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Bioterrorism: intentional introduction of animal disease

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Summary

The possibility of the intentional introduction of animal disease as an act of bioterrorism adds a new dimension to the development of strategies for assessment, prevention, response and recovery from exotic diseases, including the zoonoses. The vulnerability of livestock operations, the likelihood of success, the possibility of the use of genetically engineered organisms and limited resources to handle multiple outbreaks place new pressures on policy-makers and emergency responders to make best use of limited resources. The methods for managing a natural occurrence or accidental introduction of high-consequence diseases are generally applicable to containment and recovery from outbreaks of intentionally introduced animal diseases. Zoonotic agents increase the complexity at both international and national levels. Modern biology provides both increased threat of new disease entities and methods for earlier and more effective detection and intervention. Improved methods are emerging for defining trade restrictions and animal movement and for determining when it is safe to resume normal trade.

Keywords

Biotechnology – Bioterrorism – Detection – Intentional introduction – Recovery – Trade restrictions.

Introduction

Historical perspectives

The domestic and international spread of infectious animal disease may occur through natural, accidental, or intentional means. Transnational spread of disease may result from movement of animals, animal products or cultures of infectious organisms. The intentional introduction of animal disease has an interesting history going back to the Middle Ages, when diseased carcasses and bodies were catapulted over enemy walls in attempts to induce sickness in humans or animals (2). Developed nations have, over the course of more modern history, engaged in the active development of offensive biological weapons affecting both animals and humans. In an extensive review of the subject, Wilson *et al.* (14) list several instances in which livestock have been the targets of biological warfare or bioterrorism. Biological warfare programmes are now prohibited by the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction (the Biological and Toxic Weapons Convention), which became effective on 26 March 1975 and which currently has a membership of 163 countries (11). However, there is clear evidence that the development of biological warfare agents continues in some countries. While the intentional introduction of infectious animal disease is likely to result in different, if not unique, initial conditions of the outbreak(s), the local, national, and international responses will be generally similar to those involved with natural or accidental introduction(s). However, intentional introductions could follow unpredictable patterns and involve multiple locations or organisms, making it difficult to detect and contain an outbreak.

After clean up, gaining international recognition of freedom from disease and the resumption of normal trade between countries would involve methods based on the

recommendations of the *Terrestrial Animal Health Code* (*Terrestrial Code*) of the World Organisation for Animal Health (OIE) (16).

Bioterrorism and its manifestations

Terrorism is defined as 'the calculated use of violence, or the threat of violence, against civilians in order to attain goals that are political, religious, or ideological in nature; this is done through intimidation or coercion or instilling fear' (10). 'Bioterrorism' is defined as 'terrorism by intentional release or dissemination of biological agents (bacteria, viruses, or toxins); these may be in a naturally-occurring or human-modified form'. Unlike explosive devices used in terrorism attacks, biological and agricultural weapons can continue causing direct damage for days, weeks, or even months after their release. This is particularly true when the disease becomes widely disseminated before its presence is recognised. The results of bioterrorism may be seen in the economic or biologic effects of the introduction, or perception of introduction, of diseases. Terrorism involves perception as well as reality and, in the case of animal agriculture, it could result in consumer shifts away from consumption of products or commodities, whether or not there is a true basis for concern about human health. In the extreme case, loss of confidence in government ability to assure a safe supply of food and maintain public health can destroy, and has destroyed, standing regimes (8). The economic effects of shifts in consumption and market prices and of loss of animals through either disease or control measures are ways in which the impact of bioterrorism may become apparent. The loss of domestic and international markets through trade constraints is a key concern. As noted above, the methods for setting the limits on movement of animals or animal products, as well as the tools for defining the basis for re-establishing normal trade relations, are in place for naturally occurring disease and presumably would be used should disease be intentionally introduced (see below).

Threat and vulnerability

For planning purposes, the risk and consequences of introduction and spread of exotic disease are usually assessed in terms of the perceived threat and the vulnerability of the segment of the food and agriculture sector concerned. Threat assessment is based on the perceived ability of individuals or nation states to acquire and prepare materials suitable for intentional release, the ability to effectively deliver the materials, and the intent or will to intentionally employ such materials. Publicly available assessments, taken in the aggregate, strongly suggest that the threat of the use of biological materials is credible. The vulnerability of the food and agriculture sector to the introduction of biological agents is variable across the sector. It is generally agreed that the livestock industries are relatively vulnerable to intentional attacks, with some parts more protected than others. For instance, the intensive agricultural operations are more apt to see spread of introduced disease from animal to animal because of proximity, but these operations are often more secure, because it is possible to implement both physical and biological methods for their protection. Generally, organised methods for protection, early detection, response, and recovery are less available in the developing world for both natural and intentional introduction of disease.

