be left with permanent brain damage as a result of infection.\(^1\) In rare cases, where a mother has been infected, the child may be born with massive cerebral necrosis.\(^2\)

The disease is characterised by a sudden onset of fever, chills, headache, back ache, nausea and vomiting, which may be followed by CNS involvement. In adults, symptoms may include drowsiness, headache, mental confusion, and occasionally coma.

VEE
VEE is primarily an equine disease, but will occasionally affect humans. This usually results in a mild disease, but occasionally encephalitis may follow. Infection almost always results in an overt illness. Human infections generally resemble influenza, with fever, myalgia, nausea, diarrhoea, pharyngitis, and vomiting.\(^1\) Recovery usually occurs 3-5 days after onset of symptoms, although this may be accompanied by lethargy and asthenia. Full health is usually recovered in 1-2 weeks. Very rarely, neurological complications may arise. A fulminant form of the systemic illness may result in a rapid progression to shock, coma and death.

In some cases, the disease may be biphasic, often with CNS involvement occurring 3-7 days after the onset of the febrile illness. Symptoms may be as mild as somnolence, or as severe as encephalitis, coma, convulsions, paralysis and death. Sequelae may include personality changes. There is no evidence to suggest that aerosol infection increases the chances of CNS involvement.

The incubation period for naturally acquired VEE is around 2-5 days, although this is possibly less after inhalation of aerosolised virus (as short as 24 hours).

Mortality is usually 0.5%-1%, but may be as high as 20% in children who suffer encephalitis. Additionally, VEE in pregnancy may result in foetal encephalitis, placental damage, abortion and severe neuroanatomical abnormalities.

Chikungunya
The disease is characterised by a sudden onset of fever and severe joint pains (usually more prolonged in adults), followed by a maculopapular rash. The symptoms resemble those of Dengue fever.\(^3\) Haemorrhagic forms of the disease have been noted in South East Asia, particularly in association with outbreaks of Dengue fever. Haemorrhagic complications include haematemesis, melaena, petechiae, and shock.\(^5\)

Following the bite of an infected mosquito, and an incubation period of between 3 and 12 days, the patient experiences a sudden onset of fever, myalgia, arthralgia, and incapacitating joint pain (may be minutes to hours after initial onset of symptoms), which is usually
bilateral, involving the extremities, and more severe in adults. Headache is usually mild, and there is no retro-orbital or eye pain. Anorexia and constipation are also common symptoms. Lymphadenopathy, conjunctival suffusion, swelling of tonsils and joints, and periarticular nodules may occasionally be present.

The illness may be biphasic: the fever may abate after around six days, only to return a few days later for another several days. This second phase is often accompanied by a pruritic, maculopapular rash on the trunk and extensor surfaces of the limbs. Most patients recover completely within ten days, although some will continue to experience joint pain for weeks or months.

The disease is usually self-limiting and acute. Fatal cases are rare, and are usually associated with haemorrhagic symptoms.

Diagnosis

Laboratory diagnosis

These alphaviruses are able to multiply readily in cell cultures, and produce cytopathic effects (except in mosquito cells) which are easily detected. Vertebrate cells can also be used in plaque assays, which are highly sensitive and reproducible, and provide a convenient diagnostic method.

EEE

Positive identification is made by isolation of the virus from brain tissue (virus is rarely isolated from CSF), by detection of IgM from acute serum or CSF using immunofluorescent assays or capture ELISAs, or by an increased antibody titre with paired sera.

WEE

Identification can be made by detection of specific IgM antibodies from CSF and serum using ELISA techniques. Virus is not usually able to be isolated from brain tissue.

VEE

In VEE infections, paired antibody titres can be examined, although this may take as long as 5-7 days for a definitive result.

Chikungunya

Virus can be isolated from the blood during the first week of illness. Positive identification can also be made with a four-fold increase in titre of paired antisera, or by the identification if IgM using ELISA techniques.

Differential diagnosis

EEE

EEE may be misdiagnosed as encephalitis caused by herpes virus or other arboviruses, enteroviral infections, or bacterial meningitis.

WEE

WEE may be confused with other CNS infections caused by herpes virus, enterovirus, other viruses, or Borrelia burgdorferi.

VEE

Diseases with similar symptoms include dengue, other arboviral infections, influenza, lymphocytic choriomeningitis virus, rabies, herpes encephalitis, and cerebral malaria.

Chikungunya

Chikungunya may be confused with other arboviral infections, particularly dengue, rickettsial infections, malaria, typhoid, leptospirosis, Lassa fever, and other viral haemorrhagic fevers.

Treatment

EEE

Treatment is supportive

WEE

Treatment is supportive.

VEE

There is no specific therapy for VEE. Supportive therapy, including rest and analgesia, is recommended, and encephalitis patients should be hospitalised and closely monitored. Antivirals do not appear to have any beneficial effect, although α-interferon and interferon inducers poly(I) poly(C) have been highly effective as post-exposure prophylaxis in animal experiments if administered prior to, or immediately after exposure.

Chikungunya

Treatment is supportive.

Susceptibility of Population

EEE

All ages are affected. Most cases occur in the summer months. Children under four years of age are more likely to have an overt infection than adults.

WEE

Children, males, and people living in rural areas appear to be at higher risk. The disease seems to be more prevalent in the summer months.

VEE

All ages are affected, the incidence of the disease is higher in the rainy season, and in rural regions.

Chikungunya

There does not appear to be any appreciable difference in susceptibility with age or sex.
Prevention
The most effective method of prevention to date has been the eradication of the insect vector. Although effective vaccines are available against EEE, WEE and VEE, these have been used primarily on horses (with some testing on humans), and the effectiveness in man has not been fully elucidated.\(^2\)

EEE
An inactivated vaccine is available for at-risk laboratory workers. A live attenuated vaccine is not yet available.\(^9\)

WEE
A killed vaccine is available for at-risk laboratory workers and horses. A live attenuated vaccine is not yet available.\(^9,10\)

VEE
Two VEE vaccines are available. The first is an attenuated live strain, TC-83, which has been used since 1963 to immunise at-risk laboratory workers in the USA. This vaccine is also effective for horses. However, illness has been associated with 30–60% of recipients, with more severe symptoms, including headache, myalgia, and prostration, seen in around 5%. These side-effects are usually bimodal, peaking at day 1-2 and days 6-11. The vaccine is of a heterogeneous nature, and is not recommended for pregnant women and children. There is also the possibility that this vaccine strain may induce diabetes.

The second vaccine is a formaldehyde-inactivated vaccine (C-84) prepared from TC-83. Although it is immunogenic, safe, and non-reactogenic,\(^11\) its efficacy has not yet been tested extensively in humans, and it is used mainly as an alternative vaccine for those who failed to seroconvert with TC-83. The C-84 vaccine generally elicits a lower serum antibody titre in humans than does the TC-83 vaccine.\(^8,12\) It does not appear to be effective against aerosol challenge of VEE.\(^8\)

Research is currently underway in the USA on an infectious clone-derived live vaccine, which appears to be highly immunogenic in hamsters, mice and horses, and protective against challenge with virulent VEE virus. No human studies have been performed.

Vaccinia recombinant viruses which express TC-83 structural proteins have been tested on experimental animals with some success against intraperitoneal, subcutaneous, and intranasal challenge, although no human trials have been performed.

Polyclonal and monoclonal antibodies are effective in experimental animals as passive immunisation.

Chikungunya
A live attenuated vaccine is currently being evaluated.

Potential as BW

EEE and WEE
Little is known about the persistence of EEE and WEE viruses, or their stability in aerosol and infectivity in this form. However, their morphology is similar to that of VEE virus, and it is possible that EEE and WEE may also be transmissible in aerosol form. A biological attack could also be achieved by releasing virus-infected mosquitoes. Treatment is only supportive - no specific therapies are recommended.

EEE has a high mortality rate, and symptoms are quite debilitating. Additionally, survivors often suffer from neurological complications after recovery from the acute illness. WEE, although generally not as severe as EEE, may still cause debilitating symptoms, or even coma or death in some patients. Both illnesses would strain medical resources and manpower if a large-scale attack were to take place.

VEE
VEE has some potential as a biological agent, because it is readily aerosolised, is relatively stable in this form, and can be grown and prepared cheaply and easily. In addition, it has a high persistence in the wet, and requires a very low inhaled dose to cause infection. In the event of a biological attack of VEE, most infected personnel would develop an overt illness, and would be incapacitated for a few days to several weeks. Those patients who developed an encephalitic form of the disease would also need hospitalisation. No specific treatment is available, and there are problems with the available vaccines.

Chikungunya
A biological attack would probably involve the release of infected mosquitoes, although, as with EEE and WEE, it may be possible to aerosolise the virus. Chikungunya produces a very incapacitating joint pain, which debilitates most patients. Haemorrhagic complications would cause further problems to the patient. The fever may recur after an initial improvement, and some patients may suffer from continuing joint pain.

