

Distinguishing between natural and unnatural outbreaks of animal diseases

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Summary

An intentional outbreak of disease among livestock, or agricultural crops, will share a number of characteristics with those aimed at humans – unexpected pattern of disease in season or place, possible explosive incidence, unusual pathogen either in itself or of its genetic structure, difficult diagnosis – but there will also be notable differences: human cases, if they occur, will be coincidental and the major impacts will be delayed and of severe economic consequence. An investigative and analytical protocol is proposed for identifying such an event. Unless the nature of the event is self-declaring, such investigations necessitate a very thorough and careful investigation by a dedicated and experienced epidemiologic team. At the same time a country should take steps in advance of such an event to be prepared and to save time later, such as determining possible targets, identifying early warning indicators, establishing molecular biologic expertise and reference collections of possible pathogens, and preparing a tactical and forensic response.

Keywords

Agent weaponisation – Diagnosis – Economic cost – Molecular strain – Publicity – Target.

Introduction

This title may be better reworded as ‘What is a suspicious (agricultural) incident?’ Such a question by itself indicates that the cause of most such events is expected to be not immediately obvious.

Firstly, such agricultural incidents will differ significantly from intentional events that primarily target human beings, as follows:

- any human deaths will at worst be coincidental, even where zoonoses are concerned
- any agricultural impact may be delayed significantly and only become obvious after weeks or even months
- the major losses follow from the disease and are not directly of the disease itself, which in comparison may be relatively trivial.

An effective ‘attack’ does not necessitate massive death and destruction, quite the reverse. It is the necessary responses

to agricultural disease, to contain and clean up, to prevent further spread, and then to reclaim the previous level of disease control or freedom, lost exports, and international recognition that eat up effort and funding. There is a very different time scale and series of available tools for attacks involving animals than there are for those involving public health and human bioterrorism/biological weapons (BT/BW). The desired results from an agricultural BT/BW attack are much more complicated than the simple widespread terror induced in a human target population.

A unique and necessary characteristic of a purposeful unnatural event is that it must follow strategic objectives. By definition they cannot happen by accident – the only accident that can happen is an ‘own-goal’ or an unplanned release from a covert facility, and even these latter ‘accidents’ reflect an intended later purpose, as yet maybe unknown to the investigators. Without a strategy, without a purpose, there is no reason to have mounted such an attack.

A normal livestock disease outbreak is not without alarm and major concerns – local, national, and international –

and these fears can be manipulated if blame for such an event, real or imagined, is stage-managed to be laid at another's door. Disinformation on a perfectly normal outbreak – much less one that has been contrived – could be so structured as to be persuasive and withstand nominal investigation. The reality is surely that there will be more disinformation disseminated than actual agricultural BT/BW attacks mounted.

However, a suspicious agricultural BT/BW incident may have many of the characteristics listed below, though some may take some time to become apparent.

Characteristics of a suspicious incident

Characteristics that would be indicative of a suspicious event are as follows:

- a) unusual time and/or place, i.e. at extremes of a normal geographical or seasonal distribution for the disease, and/or
- b) in an unusual population subset, age group, or unexpected location(s), and/or
- c) explosive start, and/or
- d) atypical clinical presentation, and/or
- e) 'missed' cases and difficult diagnostics, and/or
- f) marked reversal of an otherwise steady progress in disease control or freedom, and/or
- g) epidemiologically 'weird' event; it in no way matches normal experience or knowledge, and/or
- h) unexpected strain of agent or multiple strains, or features indicating deliberate genetic manipulation, and/or
- i) location in the vicinity of a military or suspect facility.

Characteristics that would be conclusive proof of a deliberate attack would be:

- a) exotic disease agent without prior epidemiological trail, and/or
- b) evidence of weaponisation, identification as a biological warfare agent, and/or
- c) proof of release by a biological weapon.

Characteristic consequences of a deliberate attack

A deliberate attack would be likely to have the following consequences:

- a) marked economic or political costs with benefits, possibly singular, to a competitor, and/or

b) removal of target country/industry from international trade, and/or

c) target country must continue imports from competitor, and/or

d) marked social unrest, maybe with the movement of a significant part of the population as a result of losing their livestock or crops.

Additional factors

A suspicious agricultural BT/BW event would probably be characterised by most of the above factors, but there are additional factors that would add further weight to the theory that an event had been caused deliberately, for example:

- a) diagnosis in unusual circumstances
- b) publicity that is premature or from obscure source(s)
- c) coded claim(s) of authorship
- d) echoes of previous or subsequent events.

These factors will be discussed in greater detail later in this paper. It should be kept in mind that it is hard to envisage any circumstances in which a country or commercial company would publicly claim or admit to having been involved in active BT against another. The public and global opprobrium would be damning.

Intentional attacks, whether on humans or agriculture, have the potential to raise public alarm. In the case of an agricultural attack this alarm (which plays to terrorist intentions) stems from the threat to food safety and exports. There is always the concern that the perpetrator(s) may not have thought an attack through and just tried something because of the hype and the potential for making a 'big' statement. But public widespread alarm and government over-reaction are potential results from both normal and intentional events.

Monitoring suspicious activity and preparing response plans

There is a need to have done one's 'homework' well before any incident occurs, both to give a frame of reference and provide a body of updatable knowledge, but also to save time when it happens. If and when such a suspicious incident should occur there is certain to be some institutional panic and reactive demands that 'something must be done'. Maybe not. But when a decision is made to follow up such an incident the response should move with deliberate speed.

