Public Health Reviews

Smallpox and bioterrorism

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Abstract Smallpox was declared to be eradicated on 8 May 1980, during the Thirty-third World Health Assembly. However, concerns about the possible use of the virus as a weapon of bioterrorism have increased in recent years. Governments have responded by initiating selective vaccination programmes and other public health measures. This review uses historical data from 20th century outbreaks to assess the risks to current populations (which have declining immunity) from a deliberate release of virus. The data presented supports the conclusion of a previous reviewer (Mack) that "smallpox cannot be said to live up to its reputation. Far from being a quick-footed menace, it has appeared as a plodding nuisance with more bark than bite." Its R value (the average number of secondary cases infected by a primary case) is lower than that for measles, human parvovirus, chickenpox, mumps, rubella, and poliomyelitis; only the value for severe acute respiratory syndrome (SARS) is lower. Like SARS, close person-to-person contact is required for effective spread of the disease, and exposure to the virus in hospitals has played an important role in transmission for both viruses. In the present paper the dangers of mass vaccination are emphasized, along with the importance of case isolation, contact tracing, and quarantine of close contacts for outbreak control. The need for rapid diagnosis and the continued importance of maintaining a network of electron microscopes for this purpose are also highlighted.

Keywords Smallpox/diagnosis/epidemiology; Disease outbreaks/history/prevention and control; Bioterrorism/prevention and control; Mass immunization/adverse effects; Infection control/methods (*source: MeSH, NLM*).

Mots clés Variole/diagnostic/épidémiologie; Epidémie/histoire/prévention et contrôle; Terrorisme biologique/prévention et contrôle; Immunisation de masse/effets indésirables; Lutte contre infection/méthodes (*source: MeSH, INSERM*).

Palabras clave Viruela/diagnóstico/epidemiología; Brotes de enfermedades/historia/prevención y control; Bioterrorismo/prevención y control; Inmunización masiva/efectos adversos; Control de infecciones/métodos (*fuente: DeCS, BIREME*).

الكلمات المفتاحية: الجدري، تشخيص الجدري ، وبائيات (إبيدميولوجيا) الجدري ؛ فاشيات المرض، تاريخ (سوابق) فاشيات المرض ، الوقاية من فاشيات المرض ومكافحتها؛ الإرهاب البيـــولوجي (الحيوي)، الوقاية من الإرهاب البيولوجي (الحيوي) ومكافحته؛ التطعيم (التلقيح) الجموعي، الآثار الضائرة للتطعيم (التلقيح) الجموعي ؛ مكافحة العدوى، أساليب مكافحة العدوى. (**المصدر: رؤوس الموضوعات الطبية–إقليم شرق المتوسط**).

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Introduction

On 8 May 1980, during the eighth plenary meeting of the Thirty-third World Health Assembly, the president of the assembly, Dr A-R. A. Al-Awadi, signed resolution WHA 33.3. The first two sentences of the resolution read: "Having considered the development and results of the global programme on smallpox eradication initiated by WHO in 1958 and intensified since 1967 … Declares solemnly that the world and its peoples have won freedom from smallpox, which was a most devastating disease sweeping in epidemic form through many countries since earliest time, leaving death, blindness and disfigurement in its wake and which only a decade ago was rampant in Africa, Asia and South America."

The last fatal case of smallpox in the world was that of Mrs Janet Parker, who died in Birmingham, England, on 11 September 1978, after being infected by virus that had escaped from a laboratory (*1*). We could justify writing a review of the malignant nature of the virus — exemplified by the tragic events surrounding Mrs Parker's death (*2*) — and the brilliant success of WHO in eradicating it (*3*) on the basis of marking the many years of freedom from the virus. Regretfully, that is not the purpose of this review. Concern is currently being expressed that stocks of virus may be being prepared for use as a weapon (*4*), and various countries are making contingency plans against such a possibility (*5*, *6*). The abandonment of smallpox vaccination in the late 1970s has led to a steady decline in the immunity to infection of human populations everywhere, and this has made the virus more attractive to the malevolent. It is appropriate, therefore, to review smallpox in the context of a deliberate release. Even if the probability of such an event is very low, it is fitting to remind ourselves of the lessons that smallpox teaches. They are important, and are currently relevant to other communicable diseases and their control, including, in particular, severe acute respiratory syndrome (SARS).