Global implications

As is the case with natural and accidental introduction of disease within or between countries, the intentional introduction of exotic disease in any country has global economic and animal/human health implications. While trade restrictions and related market constraints may temporarily favour a country or region unaffected by the outbreak of disease in another area, the effects of health restrictions and the resulting loss of international trade make the use of bioterrorism for animal agriculture truly international in its impact. It is important to note that the threat of bioterrorism in agriculture is not unique to the developed world or a consequence of the events of 11 September 2001 in the United States. It is a global threat that has profound implications for all nations. The impact on exporting countries, including developing countries, has in fact already been felt, even in the absence of a recognised intentional introduction of animal or foodborne disease, because of the increased rigour of import standards and regulations which have been imposed to protect against such introductions. These new requirements for inspection and demonstration of freedom from disease have, in some developing countries, proved difficult to meet with available resources.

Intentional versus accidental/natural outbreaks of exotic disease

Components of outbreaks

It is, to some extent, appropriate to consider intentional and natural outbreaks of exotic disease as part of a continuum. As a valid assumption, it provides the rationale for developing a common strategy for prevention, response and recovery. However, it is important to realistically deal not only with the commonalities but also with the

substantial differences associated with the methods of introduction and the initial conditions under which an intentionally introduced outbreak is expected to occur. Natural outbreaks of exotic disease usually occur under conditions that often lend themselves to an early and effective epidemiological analysis of the source and extent of the outbreak. However, there are important exceptions where the origin of an introduced disease is never determined. Intentional introductions of exotic disease would be less predictable in terms of origin and extent. In the case of acts of bioterrorism, common scenarios in the unclassified literature assume that it is possible, and perhaps likely, that multiple introductions of the same or even different pathogens might be made concurrently, depending on the sophistication of the perpetrator. In almost all scenarios, early recognition of the disease and prompt response are important in cost-effective containment. This may be more challenging with intentional introductions. In naturally occurring outbreaks, there are often bilateral or international negotiations for regional containment and the maintenance of normal trade in unaffected areas. The uncertainties of the consequences of a recognised intentional attack and the social or psychological consequences might limit this flexibility.

Common tools for planning, training, response and recovery

The science-based principles of preventing and responding to infectious diseases are likely to apply to both intentional and accidental introductions, although the extent of the introduction may differ and there is a greater possibility that non-conventional pathogens will be used if the introduction is intentional. Similarly, the evolution of the tools for early detection of multiple organisms and for providing protection against multiple diseases with a common product, offer the expectation that dealing with the intentional attack will be similar to dealing with an accidental outbreak, except perhaps for severity, especially with multiple simultaneous introductions.

Response strategies usually draw on the principles of emergency response in general, and on the response to natural or intentional introduction of disease in particular. An important part of the national response strategies in many countries is to ensure that the normal methods for routine diagnostic laboratory support of livestock and poultry industries are expandable and flexible enough to include the use of different reagents to detect the unexpected as well as the expected (routine) pathogens. In the United States, the National Animal Health Laboratory Network exemplifies this approach, offering a common set of reagents and procedures with flexible capacities for both early detection and ongoing management of outbreaks of disease (12).

As discussed below, the underlying sciences supporting broad-based batteries of tests for detection of multiple known and unknown agents are emerging to extend these capacities as technology and funding permits. With widespread use of these capacities, there is reason to expect that their cost and complexity can be adjusted to provide for their use in the developing world. Given the relative infrequency of intentional bioterrorism attacks, and the nature of the politics of investment in systems to prevent the unlikely event, it is necessary at both national and global levels to ensure that the tools to protect against and respond to intentional attacks are used in everyday practice where their value is obvious and ongoing.

Potential perpetrators and their methods

Individuals, organisations and nations

Offensive biological weapons programmes were under development in several countries prior to the signing of the 'Biological and Toxic Weapons Convention' as mentioned previously. The former Soviet Union had active development programmes for biological weapons, including those for plant and animal agriculture, which were later revealed after its collapse. Generally, nation states and terrorist groups with even modest biological research and development capacity and the intent and will to use it could acquire and produce materials that can be used for bioterrorism. Such capacity could include the ability to use modern biotechnology to create modified biological agents which may have enhanced virulence and for which current vaccination may not be effective. Targets of these groups may be either military or civilian (4). Unlike military applications of biological weapons, the effective delivery of such biological agents in food and agriculture can be relatively simple. Terrorist organisations have the capacity to acquire naturally occurring pathogens or develop and use biological agents to attack agriculture. Experience has shown that disgruntled employees may also act as individuals to intentionally introduce disease into the food and agriculture system. In summary, there is evidence that the three main ingredients for bioterrorism in agriculture, namely technical capability, delivery methods, and will or intent, exist today.