Target pre-identification

The first step in preparing for a possible attack is to identify possible targets, by:

- a) defining the hypothetical 'goals' of potential attackers
- b) identifying their probable objectives and ranking them
- c) prioritising critical target-countries and industries
- d) following up with preparatory collection of data and confirmation of the existence of a minimal administrative/organisational infrastructure within each target-country or industry; identifying liaison persons/local guides in case of need
- e) ensuring that reference databases of strain characteristics already exist and are readily accessible – there is no point in having to do these comparison analyses on top of the urgent field samples.

Early warning indicators

In addition to normal intelligence awareness activities it is important to develop warning systems that can detect the signs that an attack may be about to happen, signs such as:

- 'own-goals': telltale accidents within a notional 'attacker' country or commercial company (maybe in relation to known institutes) or outside the country and well away from target crops or livestock
- unexpected minor events among sentinel or 'canary' animals/flocks; unsuccessful attacks with only a few cases; discovery of deployed pathogens but without clinical cases ('hang-fires')
- 'practice' events: while these 'events' may be normal outbreaks and probably are, they are not necessarily subject to detailed investigation and so their cause may be in doubt. A pattern of events might – not may – indicate that someone is getting the kinks out of a system
- travellers at airports found with pathogenic cultures, with or without adequate explanations.

National Veterinary Services should go on stand-by-alert if any of the above events are reported.

Prepared response

An appropriate game plan(s) should be agreed and ready before it is needed. The plan should be designed to:

- limit response to investigating initial events and the identification of first isolates, so that the investigators do not get in the way of the normal Veterinary Service response teams

- get people into the field quickly to collect and archive information and samples, with initial processing of samples in the field

- ensure that field workers can maintain a strict, fully documented audit trail on all materials collected, whether or not analysed, in case of the need for later recommendations or forensic investigations.

Investigating suspicious outbreaks

One must always be aware that BT/BW events will be rare and therefore any suspicious incident is most likely to have a normal if not prosaic explanation whatever the initial impression or belief. Similarly, the implications of a proven attack are so far reaching that any investigation resulting in such a conclusion must be so thorough as to survive the most rigorous of examinations. Therefore, unless the circumstances are blatantly those of an obvious BT/BW event – the biological equivalent of the recent twin-towers air crash, for example, ten widely separated cases of rinderpest across the United States of America (USA) within one week – the primary investigative position is that the situation was normal and, if unexpected, merely unusual. Thus 'rule one': look for a normal explanation. And 'rule two': try harder to find a normal explanation. Only if that fails does 'rule three' apply: 'round up the usual suspects'.

Clinical presentation

One of the very first steps in every epidemiological investigation is to confirm the diagnosis. Though most natural and possibly unnatural events will involve the same pathogens or near relatives that are well documented and that present in an almost textbook manner, some initial cases may be different. This may be clinically demonstrated by various indicators, as follows:

- a shorter than expected incubation period of many cases, not just the first of a normal Gaussian distribution
- an unexpected disease presentation, e.g. pneumonic plague in the absence of bubonic cases
- a confused symptomatology, e.g. though one agent is recovered or presumed there are lesions indicative of another pathogen
- the appearance of an increased virulence and a poor response to normally successful treatments, e.g. an increased case fatality rate
- significant numbers of cases in a population, whether human or livestock, which should have a high level of immunity

– a difficulty in getting confirmed laboratory diagnoses in cases patently and intimately co-associated with the initial outbreak or outbreaks. At the same time, inexperience in the proper collection and shipping of diagnostic samples can reduce even the best laboratory to uselessness and initiate loud agency-saving claims that everything was done correctly but nothing was found, with variations on which end is pointing the finger at the other, and therefore any failures are due to the agent. Subsequent tests will reveal the truth.

Epidemiological investigation

Based on informed epidemiological experience, literature, and databases, 99 out of 100 such outbreaks will be normal events and fully explicable from existing knowledge. Events at the extremes of normal probabilities are by their nature infrequent but not *ipso facto* abnormal. An event having a low probability of being a deliberate attack will only be regarded as such when matched or unmatched with other events. ‘Experience’ may indicate that certain infrequent events are commonly associated with a specific set of circumstances and these may be missing in a contrived and not-normal outbreak. Therefore, the events leading up to the ‘incident’ must be carefully analysed by experienced investigators. This should include examining evidence for prior outbreaks or infections indicative of an unrealised endemic or sporadic situation. This must be differentiated from the sudden appearance of a highly virulent agent and/or an abnormal reduction in the incubation period, possibly in a population with a normally protective level of herd-immunity.

Investigations should also cover commercial, legal and illegal importations of likely fomites (e.g. machinery, used sacks, harnesses), vaccines, vectors, fruits, seed, birds and poultry, eggs, livestock and livestock feed and feed components. It is a distinct advantage to know beforehand the genomic ‘fingerprint’ of all livestock and poultry authorised and unauthorised vaccines in circulation, overtly or covertly, alive or dead. Improper production of a ‘dead’ vaccine can result, and has resulted, in subsequent disease outbreaks.

Another important aspect is to investigate who or what were not apparently affected. The absence of disease can be as informative as the presence. Why was this group spared whilst another was not? The more factors the two groups have in common, the more extraordinary is absence/presence.

