Mass psychogenic illness following tetanusdiphtheria toxoid vaccination in Jordan

Saad Kharabsheh, ¹ Haidar Al-Otoum, ² John Clements, ³ Adnan Abbas, ⁴ Najwa Khuri-Bulos, ⁵ Adel Belbesi, ⁶ Taky Gaafar, ⁷ & Nora Dellepiane ⁸

Abstract In September 1998, more than 800 young people in Jordan believed they had suffered from the side-effects of tetanus-diphtheria toxoid vaccine administered at school; 122 of them were admitted to hospital. For the vast majority, their symptoms did not result from the vaccine but arose from mass psychogenic illness.

The role played by the media, the children's parents, and the medical profession in the escalation of this mass reaction appeared, at first sight, to be unusual and even unique to the circumstances in Jordan at the time. A review of the literature showed, however, that this mass reaction was similar in many ways to previous outbreaks, even though the underlying causes varied. There are about 200 published accounts of mass responses to situations involving suspected poisoning or other events. Because such mass reactions are relatively rare and the triggers so diverse, individuals faced with responding to them are unlikely to have prior experience in how to handle them and are unlikely to take bold steps to prevent their escalation. Indeed they may be unaware that such events have been recorded before. The lessons learned from this incident in Jordan may help other immunization programme managers to handle crisis situations elsewhere.

Keywords Diphtheria-tetanus vaccine/adverse effects; Psychophysiologic disorders/epidemiology; Hysteria; Students; Jordan (*source: MeSH*).

Mots clés Vaccin antidiphtérique antitétanique/effets indésirables; Troubles psychophysiologiques/épidémiologie; Hystérie; Etudiant; Jordanie (*source: INSERM*).

Palabras clave Vacuna contra difteria-tétanos/efectos adversos; Trastornos psicofisiológicos/epidemiología; Histeria; Estudiantes; Jordania (*fuente: BIREME*).

Bulletin of the World Health Organization, 2001, **79**: 764–770.

Voir page 769 le résumé en français. En la página 770 figura un resumen en español.

Introduction

The Expanded Programme on Immunization in Jordan was founded in 1979 and has developed into a mature and sophisticated immunization service. Coverage for vaccine-preventable diseases has been high and the population has participated enthusiastically. Since 1992, tetanus-diphtheria toxoid vaccine

Ref. No. **99-0271**

(Td) has been administered to all children in first grade (at the age of 7 years) and again in tenth grade (at the age of 15 years). In September 1998, the annual process of immunizing children in school started again, coinciding with the start of the school year. Vaccine coverage was very high: the number of doses administered during September 1998 is shown in Fig. 1. The number of classes participating gradually rose as the programme gathered momentum.

Until 27 September 1998, there had been no reports of adverse events during the Td vaccination programme. However, during the morning of 29 September 1998, 80 students were taken to hospital in Amman, apparently suffering from the effects of the vaccine. By the end of the following day, 122 vaccinated students from all over Jordan had been admitted. The unusual and varied reasons for this outbreak of adverse events following immunization are discussed below.

Sequence of events

The first suspected cases of adverse events following immunization occurred at Eben-Al Abas School in

¹ Director General, Primary Health Care, Ministry of Health, Amman, Jordan

² National Programme Manager, Ministry of Health, Amman, Jordan.

³ Medical Officer, Expanded Programme on Immunization, World Health Organization, 1211 Geneva 27, Switzerland. Correspondence should be addressed to this author.

⁴ Professor of Community Medicine, Jordan University, Amman, Jordan.

⁵ Professor and Head of Pediatric Diseases, Jordan University Hospital, Amman, Jordan.

⁶ Director of Disease Control, Ministry of Health, Amman, Jordan.

⁷ Regional Adviser for the Expanded Programme on Immunization, World Health Organization Regional Office for the Eastern Mediterranean, Alexandria, Egypt.

 $^{^{\}rm 8}$ Technical Officer, Vaccines and Biologicals, World Health Organization, Geneva, Switzerland.

Amman. On the morning of 29 September 1998, all 160 tenth-grade students were immunized with the Td vaccine. Two students felt faint during the session and were seen immediately by the doctor. They were soon well enough to return to their class. The vaccination session was carried out in the school library, with groups of 10 students being immunized at a time. The vaccination team left the school at the end of the session with no concerns. During the evening of the same day, several students felt unwell at home: they developed headaches and dizziness, but none was seriously ill.

