7. VHF in the Context of Bioterrorism

7.1 INTRODUCTION
Long before the terrorist attacks in New York and Washington on September 11th, 2001, and the subsequent mailing of milled anthrax spores in the United States, VHF had been recognised as potential biological weapons. The deliberate release of such agents may be overt, for example prior warning may have been given, or an explosive device may have been used. Alternatively a release may be covert, in which case the release will not be apparent until the first cases are identified.

It seems unlikely that Ireland would be a primary target for the release of such agents, but victims of exposure could travel to Ireland during the incubation period of these diseases.

Several VHFs have been weaponised by the former Soviet Union, Russia and the United States, while there are reports that North Korea may have weaponised yellow fever. Until 1992, the former Soviet Union and Russia produced large quantities of Marburg, Ebola, Lassa, Junin and Machupo viruses. Soviets researchers showed that only a few virions of Marburg virus and a small dose of Ebola in aerosol preparations caused lethal infections in monkeys. Many studies revealed Ebola, Marburg, Lassa and Junin viruses could produce lethal infections in non-human primates when administered by aerosol. The US weaponised yellow fever and Rift Valley fever viruses but the program under which they were developed ended in 1969. A Japanese terrorist cult, Aum Shinrikyo, was unsuccessful in their attempts to obtain Ebola virus as part of an effort to create biological weapons.

7.2 WHICH VHFS?
Amongst the agents that have been identified by the Centers for Disease Control and Prevention (CDC) as being Category A agents (those most likely to have greatest impact) are VHF viruses. The Working Group in Civilian Biodefense in the USA developed a list of key characteristics of biological agents that have the potential to pose serious risks if used as biological weapons against civilian populations:

1. high morbidity and mortality;
2. potential for person-to-person transmission;
3. low infective dose and highly infectious by aerosol dissemination, with a commensurate ability to cause large outbreaks;
4. effective vaccine unavailable or available only in limited supply;
5. potential to cause public and health care worker anxiety;
6. availability of pathogen or toxin;
7. feasibility of large-scale productions;
8. environmental stability;
9. prior research and development as a biological weapon.

A number of VHFs exhibit a significant number of these key characteristics and therefore, pose a serious risk as biological weapons. These include Ebola and Marburg viruses, Lassa fever and New World arenaviruses, Rift Valley fever and yellow fever, Omsk haemorrhagic fever and Kyasanur Forest disease.

VHFs that are not classified a posing a serious risk include Dengue, Crimean-Congo haemorrhagic fever and Hanta virus. Dengue is not transmissible by small-particle aerosol and primary dengue only rarely causes VHF. For these reasons, dengue is excluded. Crimean-Congo haemorrhagic fever and Hanta virus do not appear in the above list either as the technical difficulties of large-scale production currently prevents their development as mass casualty weapons. Specifically, CCHF and Hanta virus do not readily replicate to high concentrations in cell cultures, a prerequisite for weaponisation.

7.3 OUTBREAKS/CASES DUE TO DELIBERATE RELEASE
Three scenarios are outlined in the guidance Biological threats: A health response for Ireland, Expert Committee – Contingency Planning for Biological Threats produced by the Department of Health and Children in 2002:

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Health professionals have a crucial role to play in the identification of covert releases of biological agents. A high index of suspicion will be necessary for the early recognition of such covert releases. Emergency physicians, GPs or other clinicians may become aware of:

- unusual presentations of illness;
- a cluster of cases with similar symptoms;
- a syndrome suggestive of bioterrorism.

Initially, it may not be possible to differentiate between intentional and naturally occurring outbreaks. Clinical manifestations of VHF are non-specific at first which may result in a delay in diagnosis. Other reasons for delayed diagnosis include clinician’s unfamiliarity with these diseases, heterogeneous clinical presentation within an infected cohort, and lack of widely available diagnostic tests.