With true zoonotic infections it is usual for animals to be affected before humans, either because of reservoirs, vector exposure, or just being cumulatively exposed to higher ID50s/LD50s. For example, Eastern equine encephalitis

equine cases will normally appear some 14 days before any symptomatic human cases are reported. When humans are affected as the apparent primary host, it is worth searching for affected animals to determine whether in fact it is they that are the primary hosts. This can fill cartographic gaps for places where humans are not, e.g. dairy cows and sheep in the countryside and humans in villages, and gaps in time, as animals may be found dead before human cases are reported and are sometimes diagnosed faster in veterinary laboratories. Human botulism normally follows the consumption of contaminated home-made or commercial food products without animal cases, other than household companion animals. Similarly, botulism outbreaks in poultry or livestock come from feeds or forage and will not affect humans. Thus, if there are human cases associated with the latter animals it must be from a common source. Also, the spatial persistence of a biological threat in the soil, water or air will be demonstrated by sporadic illnesses in animals and grazing livestock.

Existing control programmes

When a livestock disease control programme suddenly becomes ineffective, it can raise suspicions of an external cause. One must then carefully and objectively investigate the situation and the existing programme’s surveillance system. The set-back to the programme is probably 100% expectable in hindsight, especially if the outbreak has revealed imbedded defects in the programme design, implementation, reporting cycle and response time, funding, training, or tactical control. Many national disease control programmes work well until they are challenged by a real epidemic; e.g. Taiwan and the recent foot and mouth disease (FMD) epidemic, which appears to have originated in some smuggled viraemic pigs from mainland China and then was probably exacerbated by the new owners selling ill pigs into the market system. Similarly, the present anti-rinderpest campaign in Africa could have a set-back either because of local inefficiencies or because of purposeful interference.

However, a new case in an area well cleared of disease for a number of years and with farmers experienced and knowledgeable of the costs to be incurred if the condition were to be reintroduced should give cause for concern. But farmers greed is not unknown, just as is their ability to be seduced by cheap animals with forged or absent papers. Local knowledge is a significant help in sorting out such scenarios as well as in interviewing the affected farmers.

One should never lose sight of the possibility of unexpected outbreaks following upon the illegal importation of fruit and livestock, which by definition lack the appropriate certificates and health guarantees. These will generally follow a pattern of expectations of those

knowledgeable in fighting these risks – medfly in fruit from Central America, tuberculosis in cattle crossing the Texas-Mexico border, Newcastle disease in smuggled parrots, or other pathogens contained in food being used to hide smuggle drugs. A variation on this is the present flood of bushmeat into Europe from Africa and the potential for it to contain exotic pathogens that pose a risk to humans and might also find their way to garbage-fed pigs. A similar risk is posed by any illegal smuggling of meats. What characterises these events is that there are no external beneficiaries other than those individuals directly involved in the illegal activities.

It is not impossible to conceive of a covert attack by a national Government on a sub-national group within its borders. A giveaway for this would be the intensity, or lack thereof, of the investigation as to the cause or causes. Similarly, a country might oppose such an investigation under international arrangements. Failure to cooperate would probably constitute a violation of the protocol and could be taken as confirming guilt. Therefore, even if the Government was reluctant because of internal problems of sovereignty or of revealing politically sensitive information on internal matters there would be an incentive to at least give the appearance of cooperation (8). This could involve an apparently cooperative Government steering the investigation towards certain information and away from other information; for example, the investigating group being taken unknowingly to wrong locations, different from the location where the attack was initially described as having taken place.

Inexplicable events

These are ‘weird’ events that go far beyond expectations, such as Venezuelan equine encephalitis in northern latitudes; vector-borne diseases in areas without appropriate vectors; normally feed-borne diseases in grazing stock not receiving supplemental feed; outbreaks on isolated farms or ranches, from which for a number of years animals had only been sold, not bought in. Was the spread of outbreaks in line with existing knowledge and/or was it independent of normal commercial/industrial activities, marketing, weather, and/or livestock/crop densities? For example, if the infection is normally wind-borne (e.g. with certain FMD viruses) was the initial disease spread downwind or across the prevailing wind direction; if it is a density-dependent infection, such as bovine brucellosis, was it first noted in one or more small herds with less than ten cows? Was the outbreak in the dry season while the local vectors are all wet-season breeders? Was it associated with a novel vector, even if a pre-existing vector had been well established for many decades?

One of the most fruitful epidemiological investigations is to look at outliers, i.e. cases that occur by themselves well away from the rest. Why? Because in the body of the

epidemic there are many potential modes of spread, but at the margins there can only be very few reasons as to how it got there. Thus, one can identify whether the causative agent has higher survival times or resistance, is transmitted by an uncommon or unusual route, or is the usual epidemiological opportunist.

Similarly, one may be investigating whether clusters of a similar illness in non-contiguous areas or places have a natural explanation. Usually they will. An experienced epidemiologist knows that there are always a few mysteries whose explanation comes, if at all, almost by chance at a later date.

In brief, an inexplicable event is one which does not make epidemiological sense. It is totally outside normal experience or knowledge. Obviously, this might still be a natural outbreak, amply providing a new and unappreciated insight into the disease, and must be investigated in case this is so. Even the ten rinderpest cases, mentioned earlier, might be explainable if it were found to be related to a recent importation of wildebeest from Africa that somehow were cleared from quarantine early and shipped to widely dispersed ‘wildlife’ parks with resident beef cattle or nearby dairy farms.

