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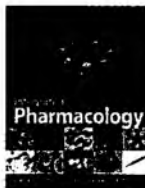
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EDITORIAL

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The possibility of a major bioterrorist attack on the British Isles is thankfully remote. Nevertheless, it casts a disproportionately large shadow. The policy and practice of many major institutions has changed dramatically in the wake of anthrax attacks in the USA last year, and public awareness of such action has soared. In this issue, Professor Crawford discusses the use of viruses as agents of mass destruction (p3).

While the threat does remain small, it is important to be informed about the issues involved. Apart from anything else, increasing our knowledge of the subject will allow us to better educate and reassure our patients, even if we never come into contact with a single case of anthrax. Dr Mike Jones has given us an overview of anthrax and how to deal with it (p14).

Those of us who travel to certain parts of the Third World on an elective are perhaps more likely to encounter this disease. What we are also likely to see is the inequality that still persists in the provision of basic health care in these countries. The continuing role of the World Health Organisation as a care provider is considered in this issue by Jane Atkinson (p8).

As usual, we welcome any comments or suggestions from our readers. Enjoy the issue.



David Griffith, Joint Editor

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Viruses as Agents of Mass Destruction

Dorothy H Crawford

Professor of Medical Microbiology, University of Edinburgh

Recent events in the US, with the release of Anthrax Bacillus from as yet unknown sources, have for the first time in most people's lifetime focussed the world's attention on the threat of biological warfare. However, such attacks are not new. From time to time throughout history peoples and governments around the world have used microorganisms as efficient and cost-effective weapons of mass destruction. Starting in a rather crude but effective way, the Greeks and Romans deposited dead animals into their enemies' drinking water. Later dead soldiers were added to this, and the technique was further refined in Medieval times when bodies of people who had died of infectious diseases were catapulted into towns under siege.

Once the true nature of microorganisms became clear in the nineteenth and early twentieth centuries, the ability to grow large stocks of bacteria and viruses meant that biological warfare assumed global significance. Although there are no clearly documented incidences of the use of biological warfare during World War I, the threat was fully appreciated, and accusations, counter-accusations and denials abounded. Hence the 1925 Geneva Protocol prohibited the use of biological methods as well as poisonous gases in warfare; but it did not ban their further development ¹.

In 1929 the Russians set up a biological warfare research station north of the Caspian Sea, prompting Britain, Japan, the USA and Canada to do the same. The Japanese developed the most extensive programme, and in the years leading up to and during World War II, they used human

subjects in open field trials to test out their lethal agents including the bacteria causing plague, cholera, glanders and typhus. Manufacture continued in some countries until The Biological and Toxic Weapons Convention came into effect in 1975. This certainly reduced the threat, but did not entirely eliminate it, and the problem of treaty verification has continued ever since ².

In the modern world the threat of biological warfare comes mainly from terrorist groups and third world dictators. For them biological weapons have many advantages over their conventional counterparts, being cheaper and relatively easy to prepare. Although new restrictions are in place, seed cultures of many dangerous microorganisms can still be obtained relatively easily from national collections. And since researching and preparing vaccines

(defensive research) is a legitimate reason for growing microbes on a large scale, biological weapons factories (offensive research) can masquerade as vaccine production plants. Clearly, Iraq is a case in point; six such facilities are known to have existed, including the Daura Foot and Mouth Disease Vaccine Facility at Al Manal. In 1991 when Iraqi troops occupied Kuwait, it was well known that they had a stockpile of weapons laden with biological agents including 200 bombs and 25 ballistic missiles. Combat troops in Operation Desert Storm were vaccinated, provided with protective equipment, and given prophylactic antibiotics. Thankfully, in the event, none of these were required ³.

“Microorganisms are ideal for selective attacks on individuals or for targeting large metropolises. They can be smuggled undetected through all traditional security devices, and tiny volumes can kill huge numbers of people.”

Microorganisms are ideal for selective attacks on individuals or for targeting large metropolises.

They can be smuggled undetected through all traditional security devices, and tiny volumes can kill huge numbers of people. Furthermore, since they are invisible, odourless, tasteless and have a delayed action, so they can be released into the air without immediate detection. A major biological attack would place untold strain on medical services which are not designed to cope with such an incident. As we have no previous experience dealing with this type of attack, it is likely that panic and psychological trauma would lead to total confusion ⁴.

Many different organisms have been tested for their potential as agents of biological warfare, including bacteria which cause anthrax, TB, typhoid, plague, cholera, gas gangrene. Candidate viruses include the haemorrhagic fever viruses, like Ebola, and smallpox. The remainder of this review will focus on these two organisms.

Smallpox

Smallpox virus was probably the first microbe to be used as a weapon of mass destruction. It is likely that deliberate release of smallpox virus occurred on several occasions during the North American Indian Wars, but the best documented incident was in 1763. At the time Indian scalping-parties were devastating European settlements in the area surrounding Fort Pitt (now Pittsburgh) causing widespread fear and panic. Sir Jeffrey Amherst, British Commander-in-Chief in North America, knowing that troop reinforcements would not be forthcoming, feared that the whole of Western Pennsylvania would soon be lost. In the knowledge that the Indians were particularly susceptible to smallpox, he authorised smallpox-contaminated blankets to be distributed among the Native American tribes-people ¹.

Until the twentieth century smallpox was a killer on a world-wide scale. The virus spread rapidly in large and crowded cities causing devastating epidemics. Case fatality rates reached 30%, or even higher in populations who had not previously encountered smallpox. The virus spread from person to person primarily through the air via droplets from the oropharynx; more rarely from direct contact with materials contami-

nated with pock fluid or scabs. In most communities smallpox epidemics occurred regularly, and since nearly all adults were immune, children were the main victims. However, unlike the other air-borne childhood infections (such as measles, mumps, chickenpox), smallpox tended to spread within households rather than in the population at large. This was probably due to the fact that sufferers only became infectious when the rash appeared, by which time they were likely to be confined to bed.

Inhaled virus particles infect cells of the upper respiratory passages, and after an incubation period of 12-14 days victims develop high fever and malaise with head- and back-aches. The characteristic pustular rash appears 1-2 days later, beginning in the mouth and pharynx and thereafter spreading to the face, arms, trunk and legs (see figure). The pustules begin to crust after 8-9 days and eventually the scabs separate leaving pitted scars, particularly on the face ⁵.

From the point of view of the aggressor, one of the main features of smallpox which make it a desirable agent for biological warfare is the fact that it remains infectious for relatively long periods of time, particularly in cold, damp conditions. This means that it could be packed into



Effects of smallpox

war-heads of guided missiles and sent to its destination still in a viable condition. Also, since smallpox was eradicated in 1977, almost half of the World's population is non immune and would by now be susceptible. Furthermore, the amount of protection afforded by a vaccination given over 20 years ago is unclear. The infectious dose of virus is thought to be very low (1-2 virus particles), and so disease would occur in almost everyone who became infected. In addition to this, although the threat of a deliberate smallpox release is well recognised by governments and stocks of vaccine have been retained for this eventuality, in reality it would not be possible to vaccinate an entire population in time to prevent an epidemic spreading, probably on a world-wide scale.