Future Directions
The use of live, attenuated vaccines for EEE and WEE could be examined more closely, and the efficacies of current vaccines on humans could be further elucidated. The live attenuated vaccine for Chikungunya, which is currently under study, may be very valuable in the future. Information on the use of interferons and other immunomodulators in the treatment of these diseases would also be of benefit.

Research is continuing into VEE vaccines, the use of passive immunisation with polyclonal and monoclonal antibodies, and the use of interferons.
References

Other Useful References

About the Author
Sue Sharpe is a microbiologist and a member of the RAN. She has contributed a series of articles on a variety of potential biological warfare agents to *AMM* in recent years.
Protecting tomorrow’s fighter pilot: Advanced Technology G Suits.
David G. Newman, MB, BS

“A desperate disease requires a dangerous remedy.”
Guy Fawkes, 1605.

Introduction
Fighter pilots regularly operate their aircraft in an environment of high gravitoinertial force, especially during air combat manoeuvring. As a result, they are very familiar with the physiological effects of high G forces. They are also well aware of the potential dangers of such exposure to high G, particularly G-induced Loss of Consciousness (G-LOC). G-LOC occurs when either the magnitude of the applied acceleration, or its rate of application, overpowers the ability of the cardiovascular system to maintain an appropriate level of cerebral perfusion.

While strictly speaking not a disease (being instead a normal physiological response to an abnormal stimulus), G-LOC nevertheless has occupied the attention of aerospace medicine researchers for many years in terms of the search for better preventive measures. These anti-G countermeasures include G-suits, various anti-G straining manoeuvres (including the L-1, M-1, and Hook manoeuvres), centrifuge training for aircrew, various physical conditioning regimes, and reclined ejection seats in some fighter aircraft. Despite these efforts, G-LOC remains a significant threat to pilots of modern high performance fighter aircraft. With the rapid advances in aerospace technology and the production of ever-more G capable aircraft, the development of effective countermeasures for +G to protect pilots from G-LOC has become even more desperate.

Fighter pilots have been operating in the +7 to +9Gz range for some decades now, and the current methods of +Gz protection have proven relatively effective (although G-LOC continues to occur). However, with fourth-generation fighter aircraft such as the Eurofighter 2000, the F-22, the Swedish JAS-39 Gripen and the French Rafale set to enter service around the turn of the century, existing anti-G measures will not provide adequate protection for pilots of these extremely high performance and agile fighters. These aircraft have greatly enhanced manoeuvrability and are capable of sustained flight operations in the +10Gz and beyond regime, and better, more effective anti-G countermeasures will be required in order to ensure that the pilot remains conscious throughout the entire flight envelope of the aircraft.

Many improvements in G protection have been considered and examined, including improving the standard G-suit, modifying anti-G valves in aircraft, and the adoption of positive pressure breathing systems for G protection (both with and without chest counterpressure systems). All of these proposed developments have advantages and disadvantages, and no one system or combination thereof has so far proven to be ideal.

The purpose of this paper is to briefly review the advanced technology anti-G suits currently being tested and evaluated for use in these future fighter aircraft. The results of some of the test programs will be examined, as well as the reported increases in G protection afforded by these new suits.

Current Anti-G Suits
The CSU-13B/P G-suit has become a standard item of flight equipment for the pilot of a high performance fighter aircraft, and will be familiar to anyone who has flown in an aircraft of this type. It consists of five interconnecting pneumatic bladders, one of which compresses the lower abdomen and the remaining four compress both thighs and both calves. The bladders are contained within a non-distensible fabric cover. Inflation of the G-suit bladder system is achieved via a source of bleed air from the compressor stage of the jet engine. This air is delivered to the bladders through a hose connected to an anti-G valve.

The G-suit is worn as a pair of trousers, in effect, over the flight suit. As the suit inflates in proportion to the +Gz load, the calves, thighs and lower abdomen of the pilot are compressed. This forces blood back to the heart, prevents dilatation of the capacitance vessels of the lower limbs, and the abdominal bladder acts to splint the diaphragm and prevent the downward displacement of the heart.

The CSU-13B/P G-suit provides in the order of about +1 to +1.5Gz protection when perfectly fitted. A well-trained and G-experienced pilot who wears his G-suit and properly executes the Anti-G Straining Manoeuvre (AGSM) can operate at Gz levels of up to +9Gz (although this is particularly fatiguing). This is of course subject to some individual variation and represents an optimal situation.

The standard G-suit does have some limitations. It is reasonably uncomfortable by its very nature, especially the abdominal bladder which can produce a significant degree of discomfort at high G levels. This has led to some pilots opting to not plug their G suits in, preferring to accept a lower G tolerance rather than experience the attendant discomfort.

The standard anti-G valve fitted to most fighter aircraft is a mechanically-operated device which controls the pressure and rate of inflation of the G-suit bladders. Inflation is generally delayed until a level of +1.75 to
+2Gz is reached. Inflation of the suit continues until a maximum inflation pressure of 1.25lb/sq inch/G (8.6kPa) is achieved.

The anti-G valve thus limits the G suit’s ability to deal with rapid onset rates of G. If a level of +5Gz is reached almost immediately (as is common in air combat manoeuvring), the pilot may have reached the stage of G-LOC before the G-suit is optimally inflated. The AGSM thus begins to assume greater importance. The difficulty with this situation is that the pilot’s principal focus of attention may well be the tactical situation he is faced with rather than on the need to properly perform the AGSM as he manoeuvres his aircraft under high G loads. With the current mechanical anti-G valve, the fighter pilot may well negate the protective effect of his +1.5Gz suit if his G-onset rate is too high.

**Advanced Technology Anti-G suits**

The advances in G-suit technology essentially represent variations on a theme. Many countries are working on such new generation G suits. While they have some inherent design differences, all of these new G suits have one thing in common: they all rely on extended bladder coverage.

While the CSU-13/5P suit covers somewhere in the region of 30% of the lower body, the various advanced technology G suits provide coverage of around 80-90%. They are thus a more complete lower-body garment than existing G suits. The bladder system of a typical advanced technology G suit traps almost completely around the thighs and calves, and in some cases has an augmented abdominal bladder.

Many countries and their defence agencies are developing these improved G suits. The United States has several under development: the USAF has its Advanced Technology Anti-G Suit (ATAGS) which is part of a wider integrated life support system known as COMBAT EDGE (Combined Advanced Technology Enhanced Design Anti-G Ensemble). The ATAGS suit is a major innovation, combining extended bladder coverage with optional pressure socks. The US Navy is working on its own version of this suit, known as the Eagle G-suit.

The Royal Air Force is also developing its own version, known as the Full Coverage Anti-G Trouser (FCAGT). This suit is ultimately destined for service in the Eurofighter 2000 aircraft. The Swedish Air Force’s Extended Coverage G-Suit (ECGS) has extended bladder coverage, as does the French Air Force’s ARZ 830 G suit. STING is the codename for the advanced technology G protective system being developed by the Canadian Armed Forces, and consists of an extended coverage G suit and a positive pressure breathing system (similar to COMBAT EDGE). The use of pressure socks is also being investigated by the Canadians.

As can be seen, the one design feature common to all of these new generation G suits is extended bladder coverage. As such, they represent a design evolution of the standard G suit to meet the demands of a more G-capable advanced tactical fighter aircraft.

Each of these advanced designs have been extensively evaluated both in the centrifuge and in some cases in high performance aircraft in operational fighter squadrons. The results of these evaluations warrant further attention. The USAF ATAGS suit has been extensively evaluated in the centrifuge, and flight-tested in both F-15 and F-16 fighters. Pilots using the ATAGS suit consistently reported an increased G tolerance when compared with the standard G suit. Ten out of 11 pilots expressed a preference to use the ATAGS suit for every high G flight. Each participating pilot reported that with ATAGS it was easier to sustain a high G loading. Ten out of 11 pilots preferred the foot pressurisation option with ATAGS. Nine out of 11 pilots reported improved tactical performance while using the ATAGS suit.

The Canadians have found that an extended coverage G suit provides approximately twice the G protection of a standard G suit. This represents a significant improvement in the level of protection against G-LOC for the fighter pilot. Furthermore, their experimental evaluation demonstrated that an extended coverage G suit with pressure socks provided a higher level of G tolerance (+10.6Gz ± 0.4) than the same suit without pressure socks (+10.1Gz ± 0.4), and both of these combinations provided more G tolerance than the standard G suit alone (+9.4Gz ± 0.5). These results were with subjects performing an AGSM. Relaxed G tolerances were reported as +5.54Gz ± 0.37 with the extended coverage G suit, and +4.66Gz ± 0.19 with the standard G suit. These centrifuge-derived results indicate a marked improvement in G tolerance with the new generation G suits.