All the students arrived at school the following day at the normal time of 0645. One of the boys who had been ill the previous night stumbled and fell as he came through the school gates, cutting his lip. The staff were alarmed, suspecting that he had fallen because he had fainted, and he was taken to hospital. At that point, the vaccine was not thought to be involved. A short while later, another boy who had also been ill in the night felt faint in the school grounds before going to his classroom. By 0730, around 20 other students had complained of feeling ill or had fainted.

Response to the index cases

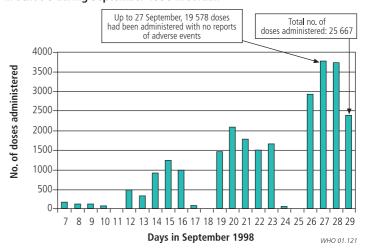
The teachers became alarmed, thinking it was the start of a disease outbreak. They called the civil defence ambulance and emergency team as the Ministry of Health had not yet opened. The team arrived at 0730 and began questioning the students and teachers in order to determine if there was an infectious basis for the illness. They initially suspected contamination of food or water but only one age group was affected and students who had not been vaccinated the previous day were not ill. They came to the reasonable conclusion that the sickness was due to the vaccination. As they assumed that they were dealing with a serious situation affecting an increasing number of individuals, and as some of the students were thought to be quite ill, they began sending them to hospital by ambulance, the first arriving by around 0800.

Effects beyond the school setting

At this point, information about the events was beginning to spread beyond the school, relayed perhaps by parents or anxious teachers. Television and newspaper staff appeared rapidly on the scene, disseminating the story by real-time television and radio coverage throughout the country and beyond.

The Ministry of Health was informed and quickly dispatched staff to the school. The Education Minister visited the school and at noon all schools in the country were told to stop using the vaccine. The Health Minister made a statement that was transmitted nationwide on the 1900 television news, announcing that any student with side-effects from the Td vaccine should be admitted to hospital for observation. He also mentioned his intention to form an investigation committee.

Fig. 1. Number of doses of tetanus-diphteria toxoid vaccine administered in schools during September 1998 in Jordan



Clinical aspects

At the hospital, the staff described the first cases as being sick enough to justify admission. All students who arrived at hospital after the ministerial statements were admitted if they had been vaccinated the day before, regardless of clinical assessment. (No criticism of the decision to admit students on this basis is intended by the authors.) In total, 55 students, all aged 15 years, from the index school were admitted to hospital. Following the minister's announcement, students from schools in other parts of Jordan were also admitted during 29–30 September.

Those admitted from the index school had the most severe adverse events (see Table 1). In retrospect, these symptoms were probably a mixture of genuine side-effects from the Td vaccine and those psychologically induced. The casualty officer treated the early arrivals with hydrocortisone and antihistamines before the chief of service was able to see them, after which time the treatment was more conservative.

The case investigation carried out by the Ministry of Health some days later revealed that 61.5% of all students identified throughout the country suffered systemic reactions (fever, headache, malaise, nausea, dizziness, arthralgia); 5.7% had local reactions (pain, swelling, erythema); and 32.8% experienced both systemic and local reactions. Not unexpectedly, the symptoms seemed to mirror those found in previous studies of adverse events to diphtheria-tetanus-pertussis vaccination. However, the students admitted to hospital represent a biased sample and showed a disproportionate level of systemic reactions (93.5%). Routine laboratory investigations of blood samples taken on admission to hospital gave results that were within the normal limits. About 70% of the students were admitted to hospital for 24 hours or less; the rest were discharged within 48 hours, there being no deaths or sequelae. One student needed treatment for an injection-site abscess. Of those admitted, 63% were male.

Table 1. Symptoms in the 55 vaccinated students admitted to hospital from the index school

-7	of vaccinated ents affected
Pyrexia more than 38.0 °C	24
Pyrexia more than 38.5 °C	8
Hypotension	1
Chest tightness (needed oxygen)	21
Chilliness	33
Feeling faint	12
Electrocardiogram changes (these were normal by the next day)	7

Official investigation

The Communicable Disease Directorate and the immunization programme manager, who were empowered to react appropriately, began a case investigation of the events which occurred on 29–30 September 1998. A questionnaire was sent to each school governerate and staff visited all schools in the country that had administered the Td vaccine between 7 and 29 September 1998. They interviewed 25 667 students from 502 classes, looking for students who had suffered adverse events. In this way 806 cases were detected and the information was submitted to the Ministry of Health in Amman. Data from the questionnaires were analysed by EpiInfo.