Ebola Haemorrhagic Fever

Viral haemorrhagic fever is a syndrome which can be caused by a number of RNA viruses from different virus families. The syndrome characteristically begins abruptly with a high fever, headache, malaise, myalgia, fatigue, diarrhoea and bleeding. Increased vascular permeability resulting from viral infection of vascular endothelium initially causes petechial haemorrhages, which progress to generalised bleeding into mucous membranes and internal organs. Depending on the particular organs affected, patients develop neurological, pulmonary and/or hepatic features, with eventual hypotension, cardiovascular collapse, shock and renal failure. Disseminated intravascular coagulation is another prominent feature, and with no specific treatment to offer, mortality is very high.

Ebola virus was first isolated from an outbreak of haemorrhagic fever in Yambuku, a remote jungle village in Northern Zaire, in 1976. However, it is probable that the virus had caused localised outbreaks in rural Africa prior to this time, and several subsequent outbreaks have been documented. On each occasion the virus has infected man from an unknown source, and this suggests that there must be a reservoir of infection, probably an animal in the rain forest which carries the virus as a harmless passenger. Until this animal is identified sporadic, unpredictable outbreaks will continue to occur.

The first outbreak of Ebola was typical. The index case was a school teacher who had just returned from a trip through the bush when he became unwell with fever and malaise. He went to the local mission station, where the Belgian nuns assumed he had malaria and gave him an injection of antimalarials. As was their practice, they then used the same needle throughout the day to inject others. By the time the school teacher died a few days later there were many other cases, including his family and several of the nuns. In all 318 people contracted the disease and 280 died. The outbreak was only brought under control when the necessary control measures were implemented.

Ebola is not endemic in the human population, and therefore any outbreak requires an initial infection, probably through a bite from the animal which harbours the virus naturally. However, once the virus has crossed the species barrier and infected man, it can spread from person to person very effectively by direct contact. Patients are highly infectious since all body fluids contain large amounts of infectious virus. Thus in the Yambuku outbreak the virus spread via a contaminated needle to other patients and through routine contact and nursing procedures to the nuns and family members.

As a weapon of mass destruction Ebola virus certainly has its attractions, in particular it's high infectivity, the devastating nature of the disease, the high mortality, and the lack of preventive or therapeutic measures. But although devastating, Ebola outbreaks generally remain localised. This is because the virus is spread by direct contact and not by aerosol, and the short incubation period (may be only 4 days) and severe symptoms prevent patients travelling far from the site of infection. Thus once the necessary isolation precautions (strict barrier nursing) are in place, it is relatively easy to bring the outbreak under control.

Conclusions

Biological weapons are primarily designed to destroy all vital activity but not necessarily to wipe out the whole human race. In this regard, smallpox, while it would certainly incapacitate,

would probably not kill all those infected because of our inbuilt resistance which developed and strengthened over the centuries when the virus was rife. We have no such inbuilt resistance to Ebola, but a world-wide epidemic of this virus would be very difficult to engineer because of its localised method of spread.

After the world-wide elimination of smallpox, the World Health Organisation (WHO) recommended that all laboratories destroy their stocks of the virus, and two WHO reference laboratories were set up: The Institute of Virus Preparations in Moscow, Russia, and the Centre for Disease Control in Atlanta, USA. These remaining stocks were due to be destroyed by the end of the twentieth century, but were in fact retained for further research when the potential threat was realised. According to a former Deputy Director of the Soviet Union's Civilian Bioweapons program, smallpox virus from these stocks has been used to grow up large quantities for use in bombs and missiles. And, to end this review with the most frightening information (hopefully only a rumour), work was apparently underway to produce more virulent and infectious strains,

perhaps even a hybrid combining the worst features of Ebola and smallpox. With the break up of the Soviet Union there are now fears as to whose hands these potentially highly lethal weapons may fall into ⁵.

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Some of the material in this review is contained in the author's book, *The Invisible Enemy: A Natural History of Viruses*, OUP, 2000.

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Health for All by the Year 2000 - Where has the WHO gone?

Jane Atkinson

“Tell the Ministry of Public Health it only works for 15% of the entire population. Furthermore, this 15% is made up of mostly the privileged. The broad ranks of the peasants can not obtain medical treatment and also do not receive medicine. The Public Health Ministry is not a people’s ministry. It should be called the Urban Public Health Ministry, or the Public Health Ministry of the Privileged, or even the Urban Public Health Ministry of the Privileged”.

Chairman Mao Dezhong, June 26, 1965 ¹

Enjoyment of the highest attainable standard of health is a fundamental human right of all people ². This is seen as an important outcome as well as a goal of sustainable human development. Yet at the dawn of the 21st century massive world-wide disparities in the provision of health care continue to exist; 800 million people still lack access to health services ³. The rate of development of the first world has been greater than that of the third world so the gap between “haves” and “have nots” is greater than ever; the richest 1.2 billion people in the world account for 82.7% of the total global wealth ⁴.

Even within developing countries there are major health disparities. In the past many governments, in striving for very visible development, have invested in building a western style medical system. As a result there are large, sophisticated hospitals often in the capital, or regional centres capable of sophisticated procedures. These services are life-saving, but only benefit a tiny minority of the population. All this time the same country neglects the vast majority who are deprived of the most basic of medical services. The traditional communist dictum of the greatest good for the greatest number is being ignored. Governments do not seem to understand that health is central to the development process.

The Road to Alma-Ata

It was in fact the aforementioned communists, in China, who first realised that the route to

development was not with fast medical development but in the provision of basic health care that was available to all. Chairman Mao Dezhong, in 1965 as part of his cultural revolution, advocated ‘barefoot doctors’ who would have only three years training but would provide inexpensive, basic health care to all, especially the rural masses ¹.

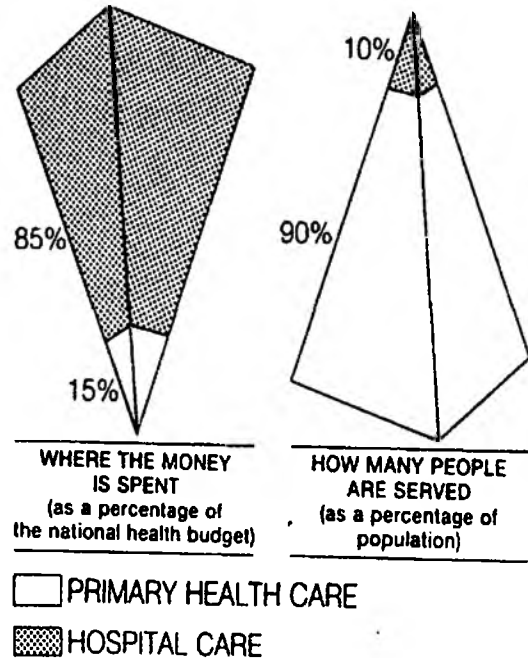


Figure 1: Distribution of health spending in developing countries ¹.

This idea lived on only to re-emerge a decade later at the 1977 World Assembly of the World Health Organisation (WHO). They decided that

their main social target should be “attainment, by all citizens of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life”; this target was summarised as Health for All by 2000 (HFA2000) ⁵. Dr Mahler (the Director-General at that time) perceived the outcome of HFA - “people will use much better approaches than they do now for preventing disease and alleviating unavoidable illness and disability and that there will be better ways of growing up, growing old and dying gracefully” ⁶.

This was an extension of WHO’s traditional role from setting normative standards and providing technical advice and assistance on medical matters to also include advocacy of health through HFA2000 ⁷. This extension was a profound change for the organisation who had previously taken “the approach to health that was largely disease orientated and it studiously avoided political or cultural controversy” ⁸.