Potential methods of introduction

Animal pathogens can be intentionally introduced via any of the routes that are associated with accidental introduction, the only difference is that the route is chosen deliberately, with malice aforethought.

Cultures of select agent organisms

Most analysts believe that this would be the most reliable and easily concealed method of intentional introduction of select agents. Given the relatively high probability of success by an informed and intentioned terrorist, the early detection of diseases resulting from such introductions is becoming increasingly important. It is commonly assumed in the lay press that it would be easy to introduce highly infectious agents, such as the foot and mouth disease virus, into a susceptible population of cloven-footed animals by simply bringing home a contaminated 'handkerchief' and exposing animals. In reality it is more difficult than this. However, acquiring such cultures from naturally occurring infections in one country and successfully introducing the material in another country without detection is quite achievable.

Contaminated animal products – raw or processed

Most developed countries have active inspection programmes intended to detect or at least discourage the importation of such products, which could be contaminated through either accidental or intentional means. However, in the case of the United States, the volume of materials coming across international borders makes it unlikely that it will be possible to detect all contaminated products, or even most of them, unless there is reasonable investment in resources.

Wilson *et al.* (14) describe the introduction of rabbit calicivirus into New Zealand as a 'well-planned organized criminal event'. The perpetrators – a group of farmers disgruntled by a government decision that deliberate introduction of a biological tool to control rabbit populations carried unacceptable risks – circumvented one of the best border biosecurity systems in the world to smuggle the virus into the country. Once it was in New Zealand, the participants were able to multiply the virus by low-technology methods and disseminate it widely around the country before its presence was recognised by the authorities.

Importation of infected animals

The spread of exotic disease, intentional or unintentional, in many parts of the developing world is not only possible, but has a historical basis in the migration of diseases across continents. For instance, in modern times, the movement of animals from the Horn of Africa to Saudi Arabia is credited with the introduction of Rift Valley fever into the Arabian Peninsula (7). In the United States, while there are procedures for quarantine of imported animals before their introduction, there are thousands of animals imported from Mexico based primarily on visual inspection by federal officials. There are records of unintentional migration of animals across the Rio Grande River into the permanent quarantine zone for *Boophilus* ticks along the Texas border. Clandestine introduction of animals along unprotected coast lines, particularly of psittacine and other pet birds of high market value is routine. This could also be a route of introduction for intentionally infected animals. While this is one of the important methods of importation of naturally occurring disease, it is perhaps less attractive as a means of intentional introduction because of the relative uncertainty of success.

Wildlife as vectors of livestock and poultry disease

Wildlife are the natural reservoirs for many diseases of domestic animals and fowl. The accidental or intentional introduction of exotic animal diseases (with mainly economic or zoonotic effects) into indigenous populations of wild animals is a potential threat. Once introduced, the eradication of such diseases from wildlife has proven very challenging in previous experience.

Priority diseases

The OIE has summarised its role, as regards intentional acts of bioterrorism, in a fact sheet, noting the importance of actions of Member Countries in preventing, detecting and responding to such acts (17). The diseases of concern to the OIE, and those that require notification of occurrence, are a major input into the development of lists of diseases of bioterrorism concern (18). Implicit in the development of such lists is the recognition of the relative importance of the economic and animal/human health implications of outbreaks of these diseases. Accepted laboratory methods for initial diagnosis and ongoing surveillance have been established. Ongoing formal and informal systems for monitoring and reporting the incidence and status of these diseases are in place.

Select agents

Within and among the developed nations specific plans for dealing with high-consequence pathogens have been put in place. Across nations with similarly developed procedures to reduce the impact of bioterrorism, relatively consistent lists of agents referred to as 'select' or 'high-priority' agents have been defined. These are organisms that pose a significant threat to human, animal, and plant health. There are specific plans, either in existence or under development, for handling them under experimental conditions and for prevention, intervention, and recovery from diseases (13). Identifying and prioritising agents for inclusion on the select agent list requires consideration of the organism involved and the consequences of its introduction, global surveillance, intelligence estimates, and the advice of panels of subject matter experts. Thus far, in most countries, the list of select agents for bioterrorism more or less mirrors the list of

select agents pertaining to natural or accidental introduction of exotic diseases. In the case of animal agriculture, the emphasis is placed on the highly virulent, highly contagious viral diseases that affect multiple species. In the case of plant agriculture, emphasis has been placed on the highly contagious and infectious fungal diseases that affect the cereal grains. Approximately 60% of the pathogens affecting public health, as noted by the Centers for Disease Control in the United States, are zoonoses (5). Models for making more quantitative estimates of the consequences of introduction of these diseases are being developed to provide assistance to policy-makers in establishing priorities as a means of guiding investment strategies for mediation (3).