Genetic evidence

Strain identification

Isolates from the initial outbreaks should be compared rapidly with known isolates in the pathogen archives. The molecular and polymerase chain reaction structure based on standardised techniques should be compared with the library of known markers and sequences. This comparison could produce any number of results on the origin of the isolate, for example:

- with luck and a comprehensive collection, it may exactly match a known strain with a documented origin, e.g. from outbreaks in a distant country or from prior outbreaks in the affected country or a neighbouring country;
- it may be ‘new’, but it might lie within a group of strains whose regional or national origin is known;
- with a measurable variation it may be possible to place it both in a general area and within a geographical radius of one strain or within radii of other known strains;
- the genomic markers may be associated with a specific ecology and/or host species, further defining its natural origin;
- the same unstable genome in two geographically distant isolates or from outbreaks years apart would indicate stable storage and release in several areas simultaneously or on separate occasions;

– if multiple strains are identified, are they logical? Do they have any other characteristics, such as resistance to a number of antibiotics, a documented collective availability to one institute, or an unusual common ability such as to successfully withstand freeze-drying while others commonly do not? If they are very diverse, their likelihood of naturally occurring together must be regarded as remote, at least until other evidence is available. However, in some cases there may be an epidemiological explanation for the presence of diverse strains, e.g. many different strains are recovered when anthrax outbreaks occur on several farms as a result of the common use of contaminated food: there can be different strains on different farms, different strains from individual animals in the same herd, and even varied strains in individual animals. It derives from the multiple sources of contaminated bones in the same batch of bone meal.

There is always the possibility that Country 'A' in 'attacking' Country 'B' may use strains or vectors from Country 'C'. Therefore, just because the identified strain is associated with one origin does not mean with certainty that it came directly from there. Nonetheless, once the strain has been identified it can provide useful clues as to who the attackers, or their contractees, may be, i.e. people/organisations who have documented ownership or access to the strains, who have the technical and scientific capacity to mount such an attack, and who have travelled in the area from where the strain originates.

The results of any successful strain identification must be promptly transmitted to the investigation team as it may open up a series of new questions and probabilities.

Purposeful genetic modifications affecting virulence

The virulence of a pathogen could be affected by genetic modification (1). The following characteristics would suggest a genetically modified pathogen:

- a) resistance to antimicrobial agents, especially to multiple antibiotics
- b) increased pathogenicity through
 - expression of new pathogenic factors, producing a novel clinical mix of lesions
 - enhanced effect of established pathogenic factors
 - altered innate immune responses to the microbe
- c) expression of biologic-response modifiers
- d) expression of immune-response modifiers
- e) altered antigenic characteristics, e.g.
 - decreased recognition by diagnostic reagents
 - avoidance of vaccine-induced immune recognition.

Vaccines depend on a suitable adaptive immune response to identified vaccine-preventable infections or intoxications. Pathogens may avoid immune protection if the genes encoding or regulating the expression of the immune targets are altered or if immune regulating genes are expressed by recombinant microbes. While several recombinant organisms capable of avoiding vaccine-induced immune responses have been reported (3, 7) the existence of naturally occurring genetic variants able to escape immune recognition (5) should not be forgotten.

Purposeful genetic modifications affecting diagnosability

If diagnosis by the normal laboratory procedures can be made less efficient or neutralised, it will immediately put a major stumbling block into any responding control activity (1). And the need to mobilise new or novel procedures will increase the cost and negatively impact the laboratory surge capacity. Thus the following diagnostic tests may give false-negative results in detecting genetically altered pathogens:

a) immunity-based diagnostic tests – this type of test will give false-negative results if the pathogen was altered to express antigens that do not bind the specific antibodies used in the assays or stimulate antibodies that do not bind standard detection targets. Examples of immunity-based diagnostic tests are:

– antigen detection assays (immunohistochemical analyses, direct immunofluorescence assays, antigen-capture enzyme-linked immunosorbent assays [ELISAs], bacterial agglutination assays)

– antibody-response detection assays (ELISAs, complement fixation assays, passive haemagglutination assays, indirect immunofluorescence assays, haemagglutination inhibition assays, and plaque-reduction neutralisation tests);

b) biochemistry-based bacterial identification tests – if the test depends on bacterial enzymes or specific viral encoded proteins it may be nullified if these products are genetically altered so that the products are either not expressed or are altered in structure or function;

c) nucleic acid-based diagnostic tests – these tests may fail because they are designed to detect specific gene regions dependent on reagents that hybridise to specific nucleotides. Similarly, digestion products of assays based on restriction fragment-length polymorphisms may not be of the expected size or may not hybridise to organism-specific probes.

Evidence of weaponisation

In spite of the events of 2001 and the intelligence fears of fall out from offensive research the probability

of weaponisation should not be presumed. Much can be achieved with pathogens off the shelf, out of the ordinary laboratory refrigerator or deep freeze; however, if a pathogen has been 'weaponised' there may be markers. The internal organisation of the genome may exhibit areas of discontinuity or heterogeneity reflecting purposeful manipulation. The discontinuities should be examined for obviously artificial junction sequences or rare restriction sites. Detailed genomic analysis may reveal whether the recovered isolates are 'normal' or whether they contain genes which are unusual and/or add virulence beyond the normal range, or have evidence of sequence insertions, deletions, or inversions, or contain episomes that are preferred vectors for genetic engineering. Similarly, finding an unstable genome in two distant sites or from outbreaks years apart would indicate stable storage and release in several areas simultaneously or on different occasions. Finally, dependent on how the micro-organism is grown, the genome may adapt and reflect the means of production. This would be demonstrated by subtle genomic changes between the primary outbreak(s) at the epicentre and subsequent spread. If the original inoculum can be found, say in feedstuffs or even in a suspect 'device', it may demonstrate the methods of storage and/or delivery. For example, additives to render the agent resistant to freeze-drying and aerosolisation such as microencapsulating reagents (poly DL-lactil-co-glycolic acid, sorbitol, trehalose) would be evidence of weaponisation, as would any genetic manipulation intended to increase the survival time of the pathogen in adverse environmental conditions.