**Anti-G valves**

The anti-G valve (AGV) in an aircraft is an essential part of the overall anti-G system, as it is this which allows the G-suit to operate. As discussed previously, the current pneumatic anti-G valve is not fast enough to ensure optimal inflation of the G-suit under very high G onset rates. While a lot of attention has been directed at improving the G suit itself, some research attention has also been focused on improving the performance of the anti-G valve. The need for faster inflation of the G suit has led to many innovative improvements.

The French ARZ 830 is an extended coverage G suit which is associated with an electronically controlled anti-G valve. This valve is capable of very rapid inflation rates, in the order of 100hPa/G. Experimental studies in the centrifuge suggest that it will be used at an inflation rate of only 70hPa/G and still afford improved G protection. The ARZ 830 system with its electronic AGV is destined to be standard equipment in the Rafale advanced tactical fighter.

The USAF has also been developing an improved AGV, which also relies on sophisticated electronics. The Rate Sensitive Anti-G Valve (RSAGV) is electronically controlled and is very responsive to both high absolute levels of G and high onset rates. During centrifuge testing it demonstrated a 0.5G increase in protection over
the current AGV. It has also been extensively tested in-flight.\textsuperscript{12}

Other work in the United States has involved matching digital electronics to the valves in order to produce variable inflation rates that correlate with the G-onset profile of the aircraft. Microprocessor-controlled systems have also been designed to "pulse" the G suit pressure, to produce, in effect, a venous return pump.\textsuperscript{11,13}

Conclusion

There is little doubt that the high performance fighter pilot of tomorrow will require more in the way of anti-G protection than is presently available. The optimum anti-G protective system has so far not been developed, but the several advanced technology G-suits currently being developed, tested and evaluated around the world seem to provide a higher level of G protection than the standard G-suit used today. It seems likely that whatever G-suit system ultimately becomes standard in the next century it will consist not just of an extended coverage G-suit but will also involve the incorporation of an electronic rate-sensitive anti-G valve. Only in this way will maximum G protection be afforded to the fighter pilot.

Any advanced technology anti-G suit is likely to be part of a more fully integrated life support package for the pilots of the next generation of high performance advanced tactical fighter aircraft, incorporating not only advanced technology G suits and anti G valves, but also positive pressure breathing systems with chest counterpressure for both G (PG) and altitude (PBA) protection. Such integration of protective systems will allow the fighter pilot to operate in the +10Gz and beyond regime.

When it comes down to the final analysis, in an air combat engagement, with all other things being equal, the fighter pilot who is able to remain conscious at a very high Gz level while causing his opponent to G-LOC will achieve a significant tactical advantage. He will not only survive but will almost certainly win the fight. Thus, advanced technology life support systems for the fighter pilots of tomorrow may well hold the key to success in air combat.

References


About the Author

Flight Lieutenant David Newman joined the RAAF in 1987 and graduated from Monash University Faculty of Medicine in 1989. He has been at RAAF Base Williamtown since January 1994, and will become the Senior Medical Officer in January 1996 on promotion to Squadron Leader. During 1995 he completed the USAF Flight Surgeon's Course at Brooks AFB, Texas. He received the 1993 Weary Dunlop Award for his paper on ejection seat injuries.
Medical aspects of parachuting
Stephen Robson

Introduction
The first military parachuting operations were conducted in Italy in 1977, using modified versions of the parachutes issued to balloon aircrew. Although the United States and Russia were conducting experiments in military parachuting, it was the German military who first recognised the enormous potential of battalions of airborne troops. German paratroopers first played a small but important role in the Scandinavian campaign beginning World War II, but it was the German invasion of Crete that spurred the formation of airborne forces in both Britain and the United States. Mass drops of paratroopers have figured as recently as Operation Just Cause, the American operation in Panama, which was the largest night-time parachute operation since World War II.

The Australian Army maintains parachute expertise in the 3rd Battalion, Royal Australian Regiment (3RAR), the Special Air Services (SAS) and through the Parachute Training School (PTS). Since the RAAF provides the aircraft, the PTS is a lodger unit at the Naval Air Station Nowra, and a number of RAN and RAAF personnel are parachute qualified, it seems timely to review the state of knowledge of the medical aspects of parachuting.

The Physiology of Parachuting
Parachuting physiology crosses the borders of several disciplines. During the ascent phase of operations, the parachutist works in the hypobaric environment of the aviation physiologist. Whilst most training and operational static-line activities are conducted at or below 1,500 feet where hypobaric stress is minimal, freefall jumps are commonly made from 10,000 feet, and often from greater altitudes. There is now worldwide military expertise in high altitude freefall jumps (with supplemental oxygen), both with low opening (HALO) and high opening (HAHO). There is little new in terms of hypobratic physiology, and high altitude parachuting is deserving of a specialised paper in itself.

Studies of Hoffian (H) and Achilles tendon reflexes in falling subjects have shown reflex muscle activity beginning between 74 and 81ms after the fall begins, with a second peak after the first 200ms of the fall, thought to be initiated by signals from the vestibular apparatus. Acceleration to terminal velocity usually occurs during the first 10 to 12 seconds of a freefall jump, and thereafter the condition of the body approximates weightlessness (which is possibly what a large number of overweight instructors appreciate!).

A number of studies have been performed involving telemetric electrocardiograph recordings during parachuting. Perhaps it is not surprising to learn that parachute jumping is associated with tachycardia, especially during the exit, canopy opening and landing phases. In a study of 13 first-time jumpers (12 male and one female), their mean resting rate one week before their first jump was 64.5/min. At the drop zone prior to the jump it was 112.8/min, and 170/min during the jump, then 122.8/min afterwards. No significant disturbances of rhythm were detected in this study. A marked increase in urinary catecholamines (mean 51.2μg/100ml) was noted, compared to a baseline level a fortnight after the jump (mean 10.3μg/100 ml), a finding that has been confirmed in other studies. ST segment changes suggestive of ischaemia were detected in 7 of 15 subjects during freefall jumps in one study. Another study of parachutists during a competition detected periods of striking sinus arrhythmia with slow atrial rhythm just prior to exit in three of seven subjects. In one of the subjects a main parachute malfunction occurred necessitating cutaway and deployment of the reserve parachute - the subject's heart rate rose to 200/min during this procedure.

Electroencephalogram (EEG) studies during freefall parachuting have been reported. In this interesting study of 35 freefall parachutists, χ-rhythms were recorded when some χ-reactive subjects closed their eyes after stabilisation in freefall. No pathologic recordings were reported.

The freefall environment does not lend itself to study of respiratory or cardiac physiology, but a number of important physiological changes have been reported in other systems. It is clear that stress may influence function of the immune system, and there is no doubt that parachuting is stressful. A study of 45 first-time tandem parachutists found a significant rise in serum adrenalin and noradrenalin levels during the jump, and a rise in cortisol levels immediately after the jump. An increase in lymphocyte subsets and Natural Killer (NK) cell function capacity immediately after jumping was reported. These cellular parameters decreased significantly below baseline levels one hour after the jump, and close correlation between the cellular changes and the serum noradrenalin values was described, suggesting that the noradrenalin was responsible for the cellular effects. Prolactin, thyrotropin and growth hormone levels in the blood also increased significantly in response to parachute jumping in a study of first-time military parachutists. Rises in serum cortisol during parachuting have been demonstrated to be associated with increased levels of C-reactive protein, vasopressin and interleukin-1β. β-endorphin levels also increase, although blood levels of substance P have not been shown to change.

The level of experience of parachuting does not seem to affect these neuroendocrine responses. A well-designed study involving 12 novice and 11 experienced military parachutists each undertaking two jumps, showed significant rises in serum cortisol, prolactin and thyrotropin, with no change in luteinizing hormone or somatotropin, irrespective of experience. Similarly,
levels of experience do not seem to alter the heart rate profiles during jumps between inexperienced and seasoned jumpers, although the two groups rate their anxiety scores differently.13

Other experiments involving combat troops have failed to show any change in blood lipids (cholesterol, HDL, LDL, apo-A, apo-B and triglycerides) in response to jumping.14 Interestingly, repeated parachute jumping seems to decrease the concentrations of peripheral platelet benzodiazepine receptors,15 and enhances blood nerve growth factor levels and the distribution of nerve growth factors in lymphocytes.16 To summarise all of this, it seems fair to say that parachuting, whether by novice or experienced persons of either sex, sees a high level of neuroendocrine response and a marked alteration of physiology in response to the acute stress.