Historical data from smallpox outbreaks

Outbreaks of smallpox continued to occur in Europe long after the virus had ceased to circulate there naturally (*3*).

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The circumstances that led to them and the outbreak control procedures adopted were often documented in detail and described in scientific publications and reports to governments. These documents provide a detailed source of information about how the virus spread, the outcome of infection in individuals with different vaccination histories, and the effectiveness of preventive and control measures in countries with well-developed medical services. The regular occurrences of outbreaks in Great Britain during the third quarter of the 20th century led to the generation of many such reports (*1*, *3*, *7*, *8*). The status of Great Britain as a colonial power in the Indian subcontinent and Africa at the beginning of this period, and the consequent regular flow of personnel from regions where smallpox was still endemic, are sufficient to explain the frequency of virus importations, although at the end of this period the escape of virus from laboratories was also important (*1*, *8*).

The Todmorden outbreak

The Todmorden outbreak of 1953 provides an excellent example of an outbreak in a non-endemic region (*9*) and illustrates the properties of smallpox particularly well. In addition, the source of the virus was never established, so the outbreak also serves as a model for an unannounced, deliberate release of a small amount of virus. In 1953 Todmorden was a town of 19 000 inhabitants, and its main industry was the spinning and weaving of cotton. Its location at the confluence of three valleys in the Pennine Hills placed it roughly mid-way and 30 km from each of two major northern English conurbations: Manchester to the west and Leeds-Bradford to the east. The last fatal case of smallpox in Todmorden was in 1893, and there had been no cases recorded since the 1920s. About 20% of infants were vaccinated during the period 1947–52, 40% in 1947, the last complete year of a "compulsory" vaccination policy, and 14% in 1948. It was estimated that about half the adult population had been successfully vaccinated at some time during their lives, usually in infancy or early childhood.

The first identified person with smallpox in 1953 recovered without being diagnosed. J., who worked at a spinning mill, had been vaccinated in infancy and revaccinated twice, most recently during the 1914–18 war. In mid-February he had developed a rash on his forehead and arms, but did not consult a doctor. He infected his wife and three workers at the mill (H., A.J., and N.) with whom he had intermittent contact. Two of these people died undiagnosed; for the other two, smallpox was only recognized very late and only after they had infected others with whom they had had contact. On 2 March J.'s wife was admitted to hospital with a three-day history of anorexia, vomiting, abdominal discomfort, fever, and toxaemia, and died four hours later. Her death was thought to be from "toxaemia due to acute enteritis". H. fell ill on 26 February. He developed headache, backache, vomiting, and a blotchy red rash, and died on 3 March. Following a postmortem examination, he was diagnosed as having had bronchopneumonia, and was subsequently cremated. Fourteen days after the start of his illness his son and daughter, who had looked after him during his illness, fell ill with "influenza". Both had been vaccinated years previously; neither developed a rash but their post-illness serology was strongly suggestive of recent smallpox. H. also infected T.B., who died with a petechial rash — diagnosed as severe scarlet fever — 24 hours after admission to an infectious diseases hospital. T.B. infected his wife and two paediatric patients in the hospital.

