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EDITORIALS

The explosion at Vector: hoping for the best while preparing for the worst

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Abstract

This commentary reviews the implications of the gas explosion at the Russian State Research Centre of Virology and Biotechnology building (Vector) on September 16th, 2019. Public health and engineering perspectives are provided on the implications of the explosion causing a physical breach of the building, and the potential for dispersion of pathogens in the surrounding area. A global public health and risk analysis perspective is taken in discussing preparedness planning around this event.

On September 16th, 2019, an explosion occurred at the State Research Centre of Virology and Biotechnology building (Vector) in the city of Koltsovo, in the Novosiberisk region of Siberia, Russia (1). The affected building was a BSL 4 virology research centre, and one of only two known sites housing variola virus, the cause of smallpox. The facility has one of the largest collections of dangerous pathogens in the world. Whilst laboratory safety breaches are common and do not usually result in epidemics, explosions are rare. Unlike a needlestick injury or an accidental shipping of live anthrax, an explosion of this magnitude is likely to lead to a physical breach of the integrity of the laboratory, possibly affecting multiple parts of the structure and equipment within. An explosion is sudden, uncontrolled and unpredictable, and involves force which may result in pathogen release into the surrounding environment. An epidemic which arises in close proximity to the explosion could spread beyond the affected region or even globally, which makes this event a concern for global public health.

The explosion was allegedly caused by a gas cylinder or gas tank, according to reports, and was followed by a fire. The fire reportedly spread through the ventilation system of the building and affected an area of 30 square meters before it was extinguished. The explosion on the fifth floor was reported to have shattered the glass in the six-storey building. According to Russian authorities, no biological agents were housed in the affected area. We do not know if this is the case, but it is in the global interest to understand the risks if there were pathogens released. The affected facility was a virology research centre, so we may assume that viruses (rather than bacteria) were present in the building but cannot exclude non-viral pathogens being present. Neither can we exclude theft of pathogens during the chaos and aftermath of the explosion, or that the explosion itself was deliberate to enable theft.

From a risk analysis perspective, an explosion at a BSL 4 facility for dangerous, contagious pathogens is a risk for global health. Despite the Russian government assertion that there is no risk to public health, it would be wise to assess the risk as objectively as possible, given the global community is a stakeholder if an epidemic arises from this accident. In the best-case scenario, there were no pathogens in the affected part of the building, no pathogens released, the situation has been contained and there is no risk to local or global public health. In the worst-case scenario, there were pathogens present at the time, which were aerosolised and propagated outside the building as a result of the explosion. The principle of pandemic and preparedness planning considers the worst-case scenario, rather than hoping for the best-case scenario. So, we need to consider what a worst-case scenario would look like and how best to be prepared and mitigate it.

A gas explosion of this scale can result in propagation of a detonation/shock wave at speeds of 1500-2000 metres/second. The flame on the other hand propagates at a slower speed (typically 20-25 m/second and up to several 100 m/second) (2). In a deflagration, the commonest way a flame propagates in a gas explosion, unburned gas is propagated ahead of the flame. Therefore, in this instance, if any biological material were present, it could have been propagated and aerosolised well ahead of the fire and before the fire was widespread. The reports of shattered glass across multiple floors in the building is indicative of a sufficiently strong explosion that could lead to the dispersion of contagious pathogens to surrounding areas. An explosion interacting with a vial of liquid or frozen pathogen will quickly and completely rupture the contents, creating tiny droplets or particles in the order of microns that could, conceivably, be projected well clear of the building and resulting fire by the shock wave. Pathogens present in liquid or solid media, even frozen pathogens, could be at risk of dispersion during an explosion. A blast that shatters the windows in a building would equally be expected to shatter freezers, fridges, biosafety cabinets and incubators. We do not have adequate research data on the effect of explosions on pathogen dispersion to make confident assertions about the safety to the public following this incident. BSL 4 laboratories are generally not designed to withstand explosions, so we should assume that secure structures, equipment and workspaces were affected.