Parachuting Injuries

While the climb, exit, fall and canopy phases of parachuting are of interest to the physiologist, it is the landing phase that generates most work for the medical officer. As the old saying goes, “Of the whole 10,000 feet, it’s the last inch or so that hurt the most”. Patterns of injury from parachute landing have been well-studied since the advent of military parachuting. A retrospective study of over 200,000 male military parachutists over 10 years found significant differences in the rate of serious injury depending on the type of parachute, whether the jump was made at night or during the day, and whether the parachutist was carrying extra equipment or not.17 The lowest rate of severe injury was 0.17/1,000 jumps for day jumps from a balloon without extra equipment, while the highest was 1.9/1,000 for day jumps from a plane without extra equipment. There was a marked increase in injuries with a wind speed on the ground of greater than 12 knots (from less than 1/1,000 jumps in nil wind conditions to almost 4/1,000 jumps in 15-16 knot winds). Differences in ground temperature and humidity were not associated with injury rates. A large prospective study of Australian military parachutists involving almost 9,000 static line jumps in experienced jumpers found an injury rate of 7.1/1,000 jumps. The rate was significantly higher (13.7/1,000 jumps) when combat equipment was carried, and rose to 16.6/1,000 jumps for simultaneous door exit operations from C-130 aircraft.18 Most of the minor or moderate injuries were to the lower limb or back, and more major injuries included closed head injuries and a range of lower and upper limb fractures and dislocations. The more serious injuries were generally associated with higher wind speeds on the drop zone. Fortunately, fatalities in military parachuting are rare. A comprehensive study from the Armed Forces Institute of Pathology identified 49 fatal parachuting mishaps between 1964 and 1989.19 Twenty-four cases were in freefall descents and 16 were static line. The causes of deaths were diverse, from accidental deployment of reserve canopies in the aircraft, static line failure, canopy failure, injuries on landing, and drowning. The study concluded that most of the fatalities were probably preventable by rigid adherence to procedures and supervision of training.

Military parachuting is normally undertaken by fit, well-trained individuals working under close supervision. In contradistinction, civilian parachuting activities are usually characterised by a broader range of age and fitness levels amongst the jumpers, and less vigorous training. A prospective study of 9,211 civilian parachute descents documented a serious injury rate of 0.35%/20. The ankle was the main site of injury in 41.5% of cases, and injuries to the ankle, foot, tibia/fibula, femur, pelvis and spine comprised over 80% of the injuries. The major associations with serious injury were jumps made in the late afternoon, increasing age of the parachutists, and increasing weight of the parachutists. Another review of 110,000 civilian descents found a fatality rate of 0.005% (six deaths) and an injury rate of 0.14% (155 cases requiring medical treatment).21

Conclusions

Parachute operations play an important part in military strategy, and a wide variety of personnel within the Australian Defence Force will participate in parachuting, both military and civilian. “Skydiving” is one of the fastest growing civilian “adventure sports”. It is clear that there is now enormous knowledge of the physiology and pathology of parachuting. The major conclusion is that, when high standards of fitness are maintained and training is intensive, the chances of injury are low. As more medical officers come into contact with parachutists, and perhaps undertake parachute descents themselves, they will come to appreciate the rich and varied physiological responses to a new and exhilarating environment.

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References


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**About the Author**

Steve Robson joined the RAN as an medical undergraduate in his final year at the University of Queensland in 1986. He served in the PNF from 1989 to 1991, and served at sea in HMA Ships SUCCESS and SYDNEY. He is now a member of the Reserves, and is a Registrar in Obstetrics and Gynaecology at the Queen Elizabeth Hospital in Adelaide. He has completed the Army's Basic Parachute Course, and is now an occasional civilian skydiver. His highest jump to date is from 14,000 feet, exiting a Pilatus Porter. His most recent article in *AAMC* concerned ECG changes in asymptomatic aircrew.
Ricin - A research review
Maria Szilagyi and Raymond M Dawson

Abstract
Ricin is a toxin of plant origin which causes fatal permeability-type (non-cardiogenic) pulmonary oedema on inhalation of the aerosol. Ricin is composed of two chains, linked by a disulfide bond. The B-chain acts to bind the toxin to cell membranes and assist in internalisation of the A-chain, which inhibits protein synthesis by an enzymatic action on ribonucleic acid. There is no known effective therapy for ricin intoxication. However, immunisation is feasible.

Introduction
Ricin is a toxic protein and lectin extracted from the endosperm cells of the seeds of the castor oil plant, *Ricinus communis*. This plant is cultivated commercially for its oil, but is also widespread as a weed and as an ornamental plant. It flourishes in most subtropical and some temperate climates. Ricin was considered a candidate warfare agent during World Wars I and II and after World War II. Under the 1993 Chemical Weapons Convention, ricin is classified as a Schedule I chemical, defined as one which has been developed, produced, stockpiled or used as a chemical weapon specifically to cause death or other harm through its toxic properties. Ricin consists of two haemagglutinins (RCL I and II) and two toxins (RCL III or I and IV). The agglutinins are tetramers (MW 130,000) and the toxins are dimers (MW 66,000). Ricin shares a similar general structure and function with several other dimeric toxins. Each toxin is composed of two small (approximately 32 and 34 kD) protein chains, denoted A and B, joined by a disulfide bond.

Toxicity
Ricin is an extremely toxic substance. A few picograms of the toxin per milliliter will kill most cells in culture within 24h. One internalised molecule of ricin is sufficient to kill a cell, while it has been estimated that the minimum amount of toxin to kill HeLa cells in culture is <10 molecules per cell. Ricin inhibits the growth of various murine tumours and of several human tumour xenografts in athymic mice. It appears to be more toxic to certain malignant cells than to normal cells. Ricin is also immunogenic, and the dust generated from extraction of castor oil from castor bean seeds is a potent allergen. Ricin has no effect on the growth of bacteria.

Table 1 lists the lethal doses of ricin in different species.

<table>
<thead>
<tr>
<th>SPECIES</th>
<th>ROUTE</th>
<th>LETHAL DOSE</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse CD-1</td>
<td>ip</td>
<td>LD_{50} 7.5 μg/kg</td>
<td>Richer et al(^{10})</td>
</tr>
<tr>
<td>Mouse</td>
<td>iv</td>
<td>LD_{50} 16 mg/kg (A-chain)</td>
<td>Richer et al(^{10})</td>
</tr>
<tr>
<td>Mouse</td>
<td>inh</td>
<td>LD_{50} 8 mg/kg (B-chain)</td>
<td>Richer et al(^{10})</td>
</tr>
<tr>
<td>Mouse</td>
<td>ip</td>
<td>LD_{50} 100 ng</td>
<td>Olms et al(^{1})</td>
</tr>
<tr>
<td>Mouse</td>
<td>iv</td>
<td>55-65 ng</td>
<td>Fosdul et al(^{11})</td>
</tr>
<tr>
<td>Mouse</td>
<td>inh</td>
<td>2.7 μg/kg</td>
<td>Hewston et al(^{12})</td>
</tr>
<tr>
<td>Mouse</td>
<td>inh</td>
<td>65 ng</td>
<td>Olms(^{12})</td>
</tr>
<tr>
<td>Mouse</td>
<td>inh</td>
<td>10 μg/l air/10 min</td>
<td>Hewston et al(^{12})</td>
</tr>
<tr>
<td>Human</td>
<td>oral</td>
<td>30 mg, 0.03-1 mg/kg</td>
<td>Klaain and Jaeger(^ {13})</td>
</tr>
</tbody>
</table>

Notes:
- **Inh**: inhalation
- **iv**: intravenous
- **ip**: intraperitoneal
- **LD_{50} or LC_{50}**: the dose required to kill 50% of the population
- **LD_{90}**: the dose required to kill 99% of the population

Ricin is toxic parenterally, orally and by inhalation, and the parenteral and inhalation toxicities are similar. On a weight basis, the guinea pig is more sensitive to ricin than the mouse, while the horse is even more sensitive. Different strains of mice show different sensitivities to ricin, DBA mice being the most sensitive. These inter-strain differences in sensitivity correlated with strain differences in the ricin concentration reached in important tissues.

When introduced intravenously or intramuscularly, the primary targets of ricin are the liver (where up to 50% of injected ricin is retained), kidney and spleen. Most of the toxin is excreted within 24h in the urine. Lesions provoked by ricin have been studied extensively and all report mention the necrosis effects on blood vessels and organ parenchyma, mainly in liver and lymphoid tissues. Large doses cause haemorrhages in the viscera and serous cavities. By contrast with the parenteral routes, exposure via the inhalation route results in the primary lesions being in the respiratory system, and death results from oedema and hypoxia. Assaad et al concluded that ricin induced-pulmonary toxicity may be divided into three phases: latent period, redistribution of lung water without an increase in extravascular lung water and pulmonary oedema.