A.J. developed severe malaise, frontal headache and fever, and a herpetic lesion on his upper lip. Two days later "red pimples" appeared on his face and lower arms and he vomited blood. His general practitioner had at one time been a resident physician in a smallpox hospital but rejected a diagnosis of smallpox because of the lesion and the timing of the appearance of the generalized rash. A dermatologist made a provisional diagnosis of generalized herpes and A.J. was admitted to a district general hospital. Discussions with a virologist led to a smallpox expert being called in and A.J. was transferred to a smallpox hospital on the same day. During his 7 hour stay in the first hospital A.J. infected three patients in nearby beds and an ambulant patient. At home he had infected his wife, his daughter, and three visitors who had come to visit him in his bedroom on the two days before his admission to hospital. One had been there for only a few minutes.

N.'s illness came to light after a search for adult and atypical cases of chickenpox by the local public health department using general practitioners. He had been vaccinated as an infant and during the 1914–18 war. He developed severe malaise and fever and a rash over the forehead, chest, and arms. By the time his case had come to light, he had recovered and was preparing to return to work. His wife was ill, however, with headaches, backache, and vomiting. She developed an erythematous rash and died of fulminant smallpox. Of the other members of the N. household, one unvaccinated son and an unvaccinated lodger died of smallpox; a recently vaccinated son escaped infection and another unvaccinated son recovered after being infected.

Other cases were undoubtedly part of the outbreak, although their route of transmission was never established. For example, a porter who worked in the postmortem room at the City of Leeds Public Mortuary pricked his finger while handling a body; a deep nodular lesion developed in the pulp and nine days later he developed a rash and a fever. The body was that of Mrs B., who had fallen ill two days before her death with a violent headache, backache, and vomiting, with some fever. At postmortem the only abnormalities were small laryngeal and subpericardial haemorrhages. A diagnosis of acute leukaemia was made on the basis of a blood film. The son and daughter of the porter were the last cases in the outbreak; both recovered, although the daughter was left with severe scarring.

Difficulties in diagnosing smallpox

The Todmorden outbreak illustrated particularly well the difficulties that attended the diagnosis of smallpox in non-endemic areas in pre-eradication times. Essentially, because the disease was not thought to be occurring in the country, its diagnosis was not entertained. This is understandable in the cases that developed suddenly, which lacked obvious smallpox-specific features, but is less so in others. For example, a doctor with extensive experience of smallpox considered A.J.'s rash to be herpetic. Evidently, the same problem of misdiagnosis could occur in cases resulting from an unannounced deliberate release of virus today. The diagnostic difficulties enumerated in Ricketts & Byles' classical early 20th century textbook on smallpox (*10*) were due to virological characteristics that have not changed in the succeeding years. Their statements that "two thirds of the errors in the diagnosis of smallpox arise from its confusion with chickenpox" and "in every epidemic cases arise at intervals in which the eruption is so highly modified and the character of the lesion is so anomalous that there is an inadequate basis for diagnosis" are still relevant. Even when smallpox was being regularly imported into Britain it was often misdiagnosed; thus,

in describing an outbreak in the English midlands in 1947 Simpson Smith (*11*) concluded that "once again an outbreak of smallpox followed a confident diagnosis of chicken-pox by competent experts. This also occurred in 1947 at Scunthorpe; in the Middlesex outbreak of 1944, the Edinburgh outbreak of 1942 and at Birkenhead in 1946."

What other lessons can be drawn from the Todmorden outbreak? Lyons & Dixon (*9*) pointed out in their account of the outbreak that classical epidemiological methods were only partly successful in tracking the spread of virus: "there were at least five known cases where infection occurred in individuals who in spite of most heroic investigations could be found to have no known connection with any other case." Nevertheless, they concluded that "in spite of many opportunities the spread of infection was more limited than is usually assumed. High attack rates only occurred in very close contacts, in the family, among personal friends, or close contacts at work." Their figures show that of 39 cases in total, 17 people contracted their infections in the domestic setting — of these, 13 were family members or lodgers and four were visitors to the sickroom.