Questionnaire design

The questionnaire asked about the types of symptoms that had been seen in the initial group of affected students, including questions about whether there had been local or systemic reactions. No case definition was created before the questionnaire was dispatched. Information on the pre-existing background rates or the nature of adverse events following immunization was not available as there was no such routine surveillance system at that time. Students were included in the survey if they had received the Td vaccine during September 1998 and had experienced any adverse signs or symptoms following vaccination. All signs and symptoms, as described by the students, were recorded. For instance, if the students said they had experienced fever, this was recorded on the form and counted as an adverse event, even if the student's temperature had not been taken.

Factors which may have lessened the validity of the survey included subjective assessment of symptoms; bias in the data, as the events occurred within days of a major media event and thus every student knew that the vaccine had been implicated by the media; lack of a pilot survey and lack of training for staff carrying out the survey, due to insufficient time; reliance on recall of events over the previous 30 days; and possible inaccurate reporting by these young students.

Analysis of survey data

For the reasons described above, the reliability of the data derived from the questionnaire is limited. While probably overestimating the overall rates of adverse events, the data nonetheless demonstrate that the rates were in the generally accepted normal range for Td vaccinations (1). They also indicate that it is likely that one batch of vaccine (lot 36) may have provoked a higher rate of adverse events than the other batches in use over the same period. Exactly what that high rate was is difficult to say, although from the survey data, it was 20.8% in tenth-graders, double that of any other batch in use (Table 2). Even so, this rate was within the expected range for adverse events and was not in itself a cause for alarm.

Of the 806 cases identified in the survey, 122 were admitted to hospital. On the face of it, this appeared to be not only a very large outbreak, but also one involving serious, possibly life-threatening, reactions. The reality was, in fact, quite different. The index cases were few in number, and had they presented in isolation, it is doubtful whether many would have been admitted to hospital. This was confirmed later by the investigating committee: the paediatrician at the University Hospital felt that only the first 5 to 10 cases warranted admission.

One of the dangers of implementing immunization schedules where large numbers of doses are given over a short period of time is that more adverse events appear to occur, simply because more doses are given over a short interval. So while the actual rate remains unremarkable, the sheer numbers involved during that period produce a "clustering" effect. So it was in this outbreak in Jordan: not only were the cases clustered in time but also in space.

Were the affected students highly immunized?

There is anecdotal evidence that some students may have received more doses of tetanus or diphtheria toxoid than they should have. However, there is no evidence that the clinical signs and symptoms of the large numbers of students admitted to hospital in this outbreak were due to hypersensitivity reactions.

Was the vaccine at fault?

If the vaccine had contained an excessively high amount of antigen from the diphtheria or tetanus toxoid, or both, or had been contaminated in some way, this could have provoked adverse events. Lot 36 produced a higher rate of adverse events than the other lots in use. The batch documentation indicated that its antigenic content was 10 Lf (limit of flocculation) units for the tetanus toxoid component and 5 Lf units for the diphtheria component — not unusually high Lf contents — and was similar to a number of other Td vaccines on the market. The values were well within the WHO recommended limits (2). A careful review of the production protocol and quality control documentation was made: no abnormality was detected. On the contrary, the vaccine was endorsed by WHO.

0.6

0.4

3.1

Vaccine lot No. of students No. of vaccinated students Overall % of vaccinated administered vaccinated with adverse events^a students with adverse events First grade Tenth grade First grade Tenth grade Undefined 725 491 1 (0.1)b 10 (2.0) 0.9 8229 4915 26 (0.3) 133 (2.7) 1.2 36 689 1345 9 (1.3) 280 (20.8) 14.2 37 1935 1903 48 (2.4) 201 (10.6) 6.4 41 1008 532 23 (2.3) 56 (10.5) 5.1

3 (0.2)

0(0)

110 (0.8)

547

1543

11 276

Table 2. Numbers of vaccinated students and adverse events by school grade and vaccine lot number

42

48

Totals

The same lot of Td vaccine was distributed to two other countries. No complaints were received by UNICEF following its use in these countries. Fortuitously, a study of the vaccine was already under way in one of the countries: the rates of adverse event were within the expected limits.