The whole ricin toxin is 2,000 and 1,000 times more toxic than the A-chain and B-chain respectively. However, all the elements of the lesions induced by ricin can be found qualitatively in the effects of each subunit.
injected independently in mice. If the separated A- and B-chains are combined again, the reconstituted protein is almost as toxic as the native protein, demonstrating that the peptide chains do not lose their activity during separation. Further, Levison and Youle showed that the A- and B-chains associate reversibly, without disulfide linkage, and that the association increases with increasing concentration in accordance with thermodynamic principles. Using inhibition of protein synthesis in cell cultures as a measure of toxicity, they found that disulfide-reduced, but reversibly-associated ricin, with most of the ricin in the associated state, was as toxic to the cells as native ricin. They reached the conclusion that the disulfide bond linking the A and B subunits appears to play no role in toxicity in this system other than to hold the two subunits together at low concentrations. It should be noted however that there is no direct correlation between toxicity in animals and in cultured cells. 4 In intact cells and living animals, only molecular species with the disulfide bridge intact have toxic effects. Different cell lines differ in their sensitivity to ricin. 5 Ricin also inhibits protein synthesis in cell-free systems (e.g., from rabbit reticulocytes), where the reduced toxin is active but not the native toxin, in contrast to the situation in vivo. 6

For parenteral administration, there is a latent period of 18 to 24 hours during which no signs of poisoning are discernible, even for high doses of toxin. Thereafter, animals show general malaise, piloerection and marked lethargy and anorexia. Other symptoms are diarrhoea, weight loss and moderate fever. 7 No animals died less than 8 to 10 hours after intraperitoneal administration of ricin in the study of Olsnes et al. 7 Survival time is dose related, and the dose-response curve is steep. 8

Clinical Manifestation

For poisoning of humans by ricin, the most famous case is that of the Bulgarian journalist Georgi Markov, who was killed by a pellet containing about 500 µg of ricin, which was implanted in his thigh via the tip of an umbrella. Five hours later he began to feel weak, and later developed a fever which continued the next day. Before death, there was a fall in temperature and in the blood pressure. 1,4,12

In most cases, however, ricin poisoning in humans is due to the ingestion of castor seeds. If they are well chewed, 2 or 3 seeds may be fatal to a child and 8 seeds to an adult. There is a latent period of 3 to 20 hours before manifestation of toxicity. The symptoms include internal haemorrhage and gastrointestinal irritation, nausea, violent vomiting, abdominal pain, severe diarrhoea, dilatation of the pupils, and shivering. Convulsions occur in severe poisoning. 12,16 The quantity of ricin available for absorption depends on the degree of mastication of the castor seeds. It resists the action of proteolytic enzymes in the intestinal tract, and presumably is absorbed without being hydrolysed. Thus, it is difficult to estimate the lethal oral dose of ricin for humans. 12

Mechanism of Action and Therapy

The main function of the B-chain of ricin is believed to be binding of the whole toxin to target cell membranes (eukaryotic cells) by lectin-type recognition of β-D-galactose contained in glycoprotein or glycolipid sequences, and the internalisation of the toxin by endocytosis. Not all eukaryotic cells are sensitive, and no prokaryotes are known to be sensitive. 17 The A-chain has highly specific N-glycosidase activity and hydrolyses the N-glycosidic bond between the base (adenine) and the ribose at position A324 in 28S ribosomal RNA (of a 60S ribosomal subunit); this renders the surrounding phosphodiester bonds highly susceptible to hydrolysis. The end result is therefore similar to that from the action of another cytotoxic protein, α-sarcin, which catalyses hydrolysis of the phosphodiester bond between A4324 and G4325. The hydrolysis prevents binding of an elongation factor and thereby inhibits protein synthesis. 17,18,19,20 The sequence of events is therefore: 21

1. binding of the toxin to cell-surface receptors
2. receptor-mediated endocytosis and intracellular transport through the vesicular system
3. translocation of the enzymatically active component of the toxin (A-chain) across the vesicle membrane to the cytosol, following reduction of the inter-subunit disulfide bond
4. enzymatic inactivation of the intracellular target.

Prophylaxis or therapy of ricin intoxication could therefore be directed at one or more of these four stages. A fifth possibility is inactivation of ricin in vivo by chemical means or immunologically. This would need to be prophylactically, or immediately after intoxication, although confirmation of intoxication will be difficult in the absence of immediate symptoms - compare nerve agent poisoning. Apart from the latent period before the effects of ricin are manifest, the clinical features of poisoning themselves give no clue as to the diagnosis. 12

A brief summary of research on the above stages in intoxication is as follows.

Binding of the toxin to cell-surface receptors

Ricin B-chain contains two galactose-binding sites. 20 Moreover, both A- and B-chains are glycosylated and expose terminal mannose residues, which can mediate binding of ricin to endocytic mannose receptors on cells that carry those, e.g., macrophages and liver endothelial cells. 21 Jang and Kim reported that the haemagglutination activity of ricin was inhibited by lactose, as well as by galactose and other sugars. 22 Fodstad et al reported that lactose inhibited binding of the B-chain of ricin, and mice were partially protected from ricin toxicity by injection of lactose with the ricin. 13 By contrast, Wannemacher et al reported that neither lactose nor the more stable synthetic disaccharide analogue lactulose was effective in protecting mice against ricin, although these compounds did reduce ricin-induced cytotoxicity in vitro. 24
Wales et al. analysed the galactose-binding site by X-ray and mutational analysis and identified key residues which hydrogen-bond to the sugar, and a conserved tripeptide Asp-Val-Arg in the binding site.25 Newton et al. studied the role of galactose binding sites of ricin A-chain in ricin toxicity by looking at a series of ricin point mutants.30 The cytotoxicity was evaluated when cell entry was mediated either by galactose-containing receptors or through the alternate mannos-1 receptor of macrophages. Even for mannose-receptor-mediated toxicity of ricin, at least one galactose binding site remains necessary for cytotoxicity and two galactose binding sites further increase potency. These results are consistent with the model that the ricin B-chain galactose binding activity plays a role not only in cell surface binding but also intracellularly for ricin cytotoxicity.

Solis et al. showed that the binding properties of ricin could be studied without undue concern about its safety in handling by modifying its carboxyl groups.37 The modified toxin was 20-fold less toxic than native ricin, but the strength and specificity of the carbohydrate-binding ability of the lectin were substantially retained.

Endocytosis and intracellular transport
Magnusson and colleagues have studied the pathways of ricin endocytosis extensively in rat liver endothelial cells, paying particular attention to mannose receptors as mediators of the internalisation, since both the A-chain and the B-chain are glycoproteins containing mannos-1 rich oligosaccharides.25,26,29 Previous research had concentrated on the galactosyl residues. Approaches adopted by these authors include binding and uptake of radiolabelled ricin, inhibition of protein synthesis, subcellular fractionation, transferrin endocytosis (i.e. the reverse pathway of endocytosis), immunocytochemistry and the role of other liver cell types. Differences were observed between the galactose and mannos-1 internalisation pathways in the transport from endosomes and lysosomes, and these were related to the different stabilities of the two binding mechanisms at endosomal pH. In particular, the binding of ricin to galactosyl residues displays unusual stability at low pH,36 although the optimum pH for ricin toxicity is between 7 and 8.4

Mannose receptors are more efficient at accumulating an inhibitory intracellular concentration of ricin than galactosyl residues, and the onset of toxicity was accordingly more rapid after internalisation via mannose receptors. Several subcellular compartments were found to be involved in internalisation, including coated pits, coated vesicles, Golgi apparatus and different types of endosomes and lysosomes. The role of the Golgi structure is controversial36 and has been studied by Sandvig et al., Ryser et al., and Bau and Draper (1993).31,32,33

Oda and Wu reported that the antibiotic cerulenin reduced the internalisation of ricin, but not its binding to cell-surface receptors, in a mutant of monkey kidney cells; however it had no effect on the parent cells.21 Naseem and Pace reported that fluconolone (an anti-inflammatory glucocorticoid) increased ricin-induced inhibition of protein synthesis by increasing the binding efficiency and internalisation of ricin.34 On the other hand, a nonsteroidal anti-inflammatory drug (indomethacin) protected macrophage cell lines against ricin. Wales et al. provided evidence in favour of their proposal that the pathway of ricin to the interior of the target cell is the exact reverse of the secretory path for toxins, via the endoplasmic reticulum.39

Translocation to the cytosol
The endoplasmic reticulum membrane may be the principle target for translocation of ricin and other toxins.35,49

Hegde et al. observed that inhibition of protein synthesis in cells by toxins, as measured by incorporation of radiolabelled amino acid, was preceded by a concentration-dependent lag phase,15,55 which they interpreted as the time the toxin takes to travel through the cytoplasmic compartments. Fluorescence techniques were used with rat thymocytes to compare the kinetics of intoxication and inter-subunit disulphide reduction by aminotransferase and ricin. The results indicated that the binding and internalisation efficiencies of the various toxins were the same, and that the observed differences in the dose-dependent lag time were causally related to the proposed intracellular processing event. Other kinetic studies also suggest that the rate-limiting step in cytoxicity under most circumstances is A-chain translocation. The B-chain appears to facilitate the transfer of the A-chain to the cytosol by insertion of hydrophobic regions into the membranes of endosomes forming a pore through which the A-chain may be delivered to the cytosol.35,56 The toxic effect of ricin can be countered by antitoxins only during the first 30 min of a 6h lag at 20°C, indicating that during the remaining 5.5h the toxin is not exposed on the outside of cells.5

Madan and Ghosh studied the ability of monensin, a carboxylic ionophore which is known to raise intravesicular pH, to reduce the lag period and enhance the cytotoxicity of ricin.37 Although this study was aimed at increasing the efficiency of ricin as an anti-tumour agent, monensin may be a useful tool for mechanistic studies.