Similar findings were made in the classical studies of smallpox in Punjabi villages by Mack and his colleagues in 1967 and 1968 (*12*, *13*). The villagers probably had similar levels of immunity to those of Todmorden in 1953; transmission within the home was so effective that the secondary attack rate among unvaccinated household members was 88%. Another kind of "sickroom" transmission not commented on by Lyons & Dixon but very evident from their account were the infections contracted in hospital or by health care workers. Six hospital patients, the postmortem room porter and two general practitioners who had attended A.J. and N. fell into this category. Mack's review of smallpox in Europe 1950–1971 (*14*), which considered 45 importations of Variola major, showed that transmissions in hospital far outnumbered those in any other category. Of the 680 cases, 339 people contracted the disease in hospital — 128 of these were staff, 193 were inpatients and 18 were outpatients, visitors, or in other hospital-related categories. Twenty other cases in laundry and mortuary workers were also occupational. Family and other intimate contacts accounted for 147 cases; only 63 cases were infected by casual contacts. Forty-four were classified as "unpredictable".

The abandonment of vaccination — its effect on outbreak size

The eradication of the virus means that evidence from well-studied outbreaks like Todmorden and detailed investigations like Mack's in the Punjab must form the basis of our understanding of the natural history of smallpox. But the smallpox vaccination of civilian populations stopped more than a quarter of a century ago, and so the outstanding question for policy-makers is what effect the consequent increase in the proportion of non-immune individuals will have on the size of an outbreak and the ability to control it. The important factor is R, the effective reproductive rate — that is, the average number of secondary cases infected by a primary case. Gani & Leach (*15*) have used historical data to estimate R to be between 3.5 and 6 for isolated pre-20th century populations with negligible herd immunity. For 30 European smallpox importations between 1958 and 1973 they estimated R to be about 5.5 for community-acquired disease; it doubled when hospital-acquired cases were included. They concluded that, under contemporary conditions in industrialized countries with low (18%) levels of herd immunity, R values would not be significantly different. Their quantitative demonstration of the importance of spread in hospitals strongly reinforces the conclusion of Mack and colleagues from their Punjabi study, which showed large variations in viral attack rates in villagers, despite their immune status being remarkably uniform, "that systematic factors other than 'herd' immunity must be important in determining the extent of spread." Because of the importance of spread in homes, contemporary trends in reductions in household size would probably reduce R for community-acquired disease, and increase the relative importance of hospitals.

An R value of 5.5 means that until the imposition of control measures, the number of cases in a given outbreak will grow exponentially. It also explains why early public health interventions had a big effect in limiting outbreak size, and, indeed, why the WHO eradication programme succeeded as quickly as it did. These things happened because R was low, being smaller than estimated values for measles, human parvovirus infections, chickenpox, mumps, rubella, and poliomyelitis (*16*).

Smallpox, bioterrorism, and government responses

In 1972 Mack concluded in his review of post-1949 smallpox in Europe (*14*) that "under contemporary conditions smallpox cannot be said to live up to its reputation. Far from being a quick-footed menace, it has appeared as a plodding nuisance with more bark than bite." Why, then, is smallpox currently regarded as a credible biological weapon and why are governments making contingency plans for its possible use? One reason is that its bad reputation persists. Thus, its case-fatality rate is very high (*3*), no therapeutic regime has ever been shown to be life-saving, and deliberate spread by aerosol is theoretically possible. It is not unreasonable, therefore, for the public to expect action to be taken once the prospect of possible malevolent use has been raised, even if the likelihood of an outbreak is remote. But Mack's review (*14*) showed that the length of post-1949 European outbreaks was weeks rather than months or years, that their size was in single figures or tens rather than hundreds or thousands, and that more than three quarters of the outbreaks ended with the generation being infected immediately after the detection of smallpox. Case-finding, isolation, and ring vaccination worked in populations in which well over half the individuals were susceptible to infection and in countries where most of doctors' lifetime experience of smallpox was only a lecture during their student days.