1494

310

14 391

The investigation committee concluded that there was no abnormality in the vaccine lots. However, use of a Td vaccine with a diphtheria toxoid level below 5 Lf units may reduce the rates of adverse events (3).

Was the vaccine administration technique at fault?

A WHO-supported review of vaccine administration in Jordan reported in October 1998 (4) that there were no programmatic errors observed by staff receiving, storing, transporting, collecting, distributing, preparing, or administering the vaccine. All staff interviewed and observed while performing these tasks were found to be competent. It was therefore considered that improper administration of vaccine did not account for the outbreak.

Were the adverse events limited to one or more lots of Td vaccines?

Table 3 shows the geographical distribution of the occurrence of adverse events following the use of six batches of Td vaccine from 29 September to 5 October 1998 in Jordan. Although most cases occurred in Amman and Zarqa, a number of batches were used in both locations. Without doubt, hospital admission followed administration of all six batches. This is not indicative of characteristics of the vaccines per se, but reflects the wider social situation at the time. However, it is interesting to note that the two schools in Amman with the most cases had both administered lot 36. Although all six batches of Td vaccine produced adverse events, with no particular pattern emerging from the geographical distribution of cases, administration of lot 36 was associated with many of the index cases.

Was administration of the vaccine just a coincidence?

9 (1.6)

7 (0.5)

696 (6.2)

The possibility was explored that the signs and symptoms experienced by some of the vaccinated students were unrelated to the vaccination. Did these index adverse events occur coincidentally with some unknown event or common environmental factor? Had the students eaten or drunk something that affected them? There were no symptoms such as diarrhoea or vomiting to support either hypothesis. The drinking-water supply was checked and found to be free of contamination. The only students affected were those who had been vaccinated the previous day; children not vaccinated were not affected.

Chain reaction causing the outbreak of adverse events

A background of distrust

Before the outbreak, there had been a strong antigovernment feeling related to the public water supply: this was to have a very negative impact on subsequent events. In the period immediately preceding the outbreak, there had been debate in the press about the reputed contamination of Jordan's water supply. This was felt by some to be injurious to the health of the nation's children. The outbreak of adverse events following Td vaccination followed hard on the heels of this discontent, with the press reporting that students had been admitted to hospital, reportedly suffering from the effects of a "bad vaccine". Thus the background mood was one of suspicion. A number of negative rumours concerning the immunization programme were also circulating at the time of the outbreak.

Reaction of students and teachers

At the index school, students may have been frightened to see their fellow students fall and receive

^a The adverse events were self-reported.

^b Figures in parentheses are percentages.

Table 3. Number of vaccinated students affected, by district and vaccine lot, 29 September–5 October 1998

District	No. of vaccinated students with adverse events $n=806$	No. of vaccinated students admitted to hospital $n = 122$	Vaccine lot administered
Ajloon	1	1	05, 41, 48
Amman	137	64	05, 36, 37, 48
Aqaba	52	7	37
Balqa	43	5	05, 36, 37, 48
Irbid	97	22	05, 41
Jarash	55	3	05
Karak	98	5	41
Ma'am	0	0	37
Madaba	0	0	05
Mafraq	0	0	05, 42
Tafileh	5	5	41
Zarqa	275	10	05, 36, 37, 42
Other	43	NAª	NA

^a NA = not available.

urgent medial attention. The teachers were alarmed at the events unfolding before their eyes and they called for help from the only service available to them at that time in the morning. Within 45 minutes of starting school, a civil defence team was called in and more and more students felt ill. Although these students had received the vaccine at the same time the previous day, it is unlikely that severe symptoms would have struck different students at almost the same minute: a psychological component is almost certain to have played a part. Teachers at the index school reported that some students laughed as they queued up to be examined, hoping for a ride to hospital rather than having to endure a day at school. One member of the hospital staff reported that it was difficult to discharge some students because they were enjoying their stay so much.

Reaction of officials

The well-meaning Ministers of Education and Health and civil defence team responded in the best way they could under the circumstances, but in their desire to prevent the spread of an outbreak, they actually contributed to it. The education and health officials were faced with several difficult decisions: to continue vaccinating when circumstantial evidence pointed to a contaminated vaccine would have been professional suicide. The ministries took the only course open to them: to stop vaccination and assure the public that a full investigation would follow.