Another factor to consider when looking for signs of weaponisation would be the physical form of the pathogen. An excellent example of this are the spores of *Bacillus anthracis* involved in the USA 2001 events. This was a highly aerosolisable product apparently consisting mainly of individual spores and few, but small, clumps; not something that one normally associates with occupational exposures, e.g. in mills and tanneries. The spores also arrived by mail.

Economic and trade analysis

Under normal circumstances all countries will try to take advantage of another country's problems whatever their cause. So judgement here has a large measure of subjectivity unless taken in regard to the previous 'event characteristics'.

There must be a concordance between the goals and objectives of a suspect organisation and the suspicious BW event; e.g. an international fruit consortium might well want to bankrupt the banana export industry in a competing region, but this would not be achieved through an outbreak of FMD in pigs in one of the latter's member countries.

A careful analysis must be made of whether the event has resulted in any of the consequences that are indicative of a deliberate attack (as described earlier in the Introduction) – to what degree did which countries benefit? For example, if Country 'B' suffers an outbreak, which countries increased – or against expectations did not decrease – their trade in the same period? By how much did they benefit from 'B's problems? Or on the other hand, in a notional prospective analysis, how much would they benefit? Nationally, the loss of exports will reverberate back reducing national demand and thereby producing excesses which can be very expensive to absorb. The suspect organisation may not be the most obvious beneficiary if, for example, it had set up others to (also) benefit at the expense of the target, i.e. as in billiards, with a bank-shot off the cushion.

Imaginary 'bank-shot' scenarios:

a) country 'N' improves its infrastructure and will soon be self-sufficient in wheat. Country 'G' uses country 'A's rust spores against 'N'. 'N' accuses 'A' and cuts off imports of 'A's grain, and probably other products as well. 'G' increases its grain exports to 'N', along with other benefiting countries;

b) country 'J' releases rust spores in country 'K', thereby reducing the latter's harvest and capability of exporting grain to its neighbour, country 'L'. 'J' increases its exports to 'L'. 'K' now cannot cover energy requirements and becomes politically unstable, thereby deflecting 'L's attention to its border with 'K', and away from 'J'.

On the other hand, a group just wanting to inflict severe economic damage but unable to financially benefit could still mount a biological attack, successful or otherwise.

People movements

Social unrest will aid terrorism and the terrorist's desire for political anarchy, opportunity, power, and change. At sporadic levels agricultural BW events will produce uncertainty and increased tension. At its most extreme in an agricultural economy when one kills the livestock and markedly reduces harvests the people must move if they are to survive. Thus it may also provide a land vacuum attracting third parties. The latter situation played a significant part in the civil wars in the former Yugoslavia.

In the Ethiopian war with Somalia, the livestock of Somalis living in the Ogaden region of Ethiopia were attacked with Napalm, with the result that the people had to take refuge with their relatives in Somalia. The influx of refugees, with some of their livestock, especially small ruminants, overloaded the governing capacity of the Somali government as well as accelerating over-grazing and the desertification of various family and clan seasonal grazing areas.

If an animal disease outbreak results in social unrest it could well be a deliberate attack, particularly if it occurs repeatedly. This is especially true in developing countries, where this type of attack can be very effective in forcing people to leave their lands. Such an event is less likely in developed areas of the world, because an attack on the high-security farms in the concentrated farming systems of these countries would require much more sophisticated planning than an attack on village livestock in low-security farms in non-intensive systems.

Diagnosis

Most agricultural costs from outbreaks are self-inflicted by the host country as they respond to the need for a rapid resolution. This response is usually out of all proportion to the number of index or primary cases. Therefore the 'initial' hit can be singular, even numerically trivial (e.g. Botswana with one FMD case; Israel and mercuric chloride [HgCl₂] in an orange; Chile and half a box of grapes). Under these circumstances the 'attacker' must aid the diagnostic process to ensure that the instance is (a) recognised and (b) reported. Therefore, what were the circumstances leading up to the initial recognition of the incident and its subsequent diagnosis and laboratory confirmation?

If a disease is not well known by professionals in the target country it may be missed. Therefore, one must keep in mind the concept of 'number needed for diagnosis'. How many cases are needed until the condition is recognised correctly? Experts in a disease always forget that their less-informed colleagues may have no idea what the disease is or even recognise the signs.

Similarly, have the surveillance and diagnostic capacities been recently improved? Therefore, could it have been a normal case that would otherwise have been missed? For example, the diagnosis of endemic cholera via naturally contaminated blue crabs in southern Louisiana is a function of physician awareness and laboratory enthusiasm. Outbreaks of human cholera follow upon hot, drier than usual summers, and the Cajun preference for not over-cooking their seafood. One successful diagnosis will beget others and soon there is an unexpected 'epidemic' and all it was was a hot, dry summer.

Therefore, one should always be aware of personnel competence, training, and technical laboratory improvements in surveillance efficiency.

Publicity

Most conditions have to be reported to national authorities and to international bodies such as the World Organisation

for Animal Health (OIE), the Food and Agriculture Organization and the World Health Organization. International reporting is frequently a monthly or annual requirement; only a limited number must be reported immediately. Any unusual departure from the conventional pattern of reporting should raise questions, e.g. was it reported 'too quickly' and what were the circumstances? If so, the appropriate investigative action can then be taken.

