The laboratory confirmation of suspected measles cases in settings of low measles transmission: conclusions from the experience in the Americas

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Abstract The Americas have set a goal of interrupting indigenous transmission of measles using a strategy developed by the Pan American Health Organization (PAHO). This strategy includes recommendations for vaccination activities to achieve and sustain high immunity in the population and is complemented by sensitive epidemiological surveillance systems developed to monitor illnesses characterized by febrile rash, and to provide effective virological and serological surveillance. A key component in ensuring the success of the programme has been a laboratory network comprising 22 national laboratories including reference centres. Commercially available indirect enzyme immunoassay kits (EIA) for immunoglobulin M (IgM)-class antibodies are currently being used throughout the region. However, because there are few or no true measles cases in the region, the positive predictive value of these diagnostic tests has decreased. False-positive results of IgM tests can also occur as a result of testing suspected measles cases with exanthemata caused by *Parvovirus* B19, rubella and *Human herpesvirus* 6, among others. In addition, as countries maintain high levels of vaccination activity and increased surveillance of rash and fever, the notification of febrile rash illness in recently vaccinated people can be anticipated. Thus, managers in the measles elimination programme must be prepared to address the interpretation of a positive result of a laboratory test for measles IgM when clinical and epidemiological data may indicate that the case is not measles. The interpretation of an IgM-positive test under different circumstances and the definition of a vaccine-related rash illness in a setting of greatly reduced, or absent, transmission of measles is discussed.

Keywords Measles/diagnosis; Immunoglobulin M/immunology; Immunoglobulin G/analysis; Immunoenzyme techniques; Measles vaccine/adverse effects; Exanthema/etiology; Measles virus/isolation and purification; Pan American Health Organization; Americas (*source: MeSH, NLM*).

Mots clés Rougeole/diagnostic; Immunoglobuline M/immunologie; Immunoglobuline G/analyse; Méthode immunoenzymatique; Vaccin antimorbilleux/effets indésirables; Exanthème/étiologie; Virus rougeole/isolement et purification; Organisation panaméricaine de la Santé; Amériques (*source: MeSH, INSERM*).

Palabras clave Sarampión/diagnóstico; Inmunoglobulina M/inmunología; Inmunoglobulina G/análisis; Técnicas para inmunoenzima; Vacuna antisarampión/efectos adversos; Exantema/etiología; Virus del sarampión/aislamiento y purificación; Organización Panamericana de la Salud; Américas (*fuente: DeCS, BIREME*).

الكلمات المفتاحية: تشخيص الحصبة؛ مناعيات الغلوبولين المناعي M ؛ تحليل الغلوبولين المناعي G ؛ طرائق اختبار الإنزيم المناعي؛ الآثار الضائرة للقاح الحصبة؛ سببيات الطفح الظاهر؛ عزل وتنقية فيروس الحصبة؛ منظمة الصحة للبلدان الأمريكية؛ البلدان الأمريكية (المصدر: رؤوس الموضوعات الطبية-المكتب الإقليمي لشرق المتوسط).

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Introduction

In 1994, countries in the WHO Region of the Americas set themselves the goal of interrupting the transmission of endemic measles by the end of 2000 using strategies developed by the Pan American Health Organization (PAHO) (*1*). These strategies included recommendations for vaccination activities intended to achieve high population immunity together with sensitive surveillance for suspected measles cases, and effective virological and serological surveillance (*2*). In the Americas, a suspected measles case is defined as any individual with a febrile rash illness

(*2*). Since 21 November 2002, no endemic measles transmission has been reported in Latin America (*3*). A key component of the programme has been a laboratory network, established in 1995, comprising 22 national laboratories, 10 of which function as reference centres, and three as specialized reference laboratories (*4*). National laboratories are responsible for the testing of blood samples for immunoglobulin M (IgM) antibodies. A case is confirmed serologically, virologically or by epidemiological linkage to another confirmed case. Commercially available enzyme immunoassay (EIA) kits for IgM-class antibodies are

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currently in use throughout the region and all network laboratories use the same test kit (5). PAHO recommends that a blood sample be taken at the first contact with a suspected case and within 30 days of onset of rash. The test kits in use have been shown to have high sensitivity and specificity. However, cross-reactions with other viral diseases, e.g. rubella and *Parvovirus*, may occur (6, 7).