While there is an extensive list of pathogens identified as select agents, there are a few that are considered to have a higher risk of being used as biological or agricultural weapons. These agents are considered to present a higher risk because:

– they are easily dispersed or obtained

– they are highly pathogenic/infective

– there are low levels of immunity to the agent in the target population

– the overall biological and economic effects of their release would be extremely negative.

Some examples among animal agents include foot and mouth disease virus, Rift Valley fever virus, highly pathogenic avian influenza virus, and anthrax. Several of these, such as Rift Valley fever and anthrax, are also human pathogens. This further increases the adverse consequences from a release of these agents.

Modern biology – threats and uses for bioterrorism

Bioengineered and other novel pathogens

Until quite recently, the majority of strategic thinking about, and plans for, prevention and response to intentional acts of bioterrorism had been based on the assumption that the same organisms involved in natural outbreaks will be involved in intentional introductions. This may continue to be the appropriate assumption for the larger part of the threat assessment and response strategy. It is usually assumed that common prevention and response methods can be used for either case (see below). However, countries considering biological weapons as a part of their offensive or defensive plans also have the scientific capacity to create new and novel organisms using relatively simple tools of the modern biotechnology revolution. Enhanced virulence or infectivity of known current threat organisms is possible, as is the creation of new pathogens comprised of combinations of existing organisms or organisms with unique signatures (6).

Application of biotechnology for countermeasures against bioterrorism

The same fundamentals of modern biology that could be used to create new biological weapons are also being used to create effective countermeasures against the threat of bioterrorism, for either natural or engineered organisms. Methods for early detection and forensics for these organisms are rapidly evolving towards combinations of tests that are able to accurately detect hundreds of pathogens and their host responses in a single array that can be applied under both laboratory and field conditions (9). Similarly, methods are rapidly emerging that will provide broad host resistance to multiple organisms with very rapid onset. The creation of novel vaccines in response to recognition of new agents, in days and weeks instead of months and years, is quickly coming into focus. These methods are emerging mainly in the field of human medicine and the challenge is to bring them to animal agriculture through the One Health initiative (1). These modern techniques offer promise of not only early initial detection of exotic disease, but also of providing the field testing ability to separate infected from uninfected animals in eradication programmes once an outbreak is discovered, thereby reducing the loss of healthy animals during the process. Initially the operational costs of using these methods may be high and there may be substantial problems with their development. As these new capacities come on line, the international community will face the serious challenge of expeditiously establishing methods for recognising, accepting, and authorising these new techniques for prevention, detection, mitigation and recovery.

One Health – One Medicine – One Biology

For many years, the concept of One Health has been emerging as the relationship between public, animal, and environmental health has become more obvious. In the United States there is an active initiative among professional societies and the Government to recognise and apply this principle to diseases affecting humans and animals (1). The underlying science that is relevant to each of these elements is increasingly recognised as having a common basis, especially as the comparability and commonality of modern genetics becomes more obvious. There is a large overlap of diseases of concern for bioterrorism between humans and animals. There is, therefore, a natural and expanding intersection that brings closer together the animal, human, and environmental

factors (including shared intermediate vectors) related to the establishment, progression, and results of the introduction of exotic diseases. From the perspective of either the perpetrator of, or the responder to, acts of bioterrorism, the underlying One Medicine approach is highly relevant. For example, the introduction of zoonotic disease in human populations via initial animal hosts and shared vectors is one method of creating human disease. The methods for mitigation of an outbreak often involve a systems approach that involves all parts of the One Biology approach, including animal, human and environmental factors.

Trade and regulatory constraints arising from concerns about bioterrorism

The involvement of international organisations in developing and implementing procedures for dealing with outbreaks of high-priority (reportable) diseases rests primarily with the OIE and the Food and Agriculture Organization of the United Nations. Most countries derive their procedures and practices from these international organisations, adding other requirements as deemed appropriate.