Since eradication, however, our memory of smallpox as a clinical entity, our technical ability to diagnose it, and our stocks of vaccine have all further decayed and declined. The USA takes the smallpox risk seriously enough to have established a programme to remedy these deficiencies (*5*). Vaccine is being purchased, vaccinia immune globulin prepared, clinicians educated, contingency plans for outbreak control re-established, and key staff, particularly hospital workers, immunized. More limited plans to control outbreaks have also been developed in the United Kingdom. Are these measures necessary? The virus no longer exists in nature and the evidence that stocks are held anywhere outside the two official repositories

at the Centers for Disease Control and Prevention in Atlanta and Novosibirsk (*4*) is purely speculative. The writer's personal experience of handling the virus supports the view that growing large amounts, while not very difficult, would be a much more challenging task than preparing weapon-grade anthrax, whose spores have the added advantage of being many orders of magnitude more stable in the environment (*17*, *18*). There is no unequivocal evidence that the aerosols of smallpox exhaled by patients, which can contain high concentrations of virus in optimal condition for transmissibility, carry infection further than a few metres (*3*). None of these factors favour smallpox as a weapon of mass destruction, but none of them rule it out as a weapon that — even if only lethal to a few — is still so feared that even a small deliberate release would cause enormous panic and have a political impact totally out of proportion to its size.

The measures taken in the US and the UK will undoubtedly re-create systems that would control an outbreak caused by a deliberate release of virus. Awareness of contingency plans may even reduce the likelihood of such an event by discouraging possible perpetrators. By raising public confidence in the ability of government agencies to protect public health, panic may be averted as well. It will enable logical arguments to be produced, based on measures already in place, to resist calls for mass vaccination, which, because of the complications caused by the vaccine should only happen if control of an outbreak has been completely lost (*19*). The New York outbreak of 1947 (*20*) and the importations of virus into England and Wales in December and January 1961–62 (*7*) are instructive. The index case in New York infected seven hospital patients, one of whom infected three others in a convalescent home, and another who infected his wife. Only three of the twelve patients had been vaccinated. Despite this, only two of them died, including one vaccinee, the index case. Following a call from the Mayor, 6 350 000 New Yorkers were vaccinated. At least three died from the effects of the vaccine. Between 16 December 1961 and 12 January 1962 five air travellers from Pakistan to the UK developed smallpox; they had probably contracted it in Karachi, where an epidemic was in progress. After arriving at Heathrow airport they dispersed to major population centres; one remained in London, two travelled to different parts of Birmingham, one went to Bradford, and one to Cardiff. Between 11 January and 15 April 62 indigenous cases of smallpox were recognized, 16 in England and 46 in Wales; 40 were of infections in hospital patients or staff, and 24 were fatal. Owing to public demand many more individuals were vaccinated than were thought necessary on epidemiological grounds, including the whole population of Bradford (250 000) and 900 000 people in South Wales. Vaccination complications killed at least 15 people.

What is to be done?