Collection of viral samples for isolation and genotyping of measles virus is recommended to establish the genotype responsible for the case or outbreak. Often, identification of vaccine virus from a sample collected from an individual who presented with rash after vaccination has provided the evidence necessary for classification of the case as vaccine-associated. Although facilities for both virus isolation and direct detection of measles virus by reverse transcription followed by the polymerase chain reaction (RT-PCR) are available in certain regional reference and specialized laboratories, only serological confirmation is performed in all national laboratories. Viral samples have limited utility in the network for case confirmation because negative results may result from poor quality of the sample and therefore cannot be used to rule out a suspected case. Thus, RT-PCR has not been utilized at the country level throughout the region. To standardize testing and control costs, PAHO elected to use a single enzyme-linked immunoassay (ELISA) test kit in national laboratories throughout the region and to rely on several specialized reference laboratories to conduct further testing if indicated.

No laboratory test is 100% sensitive or specific and false-positive results of laboratory tests do occur. The positive predictive value of a laboratory test decreases as the prevalence of the disease decreases resulting in an increase in the number of false-positive results (8). Therefore, as progress towards elimination is made, i.e. as the prevalence dramatically decreases, some false-positive laboratory results should be expected. In countries that maintain high levels of vaccination activity and of surveillance for rash and fever, the notification of febrile rash illness in recently vaccinated persons should be anticipated. This is an important consideration because at least 5% of primary vaccinations can result in a febrile rash illness (9).

Thus, epidemiologists and managers of measles elimination programmes must be prepared to interpret a positive IgM laboratory test in the setting of greatly reduced disease, or when the clinical and epidemiological data indicate that the case in question is not measles. In such situations, the dilemma is to determine whether a measles IgM-positive result occurs because:
- the subject has an acute measles infection
- the test result is a false-positive, or
- the subject was recently vaccinated against measles.

We discuss below the interpretation of an IgM-positive test in the setting of greatly reduced, or absent, transmission and reconsider the definition of a vaccine-related rash illness.

Methods

This paper describes the laboratory procedures developed by PAHO during the last 10 years. They have been implemented throughout the region as part of PAHO's measles elimination strategies. PAHO's Technical Advisory Group meets annually and makes recommendations for the region regarding all aspects of the measles elimination initiative, including laboratory procedures. Information on the laboratory network and its procedures and functions has been published elsewhere (4).

Interpretation of a positive IgM test in an individual with a febrile rash illness in the setting of little or no known transmission

Regional recommendations for measles elimination in the Americas state that, unless there is clear evidence to the contrary, all suspected measles cases with positive IgM results should be considered laboratory-confirmed and warrant immediate initiation of outbreak control activities (10). Because measles is so contagious, failure to identify the source of infection or secondary cases can occur and does not imply that the laboratory result was a false-positive. It is possible for an individual to be unknowingly infected during a very brief contact with a stranger in a public setting. Although the expected number of false-positive laboratory results should be low, the process for discarding such a case as a "non-case" with a false-positive IgM result should be standardized to ensure accurate and consistent classification of such cases.