Enzymatic inactivation
Endo et al. found that the 28S rRNA is the only target RNA for ricin and also for the ricin-related toxins abrin and modeccin.38 These other toxins also acted at a site close to the α-sarcin cleavage site. Other results suggest an important role of ribosomal proteins in inducing and maintaining the secondary structure recognised by ricin A-chain, including the fact that denatured 28S rRNA was not modified by ricin A-chain, which does not act as a ribonuclease but as a N-glycosidase.38 Endo et al. proposed that elongation factors 1 and 2, directly or indirectly via hydrolysis of GTP, initiate the reversible transition or switch in rRNA structure that propels translocation, by means of a primitive allosteric transition.17 Depurination at A4324 in 28S rRNA by ricin or cleavage at G4325 by α-sarcin might abolish the capacity to switch structure reversibly and account in this
way for the catastrophic effect of the toxins on ribosome function. In this study, Endo et al used mutants of a synthetic oligoribonucleotide, as a model of the ricin substrate, to study the kinetics of the enzymatic inactivation. This 35mer has the sequence and the secondary structure of the ricin region of 285 rRNA.

There is evidence that ricin produces an oxidative stress, mediated by free radicals, in the liver after injection intraperitoneally in mice. The lipid peroxidation which was observed in this study could be either a cause or an effect of the reactions producing toxicity. Site-directed mutagenesis has shown the importance of the carboxylate function at position 177 of ricin (Glu 177) for its enzymatic activity. The same technique, coupled with X-ray diffraction, was used by Kim and Roberts to show that Arg 180 is involved more in transition state stabilization than in substrate binding.

Hassoun et al examined specific glycosidase inhibitors as possible chaperone protectants against ricin. Six compounds, believed to form covalent enzyme linkages, were tested in an in vitro system (release of lactate dehydrogenase and aspartate aminotransferase from cultured macrophage cells). Two were found to exhibit significant activity against ricin toxicity; these were N-bromoacetyl-α-D-galactopyranosamine and the β isomer. It is plausible that these compounds inhibit ricin activity after cellular internalisation of the toxin; however it is also possible that they competitively bind to the cell membrane galactose binding site to act as a false receptor and prevent ricin transport into the cytoplasm.

Note that these compounds exhibited some cytotoxicity of their own, i.e. in the absence of ricin.

**Immunisation**

Foxwell et al prepared antibodies to ricin and its separate A- and B-chains and evaluated them in a cell-free assay, against lymphoma cells, in haemagglutination studies and in vivo (mice). The antibodies were effective in vivo (as well as in the other systems), even when given up to 640 min after subcutaneous ricin or up to 20-40 min after intravenous ricin. The use of antibodies as a treatment in cases of accidental ricin intoxication may therefore be feasible, depending on the amount of ricin absorbed and the route of entry. Houston also reported that antibodies could protect mice against ricin if given after exposure (up to 3 h in this case). Prophylaxis against ricin in mice using monoclonal antibodies (not all that successful) has been reported by Chanh et al. Other studies with antibodies to ricin are described by Colombatti et al.

Hewetson et al established the feasibility of protecting mice against intravenously administered ricin by both active and passive immunisation. It is interesting that up to 1,000-fold more anti-ricin Immunoglobulin G intravenously was required to protect mice against aerosolised ricin than against intravenous ricin. These results suggest a different mechanism of action of ricin administered by inhalation, the inability of antibody to enter the alveolar spaces at sufficient concentrations or the requirement of a different class of antibody (e.g. IgA) to protect against exposure at mucosal surfaces.

Lemley and Wright found that mice passively immunised by a protective, anti-ricin A-chain monoclonal antibody, then challenged intravenously with ricin, were protected from a subsequent ricin challenge, and were actively immunised. They concluded that the monoclonal antibody neutralised toxicity of ricin immunogen and that active immunisation was achieved with very low antigen load (~0.5 µg/mouse). As a result of its extreme in vivo toxicity, however, ricin cannot be used as the immunogen to elicit protective immunity. Chanh and Hewetson achieved anti-ricin immune responses with mouse and rabbit polyclonal anti-idiotypic antibodies, raised from protein G-purified goat anti-ricin Immunoglobulin G. A ricin toxoid has been developed which when used as vaccine protects against toxin given by inhalation and intravenously in mice.

As mentioned above, ricin binds to galactose, and if a polysaccharide of this sugar (agar as a polymer of galactose having sulphhydril groups) can be introduced into the cell, e.g. by liposome therapy, it may have some therapeutic value, as might inactivating monoclonal antibody that binds to ricin's galactose-binding domain. As there is little effective therapy once the damage has been done, the best option may be to protect troops with vaccines or protective human monoclonals.

**Therapeutic Applications of Ricin**

Immunotoxins are chimeric, antineoplastic molecules constructed by covalently conjugating monoclonal antibodies to plant or bacterial toxins. The antibody moiety allows specific targeting of the immunotoxin to tumour-associated antigens, while the toxin moiety is responsible for cell killing by irreversible inactivation of protein synthesis. In the case of ricin, monoclonal antibodies linked to ricin A-chain can substitute for the ricin B-chain binding. The potent protein synthesis inhibitory activity of ricin has been utilised as the cytotoxic effector moiety of many immunotoxins with potential use for cancer therapy. The limitation of antibody-ricin conjugates in vivo is that immunotoxins lacking the ricin B subunit have much lower toxicity to tumour cells (because of the slow rate of cell killing), and immunotoxins containing the ricin B-chain can have significant non-target cell toxicity. Attempts to circumvent non-specific cell attachment of ricin via ricin B-chain immunotoxin have included treatment of cells in the presence of high concentrations of lactose, and decreasing galactose binding by steric hindrance achieved by cross-linking ricin to the antibody. Ricin B-chain increases the specificity of antibody-ricin A-chain conjugates by increasing the rate of entry of ricin A-chain into the cytosol. Further, ricin B-chain linked to antibodies will potentiate the toxicity of ricin A-chain linked to antibodies.

*In vitro* studies have shown that ricin A-chain carried by red blood cells is able to kill efficiently erythropagocytic cells having ingested such a carrier. Ricin A-chain targeted to the erythropagocytic cells
does not seem to significantly modify the in vivo phagocytic activity and the antibody response against a heterologous cellular antigen, if there is an absence of effects on the immune system. The efficiency of this carrier devoid of side effects would be encouraging data for its use in therapeutic applications.28

References

**About the Authors:**
Maria Szilagyi is a biochemist working for DSTO at the Aeronautical and Maritime Research Laboratory (AMRL) at Maribyrnong, Victoria. Her work involves research in the area of chemical defence, and, more recently, biological defence.

Ray Dawson has a PhD in organic chemistry from the University of Western Australia, but has spent most of his 25 years at AMRL working on the biochemical pharmacology of nerve agents and their antidotes. He was attached to the University of Melbourne’s Clinical Pharmacology and Therapeutics Unit at the Austin Hospital in 1979, and to the Chemical Defence Establishment, Porton, UK in 1986-87. As a result of the Australian Government’s recent review of its policy on defence against biological warfare agents, Dr Dawson has switched fields to the study of pulmonary oedemagens and toxins.

This is the third article in a series contributed by Szilagyi and Dawson; the first two were on Phosgene and Pulmonary Oedemagens.
A Retrospective

Weary Dunlop: Surgeon
Robert D Marshall

On July 12th 1993, which would have been his 86th birthday, all Australia stopped to mourn the passing of Sir Edward ‘Weary’ Dunlop.

The state funeral held in Melbourne, at the Cathedral Church of St Paul, and the subsequent procession to the Shrine of Remembrance attracted thousands of mourners. They were of all ages and from all walks of life, not just the former prisoners of war he commanded and tended on the Burma railway 50 years ago. It is doubtful if Australia has ever before witnessed such a public outpouring of gratitude and affection. Weary was given a hero’s funeral and his life story has already become part of Australian folklore, along with other larger than life figures such as Sir Douglas Mawson and Sir Donald Bradman. Every nation needs its idols and Weary filled the bill perfectly.