The Declaration of Alma-Ata

The conference found that the key to obtaining HFA2000 was by the worldwide implementation of primary health care (PHC). This would not be yet another externally led “add-on” programme, it would form an integral and permanent part of the health care systems from the ground up of both developed and developing countries. Thus it would be a reversal of the current hospital/institution based health care system.

PHC consists of nine main areas:

- Health Education
- Environmental sanitation, especially of food and water
- The employment of community or village health workers
- Maternal and child health programs, including immunisation and family planning
- Prevention of local endemic diseases
- Appropriate treatment of common diseases and injuries
- Provision of essential drugs
- Promotion of nutrition
- Traditional medicine

HFA2000 strategy is meant to operate at three levels; locally, nationally and internationally. Ideas should be initiated nationally but planned locally, therefore being most appropriate to the people it aims to serve. Internationally there should be a flow of ideas and strategies co-ordinated by WHO. National self-reliance does imply national initiative but not national self-sufficiency and idea development. HFA was to encompass these five following concepts ⁵.

1) **Equity** – This is the foundation of the HFA2000 concept. Every individual must have lifelong access to comprehensive health care regardless of how poor or remote they are.

2) **Comprehensive provision** - Services must be promotive, preventative, curative and rehabilitative.

3) **Sustainability** – The project must be sustainable; financially, culturally and technologically to provide health for all, as well as responsive to changing conditions.

4) **Community involvement** – This promotes self-reliance and reduces dependence.

5) **Integration** – Health, as a sector can not develop in isolation; it both contributes to and is affected by other sectors such as sanitation, housing and education.

The Role of WHO

“WHO knows everything but does nothing” ⁹

The role of WHO is not to provide the primary health care for HFA2000 but to inspire and assist countries to do so themselves as well as co-ordinating the non-governmental organisations (NGOs) such as UNICEF (who incidentally “knows nothing but does everything” ⁹). In this there is a problem, WHO itself is in crisis. It is an underfunded (biennial budget for 1994-5 just \$1.8billion compared to the annual NHS budget of \$60billion), bureaucratic, overspread organisation ⁷.

Over the last decade there has been mounting

criticism of the lack of strong leadership and clear strategy; there have even been rumours of corruption⁷. The fact that pharmaceutical representatives are present at many policy-forming meetings has long been considered inappropriate³. WHO can not afford to lose its credibil-



Figure 2: Dr Nakajima – Director-General 1988-1998

ity, operating as it does through governments. It also needs to be trusted by other NGO's, such as UNICEF, who are more involved on the ground implementing the policies.

Many of the problems have been contributed to by the poor leadership of the recent director-general Dr Hiroshi Nakajima who held the position from 1988-1998. Seen by many as a reserved and a poor communicator, he himself confesses to not being a strong leader¹⁰. Dr Nakajima attempted to establish "a new paradigm for health" but he embarrassingly failed to explain what this was.

The international loss in confidence, especially by donor countries led to a demand for greater accountability. To gain more control over their donations there has been an increase in the so called 'extra budgetary contributions' for 'special programmes', accounting for 50% of WHO's income, which are outside the direct control of the management. Donors can exert political pressure by threatening to withdraw these funds¹¹.

This leads to another problem for WHO: special programmes are generally performance driven, judged by short-term outputs (such as percentage immunity achieved)¹¹. They also by-pass WHO's commitment to only working through governments and are generally non-integrated. The programmes are forced to compete with each other for funds so focus on the glamorous, attention-grabbing causes rather than the grass root development so essential for the implementation of HFA2000.

The problems of global initiatives are neatly summarised by Banerji: Firstly, how can one have a 'prefabricated' initiative given the extreme variations among and often within poor countries? Second, selection of health problems for action conformed more to the special interests of the rich countries than the poor. Third, a technocentric approach to problem solving was adopted. Fourth, there is an obvious contradiction in the scientific basis of the claim that the suggested globe-embracing programs are cost-effective given the profound variations among and within countries. Fifth, by their very nature, international initiatives cannot promote community self-reliance. Sixth, there is the key question of dependence and sustainability; 'donors' have used their tremendous influence on the pliable ruling classes of the poor countries to ensure that the ill-conceived, ill-designed, ill-managed global initiatives are given priority over the ongoing work of health organisations. Finally, and above all, these programs are the very antitheses of the Alma-Ata Declaration.

Future of WHO

Much hope was placed on Dr Brundtland the current Director-General. She is originally from a medical background and was Prime Minister of Norway for 10 years¹². Her main immediate aims as stated in her initial address in July 1998 would be to "pull WHO together by focusing on our core business", "reconnect the organisation through flatter structure, better communication, more transparency and a clearer distribution of roles", and "create an organisational structure not driven by bureaucratic rules but one that promotes performance and results"¹³. All this sounds great and is desperately needed for



Figure 3: Dr Bruntland – current Director-General ¹²

revitalising the WHO, but what has happened to HFA2000? In Dr Bruntland's 16 page opening address in July 1998 she referred to HFA only once in reference to "keeping our long term objective of HFA..." ¹³. She seems more interested in highlighting the importance of the special programmes especially relating to HIV/AIDS, which are more inclined to by-pass governments and be a "global initiative". WHO has to re-establish its two main roles; firstly to encourage governments and NGOs to work towards health for all, and secondly, to stress the need for partnerships between health and other sectors ³.

Future of HFA2000

HFA2000 was not fulfilled; child mortality is no longer dropping, per capita income in sub-Saharan Africa is lower than in the 1960s ³ and the poverty gap has increased by 30% in the past decade ¹⁴. In 1998 WHO re-christened the project Health for All in the 21st Century but this new initiative reads like the policy statement for all of WHO's interests. It is made up of Ten Global Health Targets including "reversal of global trends of the five major pandemics" "eradication and elimination of certain diseases" and "implement global and national health information and surveillance systems" ¹³. So although HFA

still exists it has become an idealistic phrase rather than an obtainable goal.

This is a tragic state of affairs; the premises on which HFA2000 was launched over twenty years ago still exist. There is still a huge unmet need for provision of basic health care for all people, regardless of how poor or how remote. The individual special programmes are valid but intrinsically focused on a particular population, be it those with HIV/AIDS, or mother and child health. WHO is at risk from losing sight of its philosophy of equity and becoming an organisation of parallel programmes.

"Before talking of the renewal of the HFA strategy, WHO has to note that it has never been completely implemented. They ought to have elicited the reasons for this sad state of affairs before coming up with yet another 'initiative'." ¹⁶

Conclusion

The principle of Alma-Ata was to develop PHC to become an integral and permanent part of the health care systems. To establish HFA2000 was hugely ambitious and although it was not obtained it does not mean it is not possible given time and enthusiasm; development occurs in

small steps rather than great leaps¹⁷. It has been estimated that \$27 billion would save 8 million lives per year; this seems like a colossal amount of money but it is still \$13 billion less than America's Congress appropriated for its "War on Terrorism" only three days after the September 11th attacks; alternatively it could be looked at as being only \$25 per rich-county citizen each year¹⁸.

WHO is in a unique position to influence the governments of developing countries to raise the status of health on national agendas and to re-structure health systems to focus on primary health care¹⁹. WHO will always be faced with problems of political instability and conflicts of interest but with perseverance governments will eventually realise that having a healthy population is the only way of obtaining long-term, sustainable, economic and social development.