Standard procedures applying to bioterrorism

Regulations pertaining to quarantine and trade restrictions arising from natural or accidental outbreaks of certain diseases also apply to intentional introductions of these diseases. There are ongoing discussions and a continuous evolution of multinational agreements regarding these restrictions, which deal with principles of detection, response, recovery, and demonstrated freedom from infection. The availability of new methods for detection, diagnosis and immunisation against the high-priority diseases is rapidly providing new and more effective methods of mitigating the impact of these diseases. For instance, the provision of vaccines and diagnostics that allow for distinguishing vaccinated from infected animals is not only drastically reducing the need for slaughter of healthy (but exposed) animals, but also providing assurance to trading partners of the healthy state of vaccinated animals. This offers the promise of more rapid and safe resumption of normal trade after outbreaks have been successfully eliminated.

Regionalisation of trade and movement restrictions

A part of the ongoing evolution of international agreements dealing with high-priority (reportable) diseases is the regionalisation of trade and movement restrictions to specific areas of nation states where the outbreak of the disease occurs. This allows other parts of the involved country to engage in normal trade, with or without testing and other procedures to further ensure the safety of such movements.

Advances in risk assessment for trade decisions

In most cases, the final decision regarding resumption of normal trade after a disease outbreak has been eliminated is based on bilateral negotiations between the exporting and importing entities. Most countries have established risk assessment procedures for informing decisions on resumption of trade and this global experience in risk analysis has been the basis for the OIE *Handbook on Import Risk Analysis for Animals and Animal Products* (15). This publication provides guidelines useful to bilateral parties considering resumption of trade after outbreaks of certain diseases. Recent research has advanced analytic methods that can be used to help inform such decisions. These methods have arisen in part from the increased concern about intentional introduction of disease and involve the combination of threat, risk, and consequence analysis.

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Bioterrorisme : l'introduction délibérée de maladies animales

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Résumé
La possibilité qu'une maladie animale soit introduite intentionnellement dans un but de bioterrorisme ajoute une nouvelle dimension à la conception des stratégies d'évaluation, de prévention, de réaction et de récupération mises en œuvre pour les maladies exotiques, zoonoses incluses. La vulnérabilité des opérations zootechniques, la probabilité incertaine d'obtenir de bons résultats, l'utilisation éventuelle d'organismes génétiquement modifiés et la disponibilité limitée des ressources consacrées à la gestion de foyers multiples sont autant de facteurs qui placent les décideurs politiques et les responsables de la gestion des crises devant de nouvelles responsabilités. En général, les méthodes utilisées pour gérer l'apparition naturelle ou l'introduction accidentelle de maladies importantes s'appliquent également au confinement des foyers épizootiques introduits intentionnellement ainsi qu'à la récupération post-foyers. Les agents de zoonose posent des problèmes encore plus complexes aussi bien au niveau international que national. La biologie moderne ouvre de nouvelles possibilités de voir surgir des entités pathogènes inédites, en même temps qu'elle permet de disposer de méthodes de détection et de réaction plus précoces et plus efficaces. De nouvelles méthodes sont actuellement mises au point pour définir les restrictions imposées au commerce et aux déplacements d'animaux et pour déterminer à quel moment les échanges peuvent recommencer normalement.

Mots-clés
Biotechnologie – Bioterrorisme – Détection – Introduction intentionnelle – Récupération post-foyer – Restriction au commerce.

Bioterrorismo: introducción deliberada de enfermedades animales

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Resumen
La posibilidad de introducción deliberada de una enfermedad animal como acto de bioterrorismo agrega una nueva dimensión a la concepción de estrategias para valorar, prevenir y responder a la eventualidad de enfermedades exóticas, comprendidas las zoonosis, y recuperarse de sus efectos. La vulnerabilidad de las operaciones con ganado, la probabilidad de ataques que tengan éxito, la posibilidad de utilizar organismos modificados mediante ingeniería genética y la escasez de recursos para hacer frente a brotes múltiples suponen una carga de presión añadida para las instancias encargadas de adoptar decisiones y responder a las emergencias, que deben hacer un uso óptimo de los limitados recursos existentes. Los métodos utilizados para hacer frente a la aparición de enfermedades con consecuencias temibles por causas naturales o introducción accidental también pueden aplicarse a la contención de brotes de patologías animales y a la recuperación de sus efectos cuando la introducción tiene un origen deliberado. Los agentes zoonóticos acrecientan la complejidad a escala tanto nacional como internacional. La biología moderna trae consigo a la vez

mayores amenazas, producto de nuevas entidades infecciosas, y nuevos métodos para detectarlas y afrontarlas con más prontitud y eficacia. Ahora están apareciendo mejores métodos para definir restricciones al comercio y al movimiento de animales y determinar el momento en el que resulta seguro reanudar las actividades comerciales con normalidad.

Palabras clave
Biotecnología – Bioterrorismo – Detección – Introducción deliberada – Recuperación – Restricciones al comercio.

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