The climactic deeds during the War that made him a folk-hero occupied only four years of a very long lifetime and, although his military career had ended in 1946, he was given a military funeral 47 years later. During the service there was little mention of the surgical work that had occupied the greater part of the next 30 years of his life. He was, however, a Fellow of the Royal Australasian College of Surgeons and an Honorary Surgeon at the Royal Melbourne Hospital, Repatriation General Hospital, Peter MacCallum Clinic and the Royal Victorian Eye and Ear Hospital, for more than 20 years, as well as having a very large private surgical practice. It therefore seems necessary for posterity that an attempt be made to appraise his purely surgical achievements and set them alongside the overwhelming ‘Christ of the Burma Railway’ image, which was to become his public persona and make him an Australian icon. The writer was Weary’s assistant for 10 years from 1953 to 1963, assisted him at most of his major operations during that time and is therefore well placed to comment on his surgical career.

Surgeons are men before they are surgeons, and they practise their craft according to their lights and their personalities. To understand Weary Dunlop as a surgeon, it is first necessary to understand the drive that made him the man he was and which made him almost a demigod to the prisoners of war he commanded. His surgical career on the other hand, although it made him many friends, also produced detractors, some of them vehement. It seems strange at first sight that a man of Weary Dunlop’s stature should have been so little involved with the Royal Australasian College of Surgeons after the War. He never served on the State Committee, much less the Council, despite serving on and presiding over innumerable non-surgical committees. He had few close friends among his surgical colleagues, particularly his seniors, and he also stood apart from the mainstream of hospital politics. Why did he choose to direct his prodigious ability to organise and to lead mostly into fields outside his chosen specialty of surgery? The answer can only be sought in his personality and attitudes.

Most of us manage to present a more or less consistent image to the world, although the mask sometimes slips. Weary never varied; he never faltered; he behaved at all times as the very epitome of the best type of British gentleman. His chosen model was Sir Thomas Dunhill, with whom he worked in London before the War, but it could as easily have been an empire builder like Clive of India or Cecil Rhodes. He was a staunch Anglophile and royalist all his life and, only a few days before his death, he commented that he was glad the republican debate would not come in his time. From early youth Weary assumed the sterling virtues of bravery, stoicism, fortitude and unflinching will. He could never ignore a challenge and would die rather than be beaten. He was a huge, slow, affable, shambling bear of a man who spoke slowly, courteously and calmly. He seemed the very personification of his undergraduate nickname, but, in the true Australian tradition, the label ‘Weary’ was no more accurate than ‘Tiny’ would have been. His apparent slowness concealed a mind like a steel trap. He was a brilliant student and won the gold medal of the Pharmacy College before switching to medicine. He gained exhibitions and honours throughout his course and breezed through his surgical training just before the War without the slightest difficulty.

His sporting career at university displayed in full measure his bulldog attitude; he was a formidable rugby player who could carry the ball straight through a pack, even with several opponents hanging on to him. He became the only Victorian ever to captain the Australian Rugby Union team. He also won the Intervarsity Heavyweight Boxing Championship and could run 100 yards in almost even time.

He was the ultimate individualist. He had an inexhaustible fund of self-confidence and an unquenchable belief in himself; this made him impatient of authority in any form. He was a great leader, but a poor follower. He was indefatigable and indestructible; he simply ignored his own discomfort or tiredness and expected that those around him should do the same. He knew that he was blessed with exceptional strength of mind and body, and felt compelled to use these talents for the benefit of others. He really had no choice but to follow what he perceived to be his bounden duty; he lived the life of noblesse oblige. These personal qualities were
tailormade for the man who was to command ‘Dunlop’s Thousand’ during the War and so defy their Japanese captors that he became a legend in his lifetime.

Weary was, of course, only one of the Australian doctors who spent the War in Japanese prison camps. ‘Bertie’ Coates, Kevin Fagan, Alan Hobbs and others were also prisoners of war and performed prodigies of selfless, devoted service for the men under their care. But of them all, it was Weary’s feats of endurance on the Burma railway that most caught the public imagination. His men regarded him as ‘a lighthouse of sanity in a world of madness’.

The whole terrible story of his prison camp years reads like ‘The Boy’s Own Paper’ and the denouement of heroism triumphant seems almost unbelievable. One can only marvel that Weary was not summarily executed for his defiance (as indeed almost happened on three separate occasions). It seems likely that he survived only because it suited the Japanese very well to have him there to preserve the morale of his troops so that they had at least some workers to build their railway. But perhaps they too realised that here was a rare example of the greatness of the vaulting human spirit.

There can be no doubt that Weary thoroughly deserved the label of a ‘great man’, in the best sense of the term. His richly merited knighthood puts him in the company of other great men: explorers, soldiers, sportsmen who really deserve a special category of their own with a different mode of address. But to say that a man is great does not imply that he is perfect. Like other great men, Weary had his faults, which in fact were merely the obverse side of the very qualities that made him capable of such great deeds in the first place.

The fact that he was never a ‘College’ man is not only understandable but inevitable when one considers his contempt for authority and his complete unruliness; he could never have worked his way patiently through the councils of the College because he was the very archetype of the individualist. He regarded College and Hospital administrative meetings as much talk and many words, which promised much but achieved little, so he left them to others and went his own way.

His enormous self-confidence and egotism made it difficult for him to regard others as his equal and this applied to his surgery, just as it did elsewhere. He preferred, for example, to perform abdominoperineal resection of the rectum single-handed, and clearly believed that the orthodox combined synchronous approach with another surgeon would have been an admission of weakness on his part and a betrayal of his duty.

He simply ignored the convenience and comfort of those who worked with him, although he also ignored his own. This made things very trying for his colleagues. The late Gordon Stanton, his permanent anaesthetist, often displayed the patience of a saint when kept waiting hours on end, but persisted for many years with total loyalty and dedication far beyond any reasonable call of duty, working on and on at all hours, day and night. Weary seemed quite unaware that anyone could regard his behaviour as other than completely normal and necessary.

During the 1930s and throughout the war, the Royal Melbourne Hospital was staffed by conservative general surgeons with little interest in the new surgical specialties that were emerging. None of them, except Edgar King, had ever attempted intrathoracic surgery, and Weary’s surgical apprenticeship was served at a time when operations within the chest were in their infancy. It was only through the efforts of Sir Alan Newton that beds were made available in 1946 for three new departments: thoracic surgery, plastic surgery and neurosurgery. The returned servicemen who were appointed to the hospital over the next few years were all innovators anxious to expand the horizons of surgery. By the early 1950s, the scope of surgical expertise had widened enormously, particularly in the new specialties. John Hayward, as a surgical resident, had pioneered the maintenance of negative pressure in the chest once it had been opened. The new Department of Anaesthesia, established in 1949 by Norman James, together with rapidly improving intravenous therapy, set the stage for oesophageal resection to become a practicable procedure. Weary was drawn irresistibly towards the new challenges posed by thoraco-abdominal surgery.

His doggedness and his refusal to accept even the thought of defeat inevitably led him towards his enduring surgical interests (distressing and often incurable complaints such as carcinoma of the larynx, oesophagus and stomach, ulcerative colitis and even abdominal aortic aneurism), all of them demanding major surgery at the limits of the possible. In his early days he treated many patients in partnership with John Hayward who taught him how to open and close the chest, while Weary for his part supplied the expertise relating to bowel resection and anastomosis. Together they pioneered oesophageal surgery at the Royal Melbourne Hospital after the War. As the years went by, Weary no longer felt the need for Hayward’s assistance and his enthusiasm and self-confidence led him to undertake massive operations, which could easily stray beyond the bounds of prudence. His patients were greatly helped by the tireless ministrations of Melbourne’s first specialist resuscitator, the late Dr E.B. Drevermann, but even so there were disasters at times.

Laryngectomy, oesophagectomy, abdominal aortic replacement and total colectomy; these were hazardous procedures in those days, and this made it inevitable that mortality and post-operative morbidity would be high in the hands of such an aggressive surgeon. It sometimes seemed that he almost welcomed intra-operative complexities for the problems they posed. He would, for example, resect part of the full thickness of an adherent aortic wall and patch the defect in the course of an oesophagectomy for carcinoma when a more cautiously orthodox surgeon would abandon the operation. These multiple procedures sometimes took an unconscionable time and stretched beyond reasonable bounds. Accordingly, his successes were punctuated by serious complications. But he continued, sparing neither himself
nor others. I vividly remember one particular operating
day at the Royal Melbourne Hospital with a proposed list
of nine major cases booked for 8am. We started 2 hours
later. The first operation took 8 hours, the second seven.
At 1am the next morning Weary was outraged that the
theatre staff flatly refused to allow the third patient to be
brought up! None of us had eaten since breakfast the
previous day.

Despite its high morbidity and mortality, it must
not be overlooked that this aggressive surgery did
produce results. His 5 and 10 year survival figures for
laryngectomy were easily the best in the world at that
time. He was determined to give his patients a chance of
‘cure’. Regrettably, this aim often proved illusory, as it so
often does, today more than ever, but at times it could
produce a brilliant success against the odds.