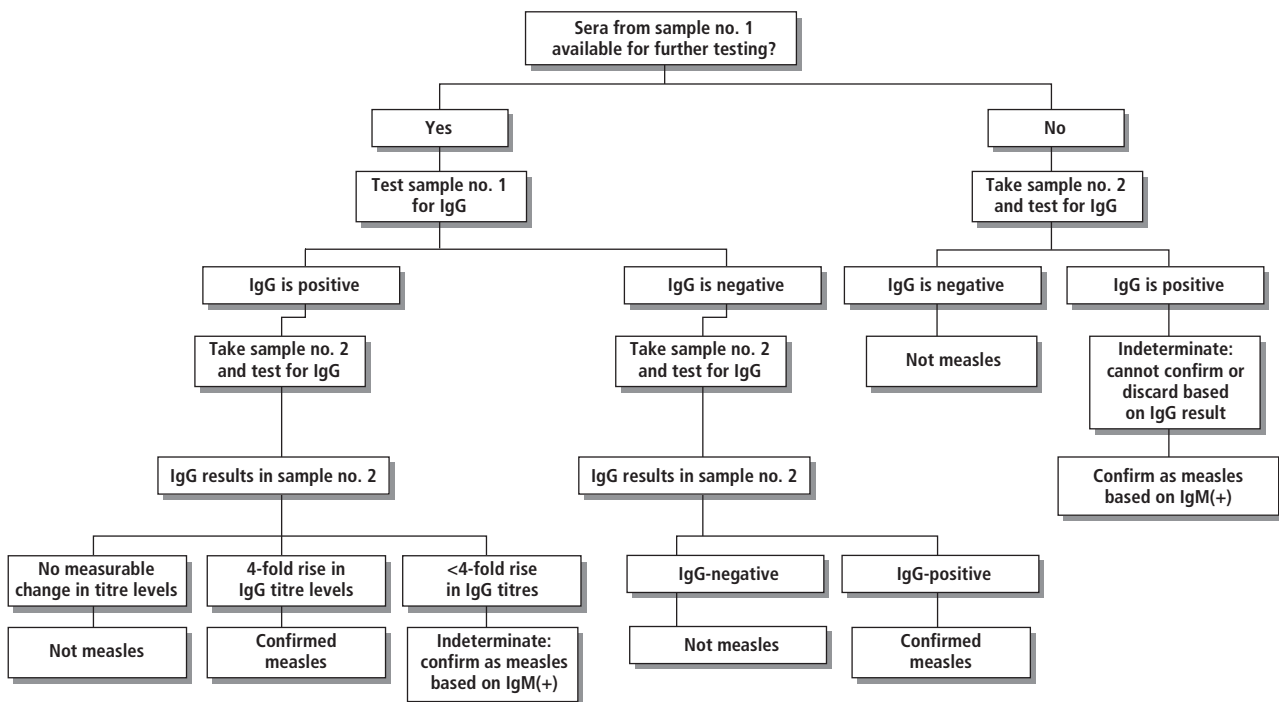### The utility of clinical data in discarding a suspected measles case

Regardless of the results of the IgM test, a suspected case should not be discarded solely on the basis of clinical data, or, because of a *lack* of clinical data supporting a measles diagnosis. Measles generally produces fever, rash and respiratory symptoms such as cough, conjunctivitis and coryza (9). However, the absence of these symptoms does not preclude the possibility of an acute measles infection. A mild infection may produce a clinical picture that differs from that of classic measles. An analysis of regional surveillance data from the Americas in 2000 showed that laboratory-confirmed measles cases ($n = 1039$) were more likely than IgM-negative discarded cases ($n = 11\ 485$) to meet eight different clinical case definitions (CDs) based on combinations of typical symptoms associated with measles (11). However, at least 37% of the laboratory-confirmed measles cases *failed* to fulfil these eight clinical CDs. Thus, the absence of the clinical symptoms typical of measles does not imply that the person being tested does not have measles. The clinical picture may vary and a laboratory result should therefore not be disregarded due to the *lack* of clinical compatibility.

Furthermore, a recent study showed that only 72% of suspected measles cases meeting a strict CD were IgM-positive for measles; 23% were IgM-positive for rubella. In this study, two of nine individuals who did not meet the CD were IgM-positive for measles. Thus, clinical CDs, while often sensitive, may be problematic in terms of the level of their specificity (12).

Laboratory testing procedures to rule out a false-positive laboratory result

An IgM-positive result from an individual suspected of having measles should trigger an investigation for additional cases and immediate initiation of control activities. However, if an exhaustive investigation fails to identify other cases, including an index case, the best serological confirmation for the IgM-positive result in this setting is to measure immunoglobulin G (IgG) antibody titres (Fig. 1), but only if the individual has not received a recent measles vaccination.