HFA needs to be separated from WHO's Global Health Targets, maybe even renamed Health by All so it is not considered a passive process²⁰. It must be re-established as a major global initiative that operates locally, nationally and internationally involving individuals, communities, NGOs and governments. It may even be appropriate to separate WHO into two sister organisations; one dealing with the shorter-term specific "special programmes", the other striving for the fulfilment of HFA through development of primary health care systems.

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Levetiracetam 1,000 mg daily did not affect the pharmacokinetics of oral contraceptives (ethinyl-estradiol and levonorgestrel). Levetiracetam 2,000 mg daily did not affect the pharmacokinetics of digoxin and warfarin and prothrombin times were not modified. **Pregnancy and lactation:** Should not be used during pregnancy unless clearly necessary. Breast-feeding not recommended. **Driving, etc:** Caution recommended when performing skilled tasks, e.g. driving vehicles or operating machinery. **Undesirable effects:** Incidence of undesirable effects considered to be at least possibly related in controlled clinical studies: **Very common (>10%):** asthenia, somnolence. **Common (between 1%-10%):** GI disturbances, anorexia, accidental injury, headache, dizziness, tremor, ataxia, convulsion, amnesia, emotional lability, hostility, depression, insomnia, nervousness, vertigo, rash, diplopia. For information on post-marketing experience see SPC. **Legal category:** POM. **Marketing authorisation numbers:** 250 mg x 60 tablets: EU/1/00/146/004. 500 mg x 60 tablets: EU/1/00/146/010. 1,000 mg x 60 tablets: EU/1/00/146/024. **NHS price:** 250 mg x 60 tablets: £29.70. 500 mg x 60 tablets: £49.50. 1,000 mg x 60 tablets: £94.50. **Further information is available from:** UCB Pharma Ltd., 3 George Street, Watford, Hertfordshire WD18 0UH. Tel: 01923 211811. medical.uk@ucb-group.com **Date of preparation:** August 2002.

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UCB-K-02-29

Anthrax after September 11th 2001

What to look for and how to treat it

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Summary

Anthrax is a serious bacterial infection with a particularly high mortality in its gastrointestinal, pulmonary, and meningitic forms with a worldwide distribution, although it is most common in the developing world. Gastrointestinal and pulmonary anthrax results in death within hours or a few days of the onset of serious symptoms and the diagnosis is usually made post-mortem. Treatment of wild type anthrax is usually with penicillin in high dose. The production of anthrax for large scale bioterrorism is difficult and requires sophisticated facilities. There is a greater risk that anthrax used as a bioterrorist weapon will be antibiotic resistant and ciprofloxacin is a more appropriate antibiotic choice until the antibiotic sensitivity of the anthrax strain being deployed becomes known. Post exposure prophylaxis should be continued for two months due to the long delay that sometimes occurs before spores germinate once within the human host. A live vaccine is available but requires a large number of injections and its use is largely limited to military personnel.

Introduction

In early October last year I was on my way back to Edinburgh from a meeting in London. A signalling failure just outside Paddington station meant that a journey on the Heathrow Express extended from 15 to 75 minutes, during which time I watched the BBC News summary more times than I would have wished, particularly since the delay threatened my return that night to Edinburgh. BBC News majored on the bioterrorist outbreak of anthrax which was then in its early phases in the USA. The index case

became ill on October 2nd in Florida and died a few days later¹. To my surprise a disease which I had treated several times at a teaching hospital in Tanzania 20 years previously was now apparently of global interest. On my return to Edinburgh I offered to give a short presentation at the Grand Round at the Western General Hospital, since if Al Qaeda was responsible it was at least remotely possible that the UK, as the closest ally of the USA, might also be a target. This paper is a direct result of that presentation and seeks to summarise what we know about anthrax, its clinical presentations and treatment, both in endemic and bioterrorist forms.

The causative organism and pathogenesis

Anthrax derives its name from the Greek word *anthrakos* meaning coal due to the appearance of a coal black centre in the lesion in the cutaneous form. Anthrax is caused by a gram positive, spore forming, toxin producing aerobic rod, *Bacillus anthracis*. Although in vitro it grows as long chains, in the human host it appears as single organisms or chains of 2 or 3 bacilli¹. The vegetative bacillus does not survive long in a putrefying carcass, only 3-4 days at 25°C². Escaping bacilli at temperatures above 20°C form spores which may survive decades, but these are destroyed by dry heat of 150°C, boiling for 10 minutes, and autoclaving. The toxin has three parts, of which two are important, an oedema factor and a lethal factor². Lethal factor stimulates the release of tumour necrosis factor and interleukin-1 contributing to sudden death².

The lethal factor is a protease with a particular amino acid substrate which could be a target for

the development of an inhibitor¹. Infection is initiated after introduction of a spore through a break in the skin or mucosa and the vegetative form is germinated after ingestion by macrophages and may then pass to regional lymph nodes and the spleen. Extracellular multiplication then occurs with toxin production². Lethal factor is produced and released in a burst, causing fever, disorientation, coma, and death. In rhesus monkeys, inhaled spores are deposited in alveolar spaces and then transported to mediastinal lymph nodes where germination occurs up to 60 days later. It was this observation that has led to the recommendation that antibiotic prophylaxis should be continued for 60 days after inhalational exposure².

Epidemiology of wild type anthrax

Anthrax has a worldwide distribution but is now most common in developing countries, principally in Africa and Asia. Historically, some outbreaks have been massive. In 1945 an outbreak in Iran caused one million sheep deaths¹, and between 1979 and 1985 an outbreak in Zimbabwe caused 10,000 human cases². Even in developed nations anthrax has continued to cause problems. Between 1944 and 1994, the USA reported 224 cases, of which 18 were inhalational³. Occasional cases have surfaced elsewhere in the developed West, for instance in 1976 fatal pulmonary anthrax was contracted from bone meal fertiliser in the UK⁴. Cutaneous anthrax occurred in a casual labourer in London in 1996⁵, and a Norwegian who skin-popped heroin in 2000⁶. The annual total for cases worldwide is estimated at 20,000-100,000².

The anthrax bacillus as a bioterrorist weapon

The use of anthrax as a bioterrorist weapon was extensively reviewed only 2 years before the 2001 outbreak by Inglesby in the *Journal of the American Medical Association*¹. There has been interest in anthrax as a weapon of war for many years. During WWII British scientists conducted experiments on Gruinard Island off the West coast of Scotland and several decades elapsed before it was successfully decontaminated. Aum Shinrikyo terrorists in Japan made at least eight unsuccessful attempts to release aerosols of anthrax spores before their more tragically ef-

fective release of sarin nerve gas in a Tokyo subway in 1995. After the Gulf War, Iraq admitted producing and deploying weaponized anthrax in missiles, lending weight to the view that a clear threat remained, a threat which has now become all too obvious¹.

A few litres of standard broth culture prepared in a kitchen can produce sufficient spores to infect a few people if sent through the post. Lyophilising cultures into powder requires simple equipment, but ultra refining spores is necessary if more extensive bioterrorism is planned. Particles need to be between 1-5µm¹ and electrostatically neutral in order to avoid clumping¹¹. This is probably beyond the ability of small groups and it has been estimated that for an attack on an urban population of 5 million, the aerial discharge of 50 kg of highly refined spore-containing powder would be needed to cause 250,000 cases².