Weary’s legendary contempt for time did not
demean him to his professional colleagues, especially his
fellow surgeons. He was apt to schedule massive
operations at a moment’s notice with a sublime disregard
for his own or anyone else’s convenience; consequently
another surgeon due to operate in the session after
Weary’s might easily find himself cooling his heels for
hours on end while he waited in vain for the theatre to
become vacant. Some of his fellow senior surgeons made
it quite clear that they regarded this as intolerable
rudeness and thoughtlessness. And indeed they had a
point!

He ate and slept at the most irregular hours and
invariably was chronically late for appointments. But he
drove himself mercilessly and would embark on a full
round of his patients at any hour of the day or night,
whenever he had finished operating. He seemed baffled
that others could regard this as unusual.

His post-operative care was thus exemplary; it was
never too late and nothing was ever too much trouble. As
a result, many patients almost worshipped him and gave
him a surgical reputation to rival his image of ‘Christ of
the Burma Railway’ during the War.

His remarkable personal qualities were really not
well adapted to produce the ‘ideal’ surgeon of the post-
war era. Such a man should display self-confidence,
aggression tempered by caution, technical precision,
deftness and delicacy, and should be a ‘team man’, even
if he is the team’s most important member. Weary’s
attributes were somewhat different; they were more
appropriate to the ‘hero-surgeons’ of the 19th century
when the surgeon really was a one-man band. He was
reluctant to delegate responsibility and believed, above
all, in his own powers.

He was therefore tailor-made for the Burma
railway, both as commandant and surgeon, where his
qualities made it inevitable that he would conduct
himself as he did. No wonder those four years dominated
his reputation for the next forty.

But the demands of improved surgery in the
jungle are very different from those in civilian practice.
Small wonder then, that Weary emerged in his surgical
persona as the most rugged of rugged individuals and
became something of a lone figure who took little part in
hospital and College affairs. Instead, he chose to direct
his energies to a multitude of committees concerned with
former prisoners-of-war, returned servicemen, Legacy,
the Colombo plan and international relationships with
South East Asia. His war experiences thus became
inextricably intertwined into his later life as an
ambassadorial figure. He never forgot his ex-POW
survivors and served them to the end of his days in many
different ways.

One final anecdote will serve to illustrate Weary
Dunlop the surgeon. He performed one of the first aortic
grafts at the Royal Melbourne Hospital, but the patient
was not originally his. Two other staff surgeons (one
general, one thoracic) were embarking on the formidable
procedure and it was necessary for the graft to be made
on the spot by winding Ivalon sponge around a metal Y
piece, which was then heated to fuse the tape into a Y-
graft. Weary volunteered to do this menial task, but an
hour later he had taken over the entire operation while
the original protagonists stood by and watched him. On
this occasion, as on others, he moved on like some
inexorable natural force.

All in all, Weary Dunlop was one of the greatest
Australians of the 20th century. It is doubtful if we shall
see his like again. His surgery was the product of all his
remarkable personal traits and was brilliant at times, but
flawed by complications made inevitable by his
uncompromising determination to succeed.

Those of us fortunate enough to have known him
and worked with him were by turns stimulated,
infuriated, instructed and exhausted.

He was the most remarkable man I have ever
known.

Abstracts From The Literature

Prepared by Andy Robertson


Secondary transmission of Ebola virus infection in humans is known to be caused by direct contact with infected patients or body fluids. We report transmission of Ebola virus (Zaire strain) to two of three control rhesus monkeys (Macaca mulatta) that did not have direct contact with experimentally inoculated monkeys held in the same room. The two control monkeys died from Ebola virus infections at 10 and 11 days after the last experimentally inoculated monkey had died. The most likely route of infection of the control monkeys was aerosol, oral, or conjunctival exposure to virus-laden droplets secreted or excreted from the experimentally inoculated monkeys. These observations suggest approaches to the study of routes of transmission to and among humans.

Comment: This is the first indication of possible aerosol spread in Ebola cases. Although there have not been documented cases of human aerosol spread, further research is required into the routes of spread, especially in regards to the index case.


The many uses of ricin for basic research and clinical studies have made it an intensively studied molecule.

Although the exact mechanism by which the toxin kills animals is unknown, ricin kills cells by entering the cytosol and inhibiting protein synthesis. In all areas of clinical use, forensic medicine and basic scientific inquiry, the capability to detect the toxin is of primary importance. Recent efforts to produce a vaccine originate from a perception that this widely available toxic plant protein could be a poor man’s weapon of mass destruction.

Comment: This article, from the Toxicology Division at USAMRIID, is a very useful review of the current research into ricin.


A study of dental bite-wing radiography was conducted covering 59 dental practices in South Australia in order to determine surface exposure to patients and some associated technique factors. The patient-surface air kerma for bite wing radiography within South Australia ranged from 1.7 to 8.5 mGy. This survey supports the view that an increase in radiation exposure to the patient is a likely technique to compensate for inadequate film processing. The percentage of dentists using unsatisfactory methods was between 15% and 32% depending on the criterion used.

Comment: Is the a problem area for ADF dentists?

Abstracts are a useful way of summarising current papers and providing succinct and useful knowledge updates. To be successful, however, they should ideally come from multiple and disparate sources. As I assume (and hope) that I am not the only person reading Journals amongst our 350 members, I encourage all members to send recent abstracts to the Editor or Assistant Editor. Only by this means will AMMA get a good representation of the advances in all aspects of Military Medicine.
AMMA 5th Annual Conference

BOOK EARLY...

By now each member will have received the Call for Papers notice and information regarding the forthcoming AMMA conference. On behalf of the 1996 Conference Committee, I would like to encourage all members to plan to attend this year’s conference. As in the past, it will be packed with interesting topics and speakers.

So far we have received a number of abstracts, but if anyone is still interested in either presenting a paper or poster session please let us know.

The program is still in the development stage, but we are pleased to confirm that Lt Colonel Frank Torova, Director of Medical Service of the PNG Defence Force will be presenting the Keynote Address on Day 1. His presentation will focus on Medical & Surgical Challenges in the PNG Defence Force. In addition, Mrs Bronwyn Bishop as Minister for Defence Industry, Science, and Personnel will be opening the Conference on Friday 6th September at 1.00pm, and Mrs Kate Carnell, Chief Minister for the ACT will be welcoming delegates to the conference and Canberra at the Friday evening cocktail party.

As another incentive to attend the conference CME points are being sought from the various colleges and faculties for the 1996 Conference. If you were thinking about taking your partner or family to the conference, this year we will also be offering an Accompanying Persons programme. Canberra as our nation’s capital has many sights to see, and there will be a great programme put together for accompanying partners and families. This information and more will be sent to you direct in the Registration Brochure at the beginning of July . . . but if you’d like to secure your registration early contact Paula Leishman on telephone (002) 47-1850 or facsimile (002) 47-1855.

The committee is attempting to again keep the registration fee to a reasonable cost, it is anticipated that the fee will be around $250.00, which will include the cost of the conference dinner.

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Write to AMMA PO Box 373, Moonah, Tasmania 7018, or phone the Conference Committee:-

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News & Views

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A reminder that the AMMA library is available for use by members. Books can be borrowed for up to 12 weeks from:

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AMMA on the Net

As more and more of our members take the plunge and place themselves on the Internet, the more scope there is for rapid communication between both AMMA and its members and between members themselves. The Internet also allows for the rapid transfer of articles, abstracts and other contributions (without the subsequent retyping by the Editor) to AMMA. It is planned to develop a directory of AMMA members and their E-mail addressees. Depending on interest, other ventures, including electronic newsletters, will be explored.

If interested, please contact Andy Robertson by E-mail at:

agrobert@canberra.DIALIX.oz.au

The AMMA home page is at:


Conference & Meeting Calendar

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The AMMA would like to welcome the following new members.

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Do you know where these members are?
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Primary Qualification

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Tu: Dr Marcus Skinner
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CONTRIBUTIONS

for the August issue should be sent to:

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Deadline is 1st July 1996.

Instructions for Authors:
Articles submitted for publication in AMM should conform to the following guidelines:

- two hard copies should be submitted, typed double-spaced on A4 paper (single-side)
- if possible, an electronic copy on an IBM formatted 3.5 inch floppy disc in a standard word processing programme should be submitted
- the text in both hard and electronic copies should be unformatted
- references in the text should be numbered consecutively as they are cited and annotation of the references should accord with the style given in Index Medicus. Where there are seven or more authors, list only the first six then et al. For example:
- figures and tables should be submitted separately with an indication in the text as to where they should be located
- the originals of all photographs, ECGs, EEGs etc should be submitted to allow high quality reproduction (originals will be returned)

Articles submitted may be subject to peer review. Articles which have been published elsewhere will only be considered if they are of importance to the field of military medicine, and publication will only proceed with the prior approval of the original publisher.
Australian Military Medicine Association

Statement of Objectives

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

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

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

The Association is totally independent of the Australian Defence Force.