Currently available tests that measure measles IgG titres include haemagglutination inhibition, plaque reduction neutralization and EIAs that compare a series of serum dilutions. These tests require the collection of two properly spaced blood specimens to observe seroconversion or to measure a diagnostic

Fig. 1. **Testing algorithm for suspected measles cases with IgM-positive test results when a false-positive is suspected[a]**

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                        ┌──────────────────────────┐
                        │   Sera from sample no. 1  │
                        │ available for further     │
                        │ testing?                  │
                        └──────────────────────────┘
                    ┌──────────────────┴──────────────────┐
                 ┌──────┐                              ┌──────┐
                 │ Yes  │                              │  No  │
                 └──────┘                              └──────┘
          ┌──────────────────┐              ┌──────────────────────┐
          │ Test sample no. 1│              │ Take sample no. 2     │
          │ for IgG          │              │ and test for IgG      │
          └──────────────────┘              └──────────────────────┘
        ┌──────────┴──────────┐          ┌───────────┴───────────┐
┌──────────────┐    ┌──────────────┐ ┌──────────────┐  ┌──────────────┐
│ IgG is       │    │ IgG is       │ │ IgG is       │  │ IgG is       │
│ positive     │    │ negative     │ │ negative     │  │ positive     │
└──────────────┘    └──────────────┘ └──────────────┘  └──────────────┘
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Sera from sample no. 1 available for further testing?
- Yes → Test sample no. 1 for IgG
  - IgG is positive → Take sample no. 2 and test for IgG → IgG results in sample no. 2
    - No measurable change in titre levels → Not measles
    - 4-fold rise in IgG titre levels → Confirmed measles
    - <4-fold rise in IgG titres → Indeterminate: confirm as measles based on IgM(+)
  - IgG is negative → Take sample no. 2 and test for IgG → IgG results in sample no. 2
    - IgG-negative → Not measles
    - IgG-positive → Confirmed measles
- No → Take sample no. 2 and test for IgG
  - IgG is negative → Not measles
  - IgG is positive → Indeterminate: cannot confirm or discard based on IgG result → Confirm as measles based on IgM(+)

[a] Applicable only to individuals with a positive IgM result not due to a recent vaccination, i.e., within 56 days.

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rise in titre. Properly spaced specimens are those for which the initial sample is obtained within 7 days of onset of rash and the second 3–4 weeks after onset of rash; the interval between the two samples should be 2–3 weeks (*11*, *13*).

As seen in Fig. 1, if the first serum sample is found to have IgG antibodies, but IgG titres in the second sample show no change when compared to the first sample, the case would not be considered measles and could be discarded. The IgM-positive test result would be considered a false-positive. However, if the second sample shows a fourfold higher IgG antibody titre than the first sample, the case should be considered an acute measles infection and confirmed. If the second sample shows an increase in IgG titres, but it is less than fourfold higher than in the first sample, it would not be possible to determine whether or not it was an acute infection. Thus, no conclusion could be reached as to the actual status of the suspected case. In this situation, for programmatic considerations, the suspect case should be confirmed solely on the basis of the positive IgM test result. For the purposes of elimination programmes, it is better to incorrectly confirm a non-case than to discard a true measles infection.

If both the first and second samples are negative for IgG antibodies, the case would not be considered to be measles and should be discarded. If, however, the second sample is IgG-positive for measles, the case should be confirmed as acute measles infection.

Sometimes there may be an insufficient volume from the first sample for IgG antibody testing, but a second sample would still be required. If the second sample is negative for IgG, the case should be discarded. If, however, the second sample is IgG-positive, it would not be possible either to confirm or discard the case, because the positive result could represent an acute or past infection. In such a situation, the case must be confirmed

based on the IgM test result. Regardless of the scenario or testing sequence results, when in doubt, the case should be confirmed on the basis of the positive IgM test result.

The use of a second IgM kit for confirmation
Experience in the Americas demonstrates that a positive IgM result in a setting of little or no transmission is generally questioned by health officials thus putting intense pressure on laboratories to demonstrate the reliability of their test results. This may create a desire to retest using a different IgM test kit believed to be more specific and/or sensitive, or one that uses another format such as an antibody capture test. The IgM kits currently used throughout the PAHO network are comparable in specificity and sensitivity to other available kits including those with a capture format (*7*). In addition, the number of false-positive results from all kits would be expected to increase where the prevalence of measles is low. Therefore, additional IgM testing should not be required nor construed as "confirmatory". However, it may be beneficial for reference laboratories to have a second IgM test option for use in the event of a disruption in the production of the standard kit or if the quality of a particular lot is in doubt.