The major experience with anthrax in bioterrorist form comes from Russia. In 1979 accidental discharge into the atmosphere occurred at a biological warfare research establishment at Sverdlovsk. Precise figures are not available but it is thought that 100 inhalational cases may have occurred of which 66 were fatal, all aged over 24 years¹. Cases in humans occurred up to 4 km and in animals up to 50 km from the factory site¹. On the basis of experiments in primates the dose in humans causing 50% lethality is between 2500 and 55,000 spores¹ and this amount is not visible to the naked eye.

The strain of anthrax used in bioterrorism in late 2001 in the USA was a derivative of Ames strain used worldwide by researchers, and first isolated from a dead animal in Ames, Iowa in the 1950s. Preliminary analysis suggested the presence of constitutive and inducible beta lactamases and for this reason treatment with penicillin, ampicillin or amoxicillin was not recommended². The CDC website does not give a clear total for the number of human cases associated with this outbreak at the point of writing this paper in May 2002 but by 28th November 2001 23 cases had been identified of which 11 were inhalational and 12 cutaneous¹.

Principal clinical manifestations

Cutaneous anthrax (Figures 1-4)

This occurs as the result of direct contact with viable organisms invading through a skin break. Person to person spread does occur but very rarely and has been documented as a result of sharing scrubbing brushes used during bathing³. The cutaneous form is referred to as a malignant pustule, but this is a misnomer since there is no pus unless secondary bacterial infection occurs. The incubation period is 1-7 days, following which a pimple grows rapidly over 2-4 days. The initial itchy painless vesicle is 1-2cm in diameter and filled with clear or serosanguinous fluid. As the vesicle enlarges satellite vesicles develop with impressive surrounding oedema. When the vesicle ruptures it forms an ulcer covered by a black eschar by day 4-5. Without the use of antibiotics resolution occurs after 10 days and in 80-90% of cases healing occurs without scarring. Ulceration may still occur after antibiotic use and total resolution may take 2-6 weeks.



Figure 1. Facial cutaneous anthrax with marked oedema.



Figure 2. Facial 'malignant pustule' with erythema and oedema spreading down onto the anterior chest wall. The patient was hypotensive and febrile.

The differential diagnosis (see over) is wide and the list is based in part on the paper by Dixon et al published in 1999¹.

Gastro-intestinal anthrax

This occurs as a result of eating infected meat and comprises 95% of cases with a mortality of only 1%. The incubation period is 1-7 days after ingestion, during which an eschar develops on the intestinal mucosa, usually in the terminal ileum or caecum but it may occur anywhere from the oropharynx downwards³. Gross mesenteric lymphadenitis follows and perforation of the intestine may occur at the site of the eschar. Gastro-intestinal anthrax is usually undiagnosed until too late. The clinical features are sudden onset of severe diffuse abdominal pain, nausea and vomiting and variably, watery or bloody diarrhoea may be present. On physical examination there will usually be fever, rebound tenderness, shock, and collapse, and ascites may be present after 2-4 days. Death occurs in a few hours or recovery may occur after 10-14 days.



Above: Figure 3a. Marked oedema in cutaneous anthrax affecting the thigh. No clear malignant pustule is seen. A BCG scar is present in the centre of the photograph.

Below: Figure 3b. Ulceration in the same patient during convalescence.



Above: Figure 4

One of four patients admitted to Kilimanjaro Christian Medical Centre, Tanzania in 1977. They had found a dead zebra, carried it to their village and cooked it over an open fire. The three patients who had eaten zebra meat developed severe abdominal symptoms suggestive of an intra-abdominal catastrophe and died in the surgical department. This patient had marked cutaneous invasion of spores as a result of having carried the zebra on his right shoulder. He has oedema of the anterior chest wall, visible as nipple oedema, and was severely hypotensive. He died four hours later.

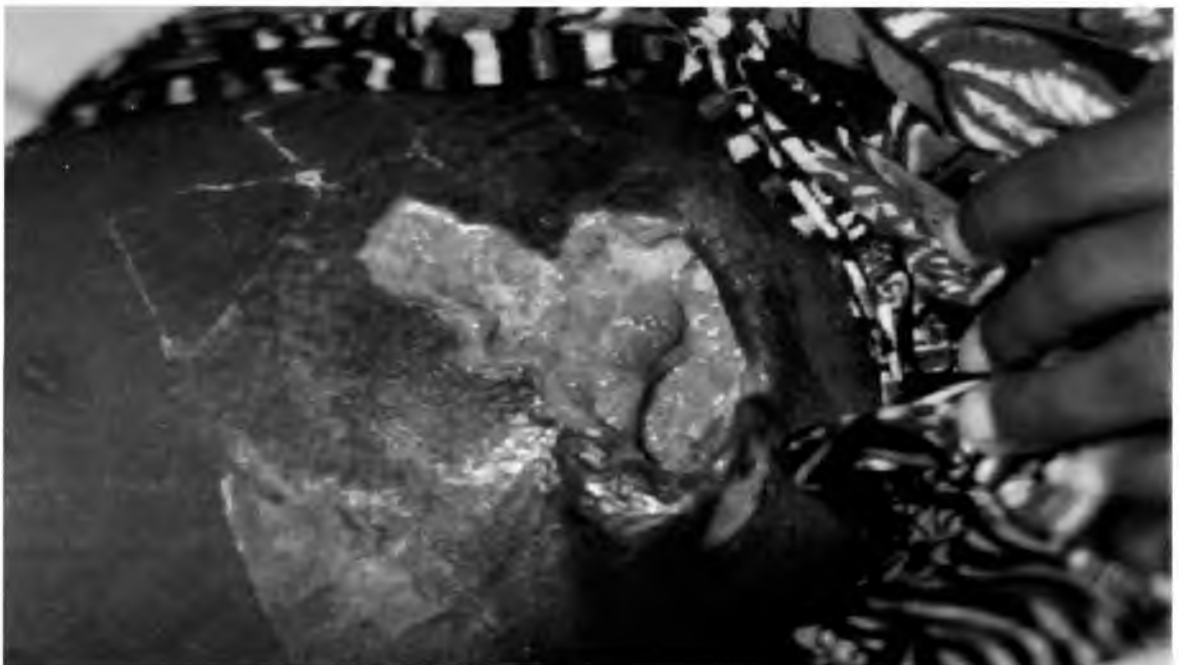


Table 1: Differential Diagnosis of Cutaneous Anthrax

Disease	Causative organism
Ecthyma gangrenosum	<i>Pseudomonas aeruginosa</i>
Rat bite fever	<i>Streptobacillus moniliformis</i>
Ulceroglandular tularaemia	<i>Francisella tularensis</i>
Plague	<i>Yersinia pestis</i>
Rickettsial pox	<i>Rickettsia akari</i>
Scrub typhus	<i>Rickettsia tsutsugamushi</i>
Tick bite fever	<i>Rickettsia conorii</i> and <i>africae</i> (Figures 5&6)
Orf	<i>Parapoxvirus</i> (Figure 7)
Staphylococcal infection	<i>Staphylococcus aureus</i>
Cutaneous TB	<i>Mycobacterium tuberculosis</i>
Leprosy	<i>Mycobacterium leprae</i>
Buruli ulcer	<i>Mycobacterium ulcerans</i>
Spider bite	<i>Loxosceles reclusa</i> ¹⁹