Latterly, there have been instances where cases of human Creutzfeldt-Jakob disease have been reported in the local USA newspapers as 'mad cow disease', sometimes with immediate effect on the price of beef futures. This is just journalistic ignorance and stupidity, but it could equally well be purposeful in the appropriate circumstances. With the internet, CNN, ProMED-mail, and modern information systems the opportunities for rapid, global dissemination of news is almost unlimited. Within ProMED-mail we have already begun to see instances of 'stirring' by certain individuals regularly referring to local news reports in distant cities that reflect very specific personal viewpoints. It would be naive to think that this was in any way new, but the growth of the global internet means that the capacity to disseminate 'news' is now available to a far greater number of people. Similarly, there have been attempts to spread disinformation via ProMed-mail, but fortunately they have been unsuccessful thanks to the experience and watchfulness of those in charge of processing incoming communications.

Keeping the reporting of disease outbreaks to the routine, usual procedure means that 'premature' reports can be detected and investigated, thus preventing the spread of disinformation and ensuring that suspicious events are identified.

Coded claims of authorship

The only groups that would admit to initiating a BW attack on agriculture, when not in wartime, would be terrorists. No country or commercial company would wish to. Such terrorist claims would reflect a grab for power, or a desire to create social unrest or to increase market share in mercenary activities.

There will be frequent false claims. However, increasingly, specific terrorist events are going unclaimed or with the perpetrators being presumed.

Echoes of previous or subsequent events

Bioterrorism and biological weapon events do not occur in isolation. A successful 'attack' follows successful research,

training and field trials. Similarly, it is unlikely that a successfully completed 'attack' will not be repeated, i.e. be a 'one-off', if the perpetrator has maintained technical competence. Any technology has a parenthood and genealogy attached to it; for example, similar research will be reported in different institutes by students of the originators; scientists are surprisingly unoriginal sometimes, such that trials get repeated and mimicked by other groups. Therefore, any event has the capacity to cast a 'shadow' forward and backwards in time. Thus a BW-suspect event without such echoes or shadows may well not be BW-related or may be merely opportunistic, which appears to be the case with the 2001 anthrax letters. 'Terrorists are tactically conservative, preferring weapons with which they are familiar. Rather than adapting entirely new techniques, most terrorists appear to prefer to adapt and improve their existing ones' (2). However, 'experience has nonetheless demonstrated repeatedly that, when confronted by new security measures, terrorists will seek to identify and exploit new vulnerabilities, adjusting their means of attack accordingly and often carrying on despite the obstacles placed in their path'. This may be facilitated by internet sources, which might cut out the need for personal contact and instruction from experts (2).

Investigating the 1973 outbreak of Newcastle disease in Northern Ireland

In November 1973, Newcastle disease (ND) suddenly appeared in Northern Ireland, where the viscerotropic disease had not been seen in three and a half years and Ireland had been regarded as essentially free for 30 years. It was successfully controlled with only 36 confirmed affected layer flocks. Contemporary investigations failed to reveal the source. The event itself was certainly unexpected as Northern Ireland did not, and does not, import animal proteins or by-products, such as bone meals or poultry offal meals. The possibility therefore existed that it might not have been a normal outbreak and it was so investigated retrospectively, using more advanced technology than that available at the time (6).

Source investigations

At the time of the outbreak, several possible sources of infection were investigated, the results of which are outlined below.

Direct infection via quarantined viraemic birds

No quarantine records supported the theory that the disease had been introduced via quarantined birds.

Legal imports of exotic birds into semi-intensive quarantine

Enquiries did not yield any support for this route of entry.

Illegal or unrecorded exotic bird importations

By its very nature this is difficult to investigate, but the investigations carried out at the time failed to reveal that anybody associated with the affected farms had been involved in this type of activity.

Imported parrots

In the early 1970s there were a series of ND outbreaks in North America and Western Europe that were associated with a sudden fad for parrots from South America and Africa. For example, in 1971 Paraguayan parrots escaped from an importer's premises and infected nearby commercial egg-laying flocks in southern California. By the time the outbreak had finished in 1973 it had cost US\$ 56 million.

Elsewhere, Switzerland had widely dispersed outbreaks, all associated with one shipment from South America; the Netherlands, in 1970, isolated Newcastle disease virus (NDV) from ten shipments of birds coming from Colombia and Paraguay, plus some of these birds were sick and infected when they later arrived in South Africa; Germany 'frequently' isolated NDV from newly imported psittacines mainly from Paraguay, but also from Colombia.

While the Antrim '73 epidemic in Northern Ireland could not be traced directly to imported parrots, it was suspected that the outbreak might in some way have been connected, but it was not known how.

Movements of people or vehicles

Extensive enquiries concentrated on 'hard-to-explain' outbreaks but failed to yield any positive information.

Feed stuffs

No feed stuffs were thought to be at the origin of the outbreak at the time. All protein meals were derived from poultry products that originated in Northern Ireland, as did meat and bone meals. Only grains were imported.

Vaccines

No vaccines were used at the index farm. Newcastle disease vaccines were not used in the province.

Human (kitchen) wastefood

No outbreak was found to be associated with the feeding of kitchen waste, nor with such materials from the nearby Aldergrove Airport.

Imported eggs

There was no commercial incentive to import eggs. Boxes with the names of Scottish or English retailers contained domestic eggs, diverted for local trade and still in their export packs.

Wind-borne virus

While winds with high humidity and adequate force were blowing in the right direction to carry the virus from infected flocks in England, the distance was considered too great.