Reaction of the media

Television, radio, and newspaper coverage of the events of 29 September 1998 played a crucial role in how the outbreak spread. Because media coverage was almost instantaneous and occurred throughout the country, a large proportion of parents, teachers, and health care staff were alerted to the situation

within hours. Unfortunately, because of the complex nature of the events, only a relatively superficial — and, as it turned out, misleading — account was broadcast. As far as the public was concerned, a faulty and dangerous vaccine had been used. It is likely that far more students were encouraged by their parents to seek health care than would otherwise have done so without the publicity. Against a background of public distrust of the government's handling of the water contamination scare immediately preceding this, the media were presented with an irresistible opportunity to report a real-life drama with strong human interest supporting their claim that the government was to blame "yet again".

Reaction of health care staff

Admissions staff at hospitals were unable to admit patients on the basis of clinical assessment of each case but were required to admit large numbers in response to the ministerial statements. Most students were seen and discharged the same day, but those with anything resembling serious symptoms, or with particularly articulate parents, were kept in overnight for observation. Some private physicians were reported to have encouraged admissions on the basis of financial gain; however, the authors cannot substantiate this claim.

Discussion

Officials who were first on the scene at the index school naturally sought an explanation for why students were feeling ill and fainting. An initial investigation seemed to rule out poison in the atmosphere, water contamination, food poisoning, or other environmental toxin. Similarly, because of the case distribution, an unknown airborne virus did not seem to be involved. Evidence seemed to point instead to the vaccine which had been administered the previous day. In a sense, those first on the scene were right: the index case and several other students probably experienced genuine, though not remarkable, symptoms as a result of the vaccination. The escalation of events, however, was not brought about by the vaccine, but by dynamics similar to those documented in many other instances and called by a number of terms including mass psychogenic illness. This phenomenon is defined as the collective occurrence of a constellation of similar physical symptoms and related beliefs for which there is no plausible pathogenic explanation (5, 6). In 1974, Sirois (7) reviewed important reported outbreaks since the Middle Ages, identifying almost 200 reports of mass reactions to suspected poisonings or other events. This phenomenon has been reported in many countries and different cultures (8-13). Symptoms vary according to the perceived threat, but those described in many other outbreaks (10, 12-18) bear a striking resemblance to those in the Jordan outbreak reported here, even though vaccines were not involved in the other mass reactions.

Mass reactions elsewhere

This was not the first mass reaction in Jordan in recent times. A mysterious gas poisoning occurred in the West Bank in 1983 affecting more than 900 people, mostly schoolgirls (18). The symptoms included headache, dizziness, weakness, and loss of consciousness. Hefez (19) described the role of the press in disseminating information rapidly about the outbreak, undoubtedly escalating the events. In the nearby Islamic Republic of Iran, a similar phenomenon was also reported in 1992 involving 26 female students who received tetanus toxoid (20).

An epidemic of hysteria was reported following a school outing in Montreal, Canada, in 1981 affecting 500 students aged 13–14 years (21). The details of this event bear remarkable similarities to the September 1998 outbreak in Jordan even though the suspected cause was different. In Montreal, food poisoning or a "mystery chemical" leaking from the air-conditioning on the train in which the girls were travelling were initially suspected. Following the fainting of one index case, 13 girls followed suite and were taken immediately to hospital. The symptoms of subsequent cases included fainting, dizziness, and weakness.

There are only a few reports of mass hysteria caused by vaccines (20, 22, 23). This is not so surprising given that the majority of vaccines are administered to infants and young children, who are not likely to react in this way given their inability to perceive vaccines as a threat and to interact as a group. In dealing with groups of older individuals receiving vaccines, extreme care is needed before attributing such mass events to hysteria. Genuine allergic or other clinical symptoms following immunization should always be considered at the outset. Symptoms suggestive of hysteria are headache, nausea, dizziness, hyperventilation, fainting (including fainting while waiting for vaccination and watching others being vaccinated), and relapse of illness (24, 25). It has been suggested (26) that in general, once the situation is recognized by a professional in authority, further investigation into the cause of the outbreak is not recommended. In the case of the Td vaccine, this would have been difficult advice indeed to follow. Only when the results of exhaustive tests on the vaccine were complete did the Jordanian Ministry of Health feel they could reintroduce the vaccine into the school immunization schedule. Thus we consider that once vaccines are identified as the perceived threat, a dismissive approach would be harmful.