Pulmonary anthrax

Pulmonary anthrax occurs as a result of the inhalation of spore-laden dust. The incubation period is 1-6 days. Prior to the 1960s in the USA, workers in goat hair mills were exposed to high concentrations of viable spores but there were few cases of inhalational anthrax. However when dispersed in the air as an aerosol anthrax spores can present a real hazard even long distances downwind, as demonstrated by the Sverdlovsk outbreak in 1979. Modal incubation is 10 days, but in the Sverdlovsk outbreak some cases occurred up to 6 weeks after accidental discharge. Longer incubation times probably occur with smaller inocula. During the first few days patients have no symptoms or 'flu' for a few days and then there is abrupt onset of chills, a strident cough, blood stained vomit due to haematogenous spread to the gut, dyspnoea and cyanosis, and on examination moist chest sounds and signs of systemic collapse. The spleen and axillary lymph nodes may be enlarged. A chest X-ray may show widened mediastinum, and



Figure 5. Tick typhus lesion in visitor to Tenerife (*Rickettsia conorii*)

blood culture becomes positive within 2-3 days of the onset of symptoms (sample chest X-rays can be downloaded from the CDC website). Death usually occurs in 2-3 days but milder cases occur with bronchitic symptoms.

Anthrax meningitis

This is rare, but may arise from any form of the disease. It is characterised by blood stained CSF and the prognosis is poor. A few cases of recovery have been recorded if antibiotics are combined with anti-toxin and prednisolone.

Laboratory diagnosis

This is usually by microscopy and culture. In cutaneous lesions gentle sampling is recommended with a moist sterile applicator. Blood cultures become positive in 6-24 hours¹², but may be negative if antibiotics have been given. The earliest that confirmation could be expected would be 48 hours but if a laboratory has not been notified about the possibility of anthrax the diagnosis may be missed¹². In gastrointestinal or pulmonary anthrax death often precedes accurate diagnosis. Dry nasal swabs allow detection of anthrax spores. Serological tests are not usually helpful. Anthrax ELISAs only rise in 70-90% of convalescent patients¹. PCR is available in only a few centres.



Figure 6. Tick typhus lesion in visitor to Kruger Game reserve (Rickettsia africae)



Figure 7. Orf virus infection (Dr Clifford Leen's patient)

Treatment for wild type anthrax

Anthrax is sensitive to penicillins, fluoroquinolones, tetracyclines, chloramphenicol, gentamycin, erythromycin, clindamycin, vancomycin and first generation cephalosporins. Isolates of natural strains are rarely resistant to penicillin, although resistance has been reported in India¹. There is some natural resistance to cotrimoxazole, second generation cephalosporins and aztreonam.

Varying advice is given for acutely ill cases in current textbooks, but initially benzyl penicillin should be given in a dose of 2.4 G 4-6 hourly, initially iv for three to five days. Cutaneous sores become sterile in one to two days. Plasma-phoresed serum from a vaccinated person 'may be lifesaving'³.

Treatment of anthrax bio-terrorism

The Russians are reported to have bio-engineered an anthrax strain resistant to tetracyclines and penicillin¹, but there is, as yet, no evidence of engineered quinolone resistance. The concerns already mentioned of delayed germination of spores carried after exposure to the primary aerosol means that short courses of antibiotic

may be insufficient. Initial treatment is ciprofloxacin 400mg iv 12 hourly, although in sensitive strains optimal treatment is with benzyl penicillin as above iv. The antibiotic may be administered orally when the patient's clinical condition improves. The total duration of therapy should be 60 days.

Supportive therapy if oedema is extensive may include corticosteroids. Other general measures include the prevention of septic shock and maintenance of fluid and electrolyte balance.

Anthrax post-exposure prophylaxis

The agent of choice is ciprofloxacin 500mg twice daily for 60 days. Alternatives are doxycycline 100mg twice daily for 60 days or amoxycillin 500mg three times daily for 60 days. Hart and Beeching have cautioned that such prophylactic treatment should be given only to those who really need it, since ciprofloxacin in prolonged courses may induce resistance in commensal organisms, and these in turn may transmit resistance to pathogenic organisms¹.

Vaccination

An anthrax vaccine consisting of an attenuated strain has been given to members of the US armed forces since 1998. Six injections are given over 18 months, the first three in the first month and aerosol challenge studies in monkeys suggest complete protection at 8 weeks and 88% protection at 100 weeks^{Swartz}. No serious adverse events have been reported but vaccine supplies are extremely limited. In the UK advice on the use of the vaccine must be obtained from the Public Health Laboratory Service¹⁴.

Web-site sources of information

www.phls.co.uk/advice/anthrax_guidelines

www.bt.cdc.gov/DocumentsApp/anthrax

www.travax.scot.nhs.uk

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266th Session - Society Events

04/10/02	FRESHERS' ADDRESS Dr Gordon Findlater	03/12/02	CLINICAL GOVERNANCE AND AUDIT Dr Dermot McKeown
11/10/02	INAUGURAL ADDRESS Mr John Rainey	10/12/02	MULLED WINE & MINCE PIES
15/10/02	A DAY IN THE LIFE OF A PRO- FESSOR OF SURGERY Professor O. J. Garden	14/01/03	GERIATRIC MEDICINE Dr Colin Currie
22/10/02	ANNUAL QUIZ Sponsored by the Medical Protection Society	21/01/03	BURNS' SUPPER
29/10/02	To be arranged	22/01/03	GLASGOW HOMEOPATHIC HOSPITAL Dr David Reilly
05/11/02	RECENT ADVANCES IN PSY- CHIATRY Professor Eve Johnstone OBE	28/01/03	SURGICAL ONCOLOGY Professor Fearon (Followed by LASERQUEST)
09/11/02	PRESIDENTS' ANNUAL DINNER At the Royal College of Surgeons of Edinburgh	04/02/03	GENERAL PRACTICE Dr Mike Waters
12/11/02	To be arranged	11/02/03	SURGERY TUTORIAL Mr Simon Paterson-Brown
19/11/02	GENETICS TUTORIAL Dr Fitzpatrick (Followed by GHOST TOUR)	18/02/03	CARDIOLOGY TUTORIAL Dr Andy Flapan
26/11/02	A DAY IN THE LIFE OF A PA- THOLOGIST Dr Basil Purdue	25/02/03	HISTORY OF THE RMS Mr Owen Dudley Edwards
		04/03/03	ANATOMY TUTORIAL Dr Gordon Findlater Summer term - to be arranged



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Bridge Problem

Ben Carrick

In the second of this series I thought it would be good to look at counting again and to cover another important area of the game: communication and how to break down your opponents' communication!

You are South, playing with;

♠ -
♥ K J 10 8 6 5 4 3
♦ 7
♣ A 9 7 3

Given this hand you open bidding strongly in hearts, and bidding ends with a contract of 5 Hearts. A difficult contract to make, but possible nonetheless...

West leads 4♣.

Q1. What can you now say about West's hand and what assumptions can you make about clubs around the table?

Dummy is revealed to have:

♠ K 9 6 2
♥ Q 2
♦ Q J 8 4
♣ Q 8 5

You play low, East plays a 10, forcing you to play the Ace. In the next hand you play 3♥, West plays 7♥, you play the Queen from North and East plays 6♦.