However, the presentation of illness due to deliberate release of infectious agents may be more sudden, more severe and involve larger numbers than is characteristic in a natural outbreak, particularly if the agent has been aerosolised. Another key difference will be the lack of usual risk factors associated with VHFs, in particular a history of travel to endemic areas in the last 21 days before onset of symptoms.

Patients may also present in Ireland having arrived from a country which was the target of a deliberate release, rather than from recognised endemic areas. The confirmed release of VHFs as agents of bioterrorism in other countries must lead clinicians to have a high index of suspicion when patients present with symptoms of VHF. Note that in the UK, guidance states that a single confirmed case in the UK, even from an endemic area, should be investigated to exclude deliberate release.

7.4 Key Medical and Public Health Interventions after Identification of a Suspected Index Case of VHF

An Garda Síochána (AGS) is the lead agency in responding to deliberate release of VHFs or any other malign chemical, biological, radiological or nuclear incident. The HSE will have a supporting role along with Local Authorities and other appropriate agencies as required.

All cases of suspected deliberate release of VHFs should be reported immediately to the DPH/MOH who will notify AGS. Once AGS have been notified of an incident they will conduct a threat analysis. If the risk is not discounted the Framework for Major Emergency Management will be activated, including actions for the HSE.

The guidance on infection control, laboratory testing and public health action as outlined elsewhere in this document would apply. In addition to the recommendations on the use of Ribavirin in the management of clinically evident cases of VHFs, a proposed dosage routine for use in the improbable event of a mass casualty setting is given below.

In situations where VHFs are released deliberately in this country then the identification of cases will need to include the additional epidemiological questions:

- Were you in RELEASE SITE on RELEASE DATE from TIME PERIOD to TIME PERIOD?
- In last 21 days, have you had close contact with a person who was present at RELEASE SITE on RELEASE DATE from TIME PERIOD to TIME PERIOD?

In addition, contact tracing should include all individuals present at the site at the time of release or in the period after the release and before access to the release site was prohibited.

In situations where VHFs are released deliberately in another country then the identification of cases will need to include the additional epidemiological questions:

- In last 21 days, have you returned from a country which has been the target of a deliberate release of VHF?
- In last 21 days, have you had close contact with a person who has returned from a country which has been the target of a deliberate release of VHF?
7.5 RECOMMENDATIONS FOR RIBAVIRIN THERAPY IN PATIENTS WITH CLINICALLY EVIDENT VHF OF UNKNOWN AETIOLOGY OR SECONDARY TO ARENAVIRUSES OR BUNYAVIRUSES

Treatment with Ribavirin should be initiated pending diagnostic confirmation. The dosage should be decided in consultation with the hospital pharmacy. In the case of pregnant women, the decision to prescribe Ribavirin should be based on individual clinical risk-benefit assessments. See table 14 for Ribavirin dosage in cases of bioterrorism.

If infection with an arenavirus or bunyavirus is confirmed, continue the 10 day course. If infection with filovirus or flavivirus is confirmed, or if the diagnosis of VHF is excluded or an alternative diagnosis is established, discontinue Ribavirin.

Table 14. Ribavirin dosage in cases of bioterrorism

<table>
<thead>
<tr>
<th>Contained casualty setting</th>
<th>Adults</th>
<th>Pregnant women</th>
<th>Children</th>
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<tr>
<td>Adults</td>
<td>See <a href="#">Chapter 2, page 21</a></td>
<td>Same as for adults after individual clinical risk-benefit assessment.</td>
<td>Same as for adults, dosed according to weight.</td>
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References


14. Leroy EM, Kumulungui B; Pourrot X; Rouquet P; Hassanin A; Yaba P; Delicit A; Pawska JT; Gonzalez; Swanepoel R. Fruit bats as reservoirs of Ebola virus. Nature 2005;438: 575-576


48. Centres for Disease Control and Prevention. *Interim Guidance for Managing Patients with Suspected Viral Hemorrhagic Fever in U.S. Hospitals*. CDC; May, 2005