The factors which may affect risk include the weather conditions at the time, the force and heat of the blast, the height of the building and affected floor, the structure, quantity, contents and type of laboratory equipment present, the extent of the breach of windows in the building, the type of pathogens present (and their propensity for aerosolization and viability in the environment), the number of people potentially exposed inside the building and the population density in the surrounding areas. It also depends on transmissibility of any pathogens present. Certain pathogens such as anthrax and variola are easily dispersed by aerosolization. Others, such as Ebola, are not primarily spread by the airborne route, but aerosol transmission is also possible (3). If hybrid, synthetic or engineered pathogens were present, this probably increases the risk because such agents may have been designed with enhanced pathogenicity or to be vaccine escape mutants or drug resistant.

Whilst anthrax was purportedly not in the building, dispersion of anthrax spores has been well studied and serve as illustrative of the potential dispersion of pathogens. The spores are less than 3 μm in diameter and can be easily aerosolised and dispersed, especially if weaponised with the use of silica nanoparticles (4). In the real example of the Sverdlovsk anthrax accident in 1979, anthrax spores were pumped out of a Soviet bioweapons facility through an air vent, at a velocity that would have been many orders of magnitude less than a gas explosion. The high-risk zone for inhalational anthrax in Sverdlovsk was up to 4km from the building, but cases also occurred well beyond this zone (5). Modelled distances of dispersion in an aerosol attack vary from 12 to over 35 km (6). Whilst these data suggest that an explosion could propagate particles to great distances, anthrax is not transmissible from person to person, so the public health impact is limited geospatially. Within the affected area, decontamination would be a challenge because of the resilience of anthrax spores and risk of secondary aerosolization (7).

If a respiratory-transmissible pathogen such as variola were aerosolised as a result of the blast, the risk includes first generation cases among people in the building and in the immediate vicinity, but also second-generation cases in others far beyond the area of initial contamination due to transmission from person-to-person. The infectious dose of variola is very small, so large quantities of virus are not required to cause infection. Local travel could see second and third generation cases occurring beyond the affected area, in neighbouring Kazakhstan, Mongolia and China, as well as further afield globally due to air travel. Failure of diagnosis of initial cases is likely, given the remoteness of the area and the unfamiliarity of clinicians with diseases such as smallpox. We have shown that even a 1-week delay in commencing vaccination and other measures for controlling smallpox can result in a more severe epidemic, and that timely response is critical (9). Failure of diagnosis in travel-related cases has been seen recurrently with emerging infections such Ebola and MERS coronavirus, and in the last European outbreak of smallpox (8). With the long incubation periods of smallpox (12 days) and Ebola (21 days), a missed diagnosis of an index case could result in a lag period of several weeks before secondary cases become symptomatic. Through international travel and trade, this could result in cases occurring far from the accident site. A mitigating factor in this instance is that Koltsovo is in a remote part of Russia and has a small population (approximately 16,000 people), and the wider Novosibirsky District has a population of about 120,000.

Relevant to the explosion in Koltsovo is the unique propensity of variola to spread over long distances, further than can be explained by direct respiratory transmission from person-to-person. This together with the low infectious dose is a serious concern. During the final 100 years of smallpox endemicity in the world, the phenomenon of "aerial convection" was observed in many different countries and settings (10). This period, approaching eradication, had a low enough incidence of smallpox to observe unusual transmissions. Long distance transmission over distances of a mile or more was observed, in the absence of other cases of smallpox in the community in Fulham (10), England (10,11), Salonika, Greece (11), Gravesend, UK (11) and Purfleet, UK (10) as well as several other settings. In 1971, a 400g smallpox "bomb" was exploded on Vozrozhdeniye Island, a Soviet bioweapons testing site. A crew member on the Lev Berg ship, which was sailing in the Aral Sea at least 15 km from the island, became infected with smallpox (12). This suggests that an explosion could disperse variola virus at least 15 km.