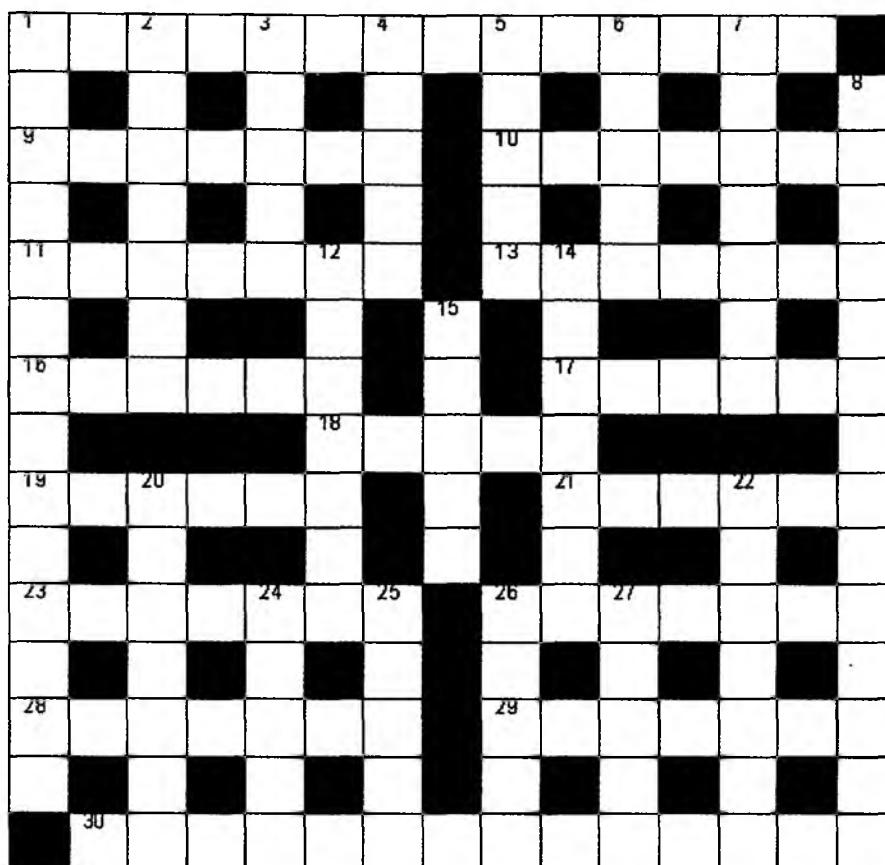
Q2. What can you now say about the hands?

Classically the next move would be to continue to deplete the trumps in play.

Q3. What is the danger in the classic move?

Answers can be found on page 28

Cryptic Crossword



CLUES

ACROSS

1. Hot wheels of the Gods, or a British film? (8,2,4)
9. Small lumps number fifty in taxes (7)
10. Shredded fuss in windy weather (7)
11. Man sees riot in a crowd (2,5)
13. Doubter can pick set apart (7)
16. Number is object I catch before start of year (6)
17. Currency between objects is worth a brain cell (6)
18. Passing on colouring without direction (5)
19. Oracle in distress - I'd help (6)
21. Lots return in party to generate power (6)
23. Advertisement - choose the queen to look after it (7)
26. Morning containing a thousand organisms makes alloy of mercury (7)
28. Chases? They're not important (7)
29. She was 100, confused and nuts (7)
30. I sit on prefects rage: not good enough for them? (14)

DOWN

1. One involved, like the Tories? (9,5)
2. In Saab, do mention the belly (7)
3. Here is the French archipelago (5)
4. Gallery holding second with flavour (5)
5. A host makes us swear (5)
6. Curve in iron - this is ridiculous! (5)
7. Concerning thespian who's gone nuclear (7)
8. Doctor confronts Simon - they don't fit in (14)
12. Under a blue one, take the plunge (with parachute) (7)
14. He rules, dominating this area (7)
15. I bail out to provide cover (5)
20. Age, in sicknote, is like a lion (7)
22. Legs ran around to catch fish (7)
24. If the contents are rumbled, it will be by him (5)
25. Antique found in barrel, iced-up (5)
26. CIA is perplexed over computer code (5)
27. Scrambled sonar shows fire (5)

For answers, see page 28

J. J. C. Cormack LVO, MD, FRCGP, FRCPEd 1934-2002

Socius Librorum Custos



When the history of the Royal Medical Society in the second half of the twentieth century comes to be written, a name which is certain to feature prominently in it will be that of Jack Cormack, whose death on 7 July 2002 is a most grievous loss not just to the Society but to the entire Edinburgh medical community. There was never a more faithful champion of the Society's highest ideals and it was this which inspired his incomparable service to it in many different capacities.

John James Callender Cormack, the son and grandson of well known and highly respected general practitioners was born in Edinburgh in 1934 and educated in his native city at the Edinburgh Academy and at Edinburgh University from which he graduated MB.ChB in 1959. As a proud and loyal Academician he was honoured and delighted at a later stage in his career to serve for 18 years on his old school's Court of Directors, to the affairs of which he made a notable contribution.

He joined the Society at the beginning of its 219th session and from the very first was a highly active member who rapidly developed an enthu-

siastic reverence for its history and traditions and a very special interest in its remarkable library. At an early stage he was appointed to the Library Committee of which in 1958-59 he became a most energetic and efficient Chairman and this responsibility stimulated him to investigate in detail the library's history. The result of these studies was the scholarly dissertation entitled simply "The Society's Library" read to the Society on 28th February 1958 for which he was awarded the Fellowship. This is not only a fascinating and highly readable account of the development of a most extraordinary collection of books but also an authoritative reference document.

After holding resident posts in Edinburgh, Jack spent two years working overseas first with the Grenfell Mission in Labrador and then in the Mission Hospital Mlanje Nyasaland (Malawi). He returned to Edinburgh in 1963 and joined his father in the Corstorphine practice which had been founded by his grandfather 38 years previously. Over the next three and a half decades this expanded progressively and at his retirement in 2000 Jack was the senior partner of a large, efficient and very highly regarded group practice.

Despite having professional commitments Jack maintained close contact with the Society and continued to be involved with the Library. The sale of the greater part of it to raise funds for the rehousing of the Society caused him no little distress but he accepted that there was no practical alternative and willingly gave expert advice on the selection of those volumes of special interest which were retained by the Society.

When the R.M.S. Trust was established in 1980 he was invited to become a Trustee and to take on the duties of Joint Trust Treasurer. It would be impossible to exaggerate the value of his services in these capacities over the next 22 years and many Senior Presidents and other office-bearers owe him a substantial debt of gratitude for the wise counsel and sound practical advice which he gave both graciously and unobtrusively.

His warm rapport with the Permanent Secretary Mrs Pat Strong ("A.P.") was immensely beneficial to the Society in all sorts of ways. Her death in 2001 affected him deeply and the very moving address which he delivered at her funeral was a truly heartfelt tribute which will be long remembered by all who heard it.

In 1985 a Steering Committee was formed to plan the celebration of the Society's 250th Anniversary and Jack undertook its Chairmanship with the utmost pride and pleasure. A year later he was appointed Vice-Chairman of the 250th Anniversary Appeal and the success of this and of the commemorative celebrations was in no small part due to his energy and enthusiasm.

Jack's higher qualifications bear eloquent testimony to his professional distinction but the ultimate accolade came in 1992 with his appoint-

ment as Apothecary to H.M. Household at the Palace of Holyroodhouse. Following his retirement this and other outstanding services were recognised by the award of the Royal Victorian Order with the rank of Lieutenant (L.V.O.).