Interpretation of a positive IgM test in a recently vaccinated individual with a febrile rash illness
It is not possible to determine whether a positive IgM test is a response to vaccination or the result of a recent measles infection. A suspected measles case for which a positive IgM test result is obtained should not be dismissed as vaccine-related solely because the individual concerned has recently been vaccinated. Such a positive IgM test result may represent a response to a vaccination in an individual who has either a non-measles infection or an acute measles infection and is therefore unrelated to

the individual's recent vaccination. The positive test result may represent a true acute measles infection because the vaccination was given during the incubation period and did not prevent the infection. IgG testing would not be useful in this situation because the results of paired IgG testing would be positive regardless of whether this was a response to a wild virus infection or to recent vaccination.

In many cases it will not be possible to determine conclusively if a febrile rash illness is vaccine-related. For the purposes of surveillance in elimination programmes, a recently vaccinated individual with a positive IgM for measles can be discarded and classified as having a vaccine-related rash if *all* of the following criteria are met:

- rash illness, with or without fever, but absence of cough or other respiratory symptoms;
- rash with onset 7–14 days after vaccination with a measles-containing vaccine;
- the serum sample taken between 8 and 56 days after vaccination is positive for measles;
- no index case or any secondary cases have been identified after a thorough field investigation; and
- field and laboratory investigations have failed to identify other causes.

Interpretation of IgM-positive result for measles but IgM-negative result for rubella in an individual who has recently received the measles–rubella or the measles–mumps–rubella vaccine

Some individuals who have recently received measles–rubella (MR) or measles–mumps–rubella (MMR) vaccinations may have a positive IgM result for measles and a negative IgM result for rubella, even when the sample was properly taken. This may create the impression that because the IgM result for rubella is negative, the individual must have a measles infection, the positive result for IgM to measles is unrelated to the vaccination, or that the rubella component of the vaccine was sub-optimal in its effectiveness. However, this interpretation may not be correct. The IgM response to rubella following vaccination rises more slowly and is of shorter duration than the response to measles (14–16). A single serum sample taken within 14 days after onset of rash (or vaccination) can be negative for rubella IgM, yet test positive for measles IgM. In fact, IgM specific to rubella vaccination may be missed altogether because the IgM may be absent in some individuals or may decline so quickly that rubella IgM antibody may no longer be detectable in a second specimen (14).

Interpretation of indeterminate IgM and/or IgG test results

Some cases will have indeterminate results of IgM and/or IgG tests on one or more samples. In the Americas, such cases have been infrequent. Even so, clear guidelines are utilized to ensure their proper management. Such samples are retested at a reference laboratory. The case in question can be discarded if: the reference laboratory reports an indeterminate (or negative) result; the investigation fails to identify a source of infection or to detect other cases; and if vaccination coverage is > 90% in the district where the individual resides.

Discussion

All suspected cases of measles with an IgM-positive test result must be considered to be measles unless proven otherwise and must prompt rapid implementation of vaccination control measures. Any delay, such as awaiting further test results, could result in the rapid spread of the virus. It is far better to misclassify a non-measles case as measles and unnecessarily initiate an investigation and control measures than to dismiss a sporadic true-positive result and fail to prevent transmission of measles virus.

Laboratory findings comprise only part of the process used to determine whether a suspected measles case is a true case. Test results are affected by the quality of samples received, inherent limitations of the test because of the low prevalence of measles and the technical expertise of the laboratory staff conducting the tests. In addition, when a sample is taken within 3 days of onset of rash, up to 30% of true measles infections may be IgM-negative (17). The proficiency of the laboratory performance can be assured through site visits, exchange of samples for re-testing, and participation in annual proficiency testing (4).