During the second half of the 20th century there was a consensus among smallpox experts that "the control of smallpox in non-endemic areas where importations may occur depends largely on epidemiological control with isolation of cases and vaccination of contacts" (*19*). The 1975 "Memorandum on the Control of Outbreaks of Smallpox" for England and Wales (*21*) said "prompt isolation of cases, combined with a policy of vaccination or re-vaccination of all contacts and the subsequent surveillance of (known or probable close) contacts will usually suffice to control an outbreak of smallpox which has been detected at an early stage. In such circumstances the hasty vaccination or re-vaccination of a large proportion of the local population … is to be deprecated because the risk of complications of vaccinations may well exceed the risk of contracting smallpox." These principles are still valid today. Early mass vaccination is not recommended by smallpox experts (*22*). However, some mathematical modellers claim that in most contemporary situations it would control outbreaks more rapidly than isolating the infected with ring vaccination around them (*23*). But some historical data does not support this view. In Scotland (*24*), for example, vaccination policy remained unchanged between the Vaccination (Scotland) Act of 1863, which made infant vaccination compulsory, with penal sanctions for failure, and the 1907 Vaccination (Amendment) Act, which allowed conscientious objection. Successful vaccinations during this time never fell below 90%. But smallpox was endemic in the country until 1904; after that time it became a largely imported disease. Its decline coincided with much more aggressive efforts to find cases and isolate them in the new isolation hospitals whose construction had been facilitated by the Public Health (Scotland) Act of 1897 (*25*). Past experience also indicates the importance of the early detection of smallpox infection. Because of the bioterrorist threat, clinicians have to return smallpox to the list of possible — if highly unlikely — diagnoses in cases of unexplained haemorrhagic fevers, severe backache with other general symptoms, and even "chickenpox" in adults. But the laboratory is needed for a definitive diagnosis. Assays for the presence of virus using the polymerase chain reaction have been developed (*26*). However, the only rapid test validated by use on material from patients with smallpox is electron microscopy. It played a vital role in diagnosis in the 1960s and 1970s (*1*, *8*). Unfortunately, in countries like the United Kingdom the network of microscopes and the expertise of their operators is in terminal decline. The writer agrees wholeheartedly with Madeley (*27*) that the reversal of this process should be given high priority.

In 2003 smallpox has been joined by SARS as a pathogen for which case isolation and quarantine of close contacts are effective control measures. Both pathogens have low R values; for SARS R has been estimated to range from 2.2 to 3.7 (*28*, *29*). For both pathogens, hospital exposure has played an important role in transmission. In Hong Kong, for example, after excluding the two "super spread" events, at the Prince of Wales Hospital where the index patient infected at least 125 people and at the Amoy Gardens estate where faecal spread was thought to have occurred, it accounted for 19% of cases (*28*).

Systems set in motion to renew traditional measures of infection control because of worries about smallpox now have added weight. They are appropriate not only as a response to a hypothetical threat, but also to a real one. ■

Conflicts of interest: non declared.

Résumé

Variole et bioterrorisme

La variole a été déclarée éradiquée le 8 mai 1980 pendant la Trente-Troisième Assemblée mondiale de la Santé. Ces dernières années, cependant, la crainte de voir le virus utilisé comme arme par des terroristes s'est amplifiée. Dans cette perspective, des gouvernements ont mis en place des programmes de vaccination sélectifs et adopté d'autres mesures de santé publique. Sur la base des données relatives aux flambées enregistrées au XXe siècle, le présent article évalue les risques auxquels seraient aujourd'hui exposées les populations (dont l'immunité est en baisse) en cas de propagation délibérée d'un virus. Les données présentées corroborent les conclusions d'une précédente étude (Mack) selon lesquelles « La variole a une réputation usurpée. De même que pour un chien qui aboie mais ne mord pas, il semble qu'on lui ait prêté une capacité de nuisance démesurée. » Dans le cas de la variole, R (nombre moyen de cas secondaires contaminés par un cas primaire) est moins élevé que pour la rougeole, le parvovirus humain, la varicelle, les oreillons, la rubéole et la poliomyélite ; seul le syndrome respiratoire aigu sévère (SRAS) a un taux inférieur. Comme pour le SRAS, la contamination n'intervient qu'entre des personnes ayant eu des contacts rapprochés et l'exposition en milieu hospitalier a joué un rôle important dans la transmission de ces deux virus. L'article insiste sur les risques associés à la vaccination de masse et sur la nécessité, pour endiguer les flambées, d'isoler les cas, de rechercher les contacts et d'isoler les contacts proches. La nécessité de poser un diagnostic rapide et de continuer d'entretenir un réseau de microscopes électroniques à cet effet est également soulignée.