Jack was a man of many parts and a list of the non-medical activities to which he made his own distinctive contribution would fill many columns. He was highly articulate with total clarity of thought and an unfailing ability to focus upon the essentials of any problem which made him a Key member of the many committees, both lay and professional, on which he served. These additional duties were invariably discharged punctually and efficiently in a straightforward self-effacing manner.

Throughout his life Jack never deviated from a personal code of conduct based solidly upon courtesy, consideration for others, and firm religious convictions but solemnity and austerity were foreign to his nature. He greatly enjoyed convivial gatherings, not least those organised by the Society and was a polished and entertaining after-dinner speaker. His splendidly dramatic rendering of "Tam o'Shanter" was an absolute tour-de-force which by itself could guarantee the success of any Burns Supper and the Society had the pleasure and privilege of hearing this on many occasions.

Jack Cormack's warm out-going personality, his easy gracious manner, his strength of character, his kindness and his compassion endeared him to his patients and his host of friends from all walks of life, who are united in mourning his untimely death. No member of our Society has served it more diligently or enthusiastically and we salute his memory.

Mr Iain MacLaren FRCS

Terrorism – a health sector response

Gillian Reeve, Deputy Director, Medact

Terrorism and war are and always have been public health issues. Health professionals are in a unique position to act on this, being able to take a public health perspective on such issues.

An open letter signed by the presidents of six of the Royal Colleges - 'health professions on the aftermath of terrorism' - was published in the key health press. It expressed concern 'that all responses should take account of the magnitude and complexity of the problem of combatting terrorism of all kinds and its causes. By virtue of their skills and experience, health professionals should take part in formulating appropriate responses to humanitarian needs in this crisis taking into account lessons learned from the past. In the longer term, building local capacity in the health care systems of affected populations will be an important contribution.'

They ended by urging that, in the longer term 'in formulating foreign policy, governments should assess the effects of their proposed actions on the health and human rights of their own people and those likely to be affected in the wider world.'

The plight of the citizens of Afghanistan, who face a humanitarian crisis of major proportions, has drawn much attention. Prior to the recent military action after three years of severe drought, 5.5 million people were partially or fully dependent on food aid for survival. As winter drew on and lawlessness increased after the departure of the Taliban, the provision of food aid and medicines became ever more urgent. The health system of Afghanistan had virtually collapsed. About 40 percent of immediate needs for medical supplies were being met by aid agencies. The UN predicted dire consequences for health, expecting outbreaks of dysentery, cholera, measles epidemics and increased maternal and perinatal deaths. As ever, women, children and the elderly were particularly vulnerable. The WHO had also warned of a large scale mental health crisis in Afghanistan which was as urgent as physical health problems.

For decades the health status of the Afghan population has been known to be one of the poorest in the world with amongst the highest maternal, infant and under-five mortality globally. The optimistic view would be that the recent conflict will have restored some sort of stability, enabling a concerted effort to reconstruct the country and its institutions. One of the key priorities must be to rebuild a health system capable of meeting the health needs of Afghanistan and its people. The people of course will take the lead in determining what kind of health system will best fulfil those needs. External assistance in terms of funds, expertise, and possibly temporary personnel will be available to support this process.

Health professionals can be involved in a number of ways. These include:

- Looking closely at the causes of terrorism - the ongoing cycle of violence caused by infringement of human rights in the areas of health, education, land and housing. Fundamental problems of injustice and inequality beset many of the poor countries of the world. Availability of resources to relieve poverty and sustain the environment are essential.
- Acknowledging that we live in an interdependent world. Reconnect with the international community in strengthening the UN and maintaining and promoting treaties which increase international confidence and prevent the spread of weapons of mass destruction.

Full information on Medact's work on all these issues can be found on our website www.medact.org or by contacting Medact at 601 Holloway Road, London N19 4DJ, telephone 020 7272 2020, email info@medact.org.

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Saturday 9th November
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Black Tie

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Bridge Problem Solution

A1.

West ideally wants to be able to use hearts to trump in clubs rather than be forced to discard – hence the play of a singleton. Since 5 clubs are accounted for 8 remain and you would assume, on roughly 2:1 odds that they are divided equally, 4 in each of North and East’s hands. However, since you can now see your dummy’s hand you can conclude that this is not the case!

A2.

The opponents have communicated very effectively – but not very secretly. All players now know that West has no Clubs left and East has no Hearts, not a common hand, but the one we have to play! Trumps first; 11 are accounted for, East has none, so West must have the remaining 2. Because West has no clubs left (meaning that he can trump in that hand) the remaining 4 must be in East. Since East discarded in Diamonds you can presume he has a longer suit there, rather than a 4:4 split of his 8 remaining cards between Spades and Diamonds; he may have had a 3 Spade: 5 Diamond hand. This is important because the remaining cards will be in West, leaving him a 6 Spade: 3 Diamond hand.

A3.

Ideally, defence will consist of playing from one hand to the next to take the requisite 3 tricks to defeat, which they can easily do with the missing 3 Aces. By playing a heart next, the obvious move is to counter with an Ace from West and to move into Diamonds, to play back to East, who would return in Clubs, allowing West to ruff.

A better response would be to play in Spades and cut off their communication (also called the “coup without a name”) by playing K♠ from North and discarding the singleton 7♦ from South. Whilst this trick would be lost to West’s Ace♠, West would then be unable to lead to East with a Diamond because South would ruff. The contract could then be made!

Crossword solution

C	H	A	R	I	O	T	S	O	F	F	I	R	E	
O		B		S		A		A		A		E		N
N	O	D	U	L	E	S		T	O	R	N	A	D	O
C		O		E		T		H		C		C		N
E	N	M	A	S	S	E		S	K	E	P	T	I	C
R		E			K		A		I			O		O
N	I	N	E	T	Y		L		N	E	U	R	O	N
E					D	Y	I	N	G					F
D	E	L	P	H	I		B		D	Y	N	A	M	O
P		E			V		I		O			N		R
A	D	O	P	T	E	R		A	M	A	L	G	A	M
R		N		H		E		S		R		L		I
T	R	I	V	I	A	L		C	A	S	H	E	W	S
Y		N		E		I		I		O		R		T
	P	E	R	F	E	C	T	I	O	N	I	S	T	S

Think maggots!

Larkspur - (l. 'Erks, at) [L. LARK sb1 + SPUR] *Bot.* Any plant of the genus *Delphinium*; so called from the spur-shaped calyx. The common larkspur is *D. consolida*.

LarvE - (l. 'Ervi) *n.* sterile maggots of *Lucilia sericata* recommended for the rapid and cost effective debridement of Diabetic Foot ulcers and other soft tissue injuries; proven to eliminate infection including those caused by MRSA; suitable for both Primary and Secondary healthcare sectors; widely used throughout the UK
LarvE *v.* To cleanse wound quickly

Larynx - (l. 'Eri, ks) A cavity in the throat with cartilaginous walls, containing the vocal cords, by means of which sounds are produced. In man and most of the higher animals this cavity forms the upper part of the trachea or wind-pipe. In birds there are two larynxes, one at each end of the trachea, the lower one, called the syrinx, is the true organ of sound.

Think

LarvE

Produced by The New York Times

For further information please contact: Biosurgical Research Unit on 01656 752820
or e-mail on maggots@smtl.co.uk



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