Wild birds

While there were historical precedents of ND being introduced via wild birds, no detailed investigations were carried out.

Sabotage

Sabotage was considered at the time both within and without the Northern Ireland Department of Agriculture. Enquiries at each infected premise covered this possibility despite that fact that disease prevention procedures on many farms were poor and it was possible that the virus could have been introduced via dirty poultry crates, muddy Wellington boots, etc. The targeted farms were largely protestant, so the involvement of the Irish Republican Army (IRA) or other nationalist paramilitary group could not be ruled out at the time, but there was no evidence to support such a hypothesis beyond mere suspicion and speculation. The attacks were a claimable success, but there were no claims of responsibility from any political association or paramilitary group.

Retrospective investigations

The initial outbreaks were all in layers that had mash, pelleted, complex rations with many components, while broilers with simple rations were not affected. This had suggested that certain feed stuffs may have been contaminated, but the affected farms bought their feed from a variety of retailers, so there did not appear to be a link. However, later investigations discovered that all feed coming into Ireland was imported via Rotterdam docks, where it may have been contaminated by infected pigeons. The Netherlands had an active vaccination programme, but it prevented disease, not infection, so there was a possibility that all feed mills in Ireland could have distributed contaminated feed.

Genomic analysis of Newcastle disease virus Antrim '73

The virus isolates from this epidemic were very similar to those of the Essex '70 epidemic in the United Kingdom

(UK), which were identical to the previous American NDV isolates. This demonstrates an epidemic commonality (Group A – Fig. 1), which is to be expected if the UK and the immediate related European outbreaks followed the movement of American parrots to Europe. Group B is a group of Hungarian isolates that were isolated some years later as the Newcastle panzootic spread eastwards across Europe. Unfortunately no intermediate virus isolates have survived.

Of course, an alternative viewpoint might suggest that varied NDV strains were characteristic of an aggressive group with tight security and three separate teams, each with their own infected eggs to be placed broken in the targeted flocks so that they would be eaten by the chickens; or however else delivery was to be achieved – a Roswellian interpretation in the opinion of the writer in the absence of any strategic or economic advantage.

Economic assessment

The costs of the outbreak in Northern Ireland were severe, but the economic assessment revealed that deliberately introducing NDV into the country would have brought little financial benefit to anyone, thus making the sabotage theory highly unlikely. The market for table eggs in the UK was declining rapidly and most countries in Europe had Newcastle disease problems of their own at that time, so there was little motivation for anyone to try to gain a larger share of the market by destroying the industry in Northern Ireland.

The final bill was £668,994 (or £4.7 million to £5.1 million in 1997 terms) (4) but efficient control meant that the uninfected flocks within the country were able to keep the domestic market afloat and Antrim quickly returned to full production. The economic costs had no obvious social or political impacts inside the country; in fact, the outbreak brought all those involved closer together. The eradication campaign left Northern Ireland free of Newcastle disease and with no need to vaccinate, and the outbreak had no other benefit to anyone outside Northern Ireland.

Conclusion

There was nothing in the investigation which provided firm evidence to support the theory that the appearance of ND in Northern Ireland had been the result of a bioterrorist attack. Moreover, the outbreak had none of the additional characteristics of suspicious attacks, e.g. no premature publicity, no coded claims of authorship, and nothing about it was reminiscent of a previous or subsequent attack. The conclusion, therefore, was that this was a natural series of outbreaks resulting from a