Resumen

Viruela y bioterrorismo

El 8 de mayo de 1980 la 33ª Asamblea Mundial de la Salud declaró la erradicación de la viruela. Sin embargo, la inquietud por el posible uso del virus como arma bioterrorista ha aumentado en los últimos años. Los gobiernos han respondido lanzando programas de vacunación selectiva y otras medidas de salud pública. En el presente análisis se utilizan datos históricos sobre los brotes del siglo XX para evaluar los riesgos que una liberación deliberada del virus supondría para las poblaciones actuales (que tienen una menor inmunidad). Los datos presentados respaldan la conclusión de un experto anterior (Mack) de que "no puede decirse que la viruela esté a la altura de su reputación. Lejos de ser una amenaza versátil, constituye una pesada molestia que ladra más que muerde". Su valor R (promedio de casos secundarios infectados por un caso primario) es menor que los del sarampión, el parvovirus humano, la varicela, la parotiditis, la rubéola y la poliomielitis; sólo el valor correspondiente al síndrome respiratorio agudo severo (SRAS) es inferior. Como en el caso del SRAS, para que la enfermedad se propague eficazmente se requiere un contacto estrecho de persona a persona, y la exposición al virus en los hospitales ha tenido un papel importante en la transmisión de esas dos enfermedades. En este artículo se resaltan los peligros de la vacunación masiva, así como la importancia del aislamiento de los casos, el rastreo de contactos y la cuarentena de los contactos cercanos para lograr controlar los brotes. Se destaca asimismo la necesidad de un diagnóstico rápido y la continua importancia de mantener una red de microscopios electrónicos con esa finalidad.

ملخص

الجدري والإرهاب البيولوجي (الحيوي)

الملخص: أعلنت جمعية الصحة العالمية الثالثة والثلاثون عن استئصال الجدري في الثامن من آيار/مايو ١٩٨٠. غير أن القلق من إمكانية استخدام فيروس الجدري كسلاح للإرهاب البيولوجي تزايد في السنوات الأخيرة. وقد استجابت الحكومات بالبدء في تنفيذ برامج تمنيع منتقاة وباتخاذ تدابير أخرى لحماية الصحة العمومية. وتُستخدم في هذه الدراسة المعطيات التاريخية الخاصة بفاشيات الجدري في القرن العشرين بغرض تقييم المخاطر المحتملة على السكان الحاليين (الذين ضعفت مناعتهم) من جراء الإطلاق المتعمد للفيروس. وتعزز معطيات هذه الدراسة النتيجة التي توصَّل إليها ماك وهو أحد النقاد من أنه "لا يمكن أن نزعم أن الجدري سيسلك السلوك المتوقع منه. فبالرغم من أن الجدري خطر سريع الخُطى، إلا أنه ظهر في شكل حيوان مزعج بطيء الخطى، ينبح أكثر مما يعض". وتقل قيمة معامل المقاومة للجدري (والذي يمثِّل العدد المتوسط لحالات العدوى الثانوية التي تنجم عن حالة العدوى الأولية) عن قيمة معامل المقاومة للحصبة، والفيروسة البشرية الصغيرة، والخُماق، والنكاف، والحصبة الألمانية، وشلل الأطفال، ولكنها تزيد على قيمة معامل المقاومة لمتلازمة الالتهاب التنفسي الوخيم فقط. ويتشابه الجدري مع مرض الالتهاب التنفسي الوخيم في ضرورة حدوث اتصال مباشر بين شخص وآخر حتى ينتشر المرض بشكل فعال، وفي أن التعرض للفيروسين في المستشفيات يؤدي دوراً مهماً في انتقالهما. وتؤكد هذه الدراسة على مخاطر التلقيح (التطعيم) الجموعي، وعلى أهمية عزل الحالات المصابة بالعدوى، وتتبُّع المخالطين، ووضع المخالطين المباشرين للمريض في الحجر الصحي تجنباً لتفشي العدوى. كما تؤكد هذه الدراسة على ضرورة التشخيص السريع للحالات، وعلى أهمية توافر شبكة من المجاهر الإلكترونية بشكل مستمر لضمان سرعة تشخيص حالات العدوى.

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