The procedure presented for retesting IgM-positive specimens thought not to be measles for IgG should be performed only in a reference laboratory. It is important to note that not all IgM-positive specimens need be tested for IgG, but only those taken from isolated, sporadic cases when there is a high likelihood that the IgM result may be inaccurate, and, only after the case has been confirmed and appropriate control measures taken, i.e. countries should not wait for final laboratory results before implementing control measures. The actual number of problem cases that will confront a programme should be small. Although more than 30 000 specimens are tested annually for measles in the Americas, few require further evaluation. However, even if the numbers are small, the implications are significant. One problematic case occurring in a country with no confirmed measles transmission can have considerable political and programmatic repercussions. Thus, clear and standardized guidelines are needed to ensure that such cases are handled appropriately.

The increased likelihood of being confronted with a false-positive IgM result as progress towards elimination of measles is made highlights the need to obtain specimens for virus isolation. These specimens should be obtained < 7 days after onset of the rash. Isolation of measles virus confirms the diagnosis. A viral specimen can be evaluated for the presence of measles virus by PCR in a specialized network laboratory if culture attempts fail. Moreover, the molecular analysis of the virus may be essential to confirm its source.

The interpretation of a positive IgM result in recently vaccinated individuals who present with rash and fever is often problematic. In general, IgM due to vaccination against measles or rubella is not detectable as early as the response following natural infection would be (15, 18). In one study, IgM to measles was detected in only 2% of vaccine recipients one week after vaccination (18). Thus, a positive IgM test result in a recently vaccinated case of suspected measles is more likely to result from wild measles than from the vaccination if the interval between vaccination and the collection of the sample is < 7 days.

Vaccine-associated rash and/or fever, observed after vaccination of non-immune individuals, is generally attributed to the measles vaccine or to the measles component of a combined vaccine (19). Fever is the most common side-effect and can occur in 5–15% of recipients; rash occurs in 5% of recipients (9, 20). Surveillance guidelines for vaccine-associated measles cases are based on studies with groups of vaccinees in which the peak period between vaccination and rash onset was observed during the second week following vaccination, but the actual range during the second week can vary, i.e. 7–10 versus 7–12, 7–14, etc. (20–23). However, in large populations, some

unusual rash reactions may occur outside of the expected 7–14-day window following vaccination. In addition, although less common, rash due to the rubella component could extend the window for vaccine-associated rash up to 30 days following vaccination (*16*).

National programme managers must understand that the presence of isolated, sporadic IgM-positive cases classified as confirmed measles cases may not represent a failure of the national elimination programme. Sporadic cases of imported measles will continue to occur. The presence of a sporadic confirmed case that does not result in further disease transmission implies that the population immunity resulting from high vaccination coverage has prevented or limited secondary disease transmission and should be considered a programme success.

Vaccination of susceptible individuals through the full implementation of the strategy recommended by PAHO in all countries remains the foundation of the regional measles elimination initiative (*24*). Until programmes for measles elimination are implemented worldwide, importations will continue to occur in the Americas. Sensitive measles surveillance and high population immunity must be maintained to prevent the resumption of endemic transmission. Laboratory surveillance remains a central activity within the elimination programme (*25*). Standardized approaches to laboratory testing and interpretation of results are critical to ensure the continued success of the programme. ■

Résumé

Confirmation au laboratoire des cas suspects de rougeole dans des contextes de faible transmission de la maladie : l'expérience des Amériques

Les Amériques se sont fixé pour objectif d'interrompre la transmission indigène de la rougeole au moyen d'une stratégie développée par l'Organisation panaméricaine de la Santé. Cette stratégie comprend des recommandations en matière de vaccinations afin d'obtenir et de maintenir un niveau élevé d'immunité dans la population et est complétée par des systèmes sensibles de surveillance épidémiologique conçus pour suivre les maladies caractérisées par une éruption fébrile et assurer une surveillance virologique et sérologique efficace. Un des éléments clés de la réussite de ce programme réside dans un réseau de laboratoires comprenant 22 laboratoires nationaux, dont des centres de référence. Des trousses de titrage immunoenzymatique indirect disponibles dans le commerce pour la recherche des anticorps de classe IgM (immunoglobulines M) sont actuellement utilisées dans toute la Région. Cependant, comme il n'existe que peu ou pas de véritables cas de rougeole dans la Région, la valeur prédictive positive de ces tests