We do not have the evidence or experience to dismiss the risk of this event. An explosion in a BSL 4 laboratory cannot be classified in the same risk category as misplaced biological samples, needlestick injuries or shipping errors, and the lack of epidemics arising from the latter examples is not grounds to dismiss the risk from this unique event. The building was physically breached by an explosion which would have resulted in propagation of aerosols at subsonic speeds. We do not know what equipment and materials within the building were breached. Preparedness planning principles can be applied to this event, starting with environmental testing, screening, surveillance and containment. Other considerations would be stockpiling of countermeasures for pathogens known to be housed in the building and planning for human resources and physical space for isolation of cases and quarantine of contacts (9).

Steps which need to be taken include:
1. Accounting for all pathogen samples and stocks in the building, and securing them while the building is breached (broken windows).
2. Perimeter security.
3. PPE and vaccination for all first responders at the scene.
4. Environmental testing for contamination inside and outside the building, including along the likely trajectory of propagation of the shockwave.
5. If any evidence of a breach of pathogens is present, depending on the pathogen, vaccination and/or chemoprophylaxis of staff in the building and the surrounding population should be considered. Smallpox vaccine, for example, is still effective post-exposure.
6. Quarantine of any potentially exposed people.
7. Fever screening and serial interval testing (for example by serology or throat swabs) of people in the building and surrounding area for exposure.
8. Stockpiling of medical countermeasures (drugs, vaccines, PPE, immunoglobulin) informed by the findings in 1-6 above, and plans for rapid deployment of stockpiles which are held far from the site.
9. Enhanced disease surveillance in the local area and beyond, for at least 6 months after the event.
10. Plans for physical space for case isolation and human resources capacity (for treatment of cases and contact tracing and vaccination) in the event of an epidemic.

Only the Russian government has the specific information required to inform preparedness around this event, and the rest of the world relies on prompt communication of any disease cases or clusters from Russia to prevent a pandemic arising. If classified biological research was occurring at Vector, there may be a powerful disincentive for the government to disclose disease occurrence. Other countries, especially surrounding countries, can use disease surveillance for early warning. Surveillance for disease events in the affected area and beyond is important, and there is a strong case for using sentinel syndromic surveillance and open source intelligence for sensitive, rapid detection (13). Syndromic surveillance should look for the most likely clinical syndromes arising from an emerging infection: severe acute respiratory syndrome; rash and fever (including haemorrhage); neurological syndromes (meningitis, encephalitis, acute flaccid myelitis, Guillain Barre Syndrome and neuropathy); and gastrointestinal syndromes; and unexplained deaths. Such surveillance should be commenced immediately to allow baseline data for comparison of any signals occurring in the coming weeks or months in Siberia, the rest of Russia, and neighbouring countries such as Mongolia, Kazakhstan and China. In the case of theft of biological materials, an index case may occur anywhere in the world, and in the case of engineered or synthetic pathogens, previously unknown disease syndromes may occur. The incubation periods of known diseases such as influenza, smallpox and Ebola provide a range of time periods within which first disease clusters may occur, if there has been a pathogen breach. It could be days in the case of influenza, or weeks in the case of smallpox or Ebola. A caveat to this is the dose-response relationship, as known incubation periods relate to doses of natural exposures. If abnormally high dose exposures occur, incubation periods can be substantially shorter. Any signals from syndromic surveillance should be investigated promptly. Epidemic diseases with a R0 >1 can grow exponentially, within weeks to months. Whilst we hope for the best-case scenario, and we may indeed see a best-case scenario eventuate, we must be prepared for the worst. In the event of a worst-case scenario, the earlier a breach of pathogens or an epidemic is detected, the greater the potential for mitigation and control with pharmaceutical and non-pharmaceutical measures.8

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