Implications for immunization programmes

Could this mass psychogenic illness have been averted by different handling of the situation? It is impossible to know with certainty. However, immunization programme managers would be able to handle crisis situations better if they already have a strong relationship with the media. One way this can be achieved is to provide a continuous flow of background information and features to key members of the media. This would produce a group of media personnel who are already well briefed on the subject and who are more likely to have a perspective in line with that of the staff delivering immunization services. Relationships with the media cannot be built up quickly during a crisis: they are long-term investments. A rapid and clear response is called for in a crisis if confidence in the national immunization programme is to be preserved. The need for a surveillance system capable of detecting adverse events is essential to manage such crises properly.

With support from WHO, the Jordanian Ministry of Health reinstated the Td vaccine and restored the shaken public confidence in immunization programmes. A surveillance and response system for vaccine adverse events is in the process of being installed so that better information on background rates of adverse events will be to hand.

Acknowledgements

The authors dedicate this article to all the students and parents who suffered distress during the outbreak, and to all the professionals who did their best to react responsibly throughout. We hope this study will reduce the chance of similar events happening in other locations.

Conflicts of interest: none declared.

Résumé

Phénomène psychogénique de masse après administration de vaccin antidiphtériqueantitétanique en Jordanie

En septembre 1998, plus de 800 enfants et adolescents ont cru souffrir d'effets secondaires de l'administration de vaccin antidiphtérique-antitétanique en milieu scolaire en Jordanie; 122 d'entre eux ont été hospitalisés. Dans la très grande majorité des cas, les symptômes n'étaient pas dus au vaccin mais traduisaient un phénomène psychogénique de masse.

Le rôle des médias, des parents et du corps médical dans l'amplification de cette réaction a semblé au premier abord inhabituel, et même unique dans le contexte de l'époque en Jordanie. Un examen de la littérature médicale a toutefois montré que cette réaction était similaire par bien des aspects à des phénomènes de ce type survenus ailleurs, même si les facteurs déclenchants en étaient différents. On connaît environ 200 descriptions de réactions psychogéniques collectives impliquant des intoxications supposées ou d'autres événements. Comme de telles réactions sont relativement rares et font suite à des facteurs déclenchants très divers, il est vraisemblable que les personnes qui y sont confrontées n'auront aucune

expérience de la façon d'y répondre et ne sauront pas prendre les mesures énergiques qui en stopperont l'escalade. En fait, peut-être ignoreront-elles même que de tels événements ont déjà été observés. Les leçons de l'incident survenu en Jordanie pourront aider d'autres responsables de programmes de vaccination à mieux faire face à des situations de crise qui pourraient survenir ailleurs.

Resumen

Reacción psicógena masiva tras la vacunación con anatoxina tetánica y diftérica en Jordania

En septiembre de 1998, más de 800 jóvenes de Jordania creyeron haber sufrido los efectos secundarios de una vacuna de anatoxina tetánica-diftérica administrada en la escuela; 122 niños fueron hospitalizados. En la gran mayoría de esos niños los síntomas no se debían a la vacuna sino a un fenómeno psicógeno masivo.

La influencia de los medios de comunicación, de los padres de los niños y de los médicos en la escalada que dio lugar a esta reacción masiva fue a primera vista inhabitual, si no excepcional, en las circunstancias de Jordania en ese momento. No obstante, el examen de la literatura reveló que esta respuesta masiva tenía muchos puntos en común con brotes anteriores, si bien las causas subyacentes eran

distintas. Hay aproximadamente unos 200 casos publicados de respuestas masivas a presuntas intoxicaciones o eventos de otro tipo. Dado que esas reacciones masivas son relativamente infrecuentes, y que los factores que pueden desencadenarlas son muy diversos, quienes deben responder a ellas difícilmente poseen la experiencia previa necesaria para manejarlas, no suelen tomar medidas contundentes para evitar su escalada, y muchas veces incluso desconocen que hay precedentes del fenómeno. Las lecciones que cabe extraer de este incidente ocurrido en Jordania pueden ayudar a otros gestores de programas de inmunización a manejar mejor esas crisis en otros lugares.

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