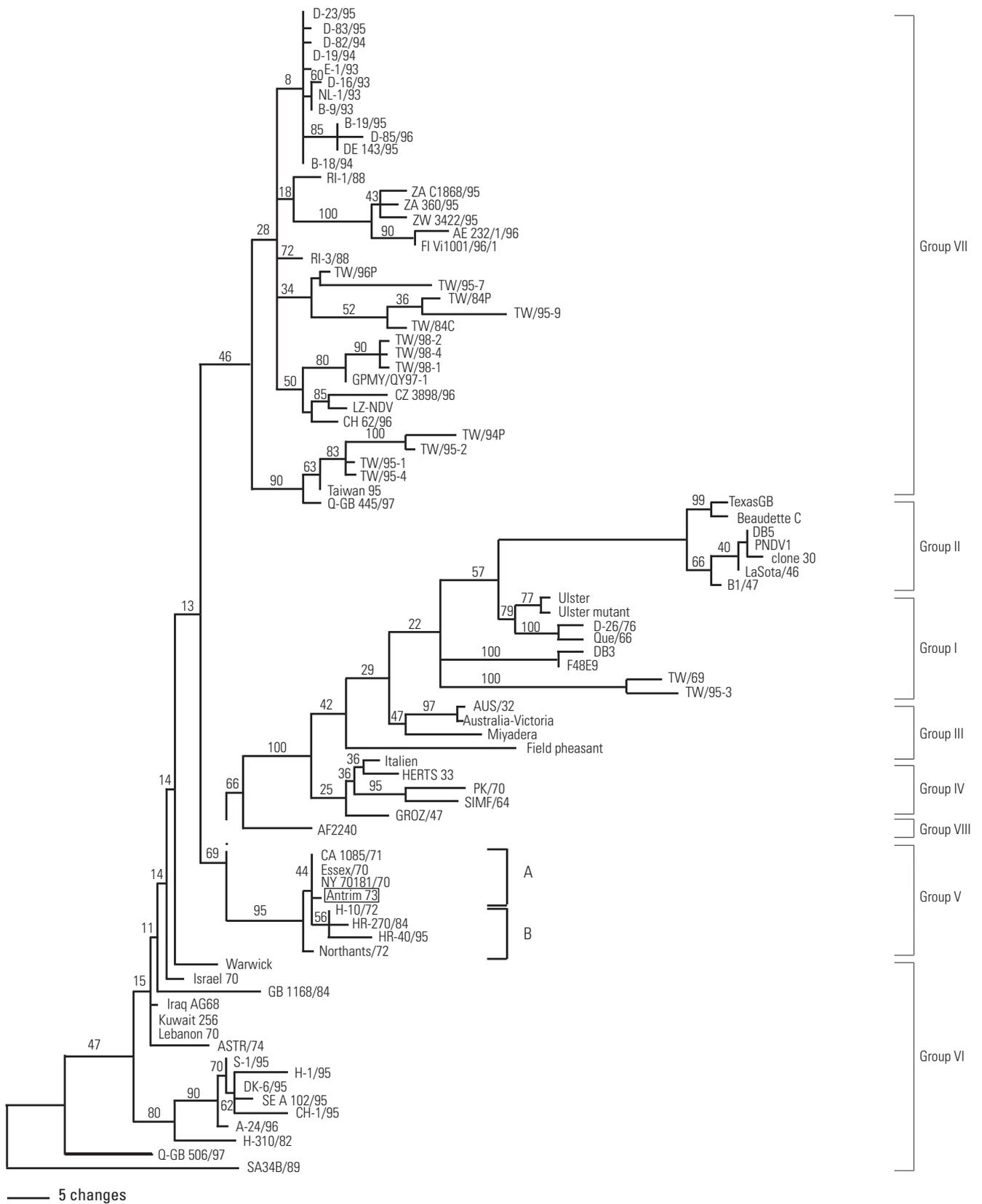


Fig. 1
Phylogenetic analysis of Newcastle disease virus (6)

conjectural source outside Antrim involving imported contaminated poultry feed.

Final remarks

While there is at present heightened awareness of the risks of BT/BW-related disease outbreaks, the reality is that we will, unfortunately, still have outbreaks, small and large, that are normal in all respects. These must be handled efficiently, cost-effectively, and quickly. But as long as the potential for unnatural/intentional outbreaks exists, we must be prepared.

Part of this preparation is to be proactive in their recognition. It is not sufficient to have a John Snow produce evidence after it has happened and explain why. It is vitally important to be realistically sensitive to possible prior signature events. And any and every prediction must be validated. On the other hand one must guard against hypersensitivity, which by definition is unnecessarily expensive and not cost effective. But be aware. Be alert. And when in doubt as to the normality of any given event investigate promptly, appropriately, and quietly.



Distinction entre les foyers de maladies animales d'origine naturelle et non naturelle

M. Hugh-Jones

Résumé

Un foyer de maladie d'origine intentionnelle apparu dans un élevage ou dans des cultures présentera des caractéristiques communes avec un foyer visant l'homme – saison ou lieu inattendus pour la maladie, caractère explosif possible en termes de fréquence, nature ou structure génétique inhabituelles de l'agent pathogène, diagnostic difficile – mais aussi des différences notables : les cas humains, s'il en existe, seront fortuits et leurs principaux effets seront différés et auront une portée économique importante. L'auteur propose un protocole d'investigation et d'analyse pour l'identification d'un tel événement. À moins que la nature de l'événement soit évidente, ces investigations nécessiteront un examen très approfondi et rigoureux mené par une équipe épidémiologique spécialisée et expérimentée. En même temps, les pays doivent anticiper ce type d'événement en prenant des mesures préventives qui leur permettront d'être prêts et de gagner du temps, par exemple en identifiant les cibles possibles, en définissant les indicateurs d'avertissement précoce, en réalisant une expertise biologique moléculaire et une collection de référence des agents pathogènes éventuels, enfin en préparant une réponse tactique et médico-légale.

Mots-clés

Cible – Coût économique – Diagnostic – Identification moléculaire de la souche – Publicité – Utilisation des agents pathogènes comme armes.



Discriminación entre brotes zoonosarios de origen natural y no natural

M. Hugh-Jones

Resumen

Un brote infeccioso de origen intencionado que afectara al ganado o los cultivos agrícolas tendría una serie de rasgos en común con los brotes dirigidos contra seres humanos (comportamiento insólito de la enfermedad por el lugar o la estación, eventual incidencia explosiva, patógeno inusual, ya sea por sí mismo o por su estructura genética, diagnóstico difícil, etc.), pero también presentaría diferencias notables, puesto que los casos de infección humana, si llegara a haberlos, serían fortuitos, y las principales consecuencias surgirían con más retraso y constituirían sobre todo un grave percance económico. El autor propone un protocolo de investigación y análisis para detectar este tipo de episodios. A menos que ello resulte obvio por la propia naturaleza del caso, las investigaciones requieren un trabajo de análisis realmente exhaustivo y cuidadoso por parte de un equipo de epidemiólogos expertos. Paralelamente, a fin de estar preparado y ganar tiempo llegado el momento, un país debería adoptar medidas para adelantarse a los acontecimientos, por ejemplo determinando posibles objetivos, definiendo indicadores de alerta rápida, consolidando sus conocimientos técnicos en biología molecular, elaborando colecciones de referencia de posibles patógenos y preparando una respuesta táctica y forense.

Palabras clave

Costo económico – Diagnóstico – Objetivo – Publicidad – Uso armamentístico de agentes biológicos – Variedad molecular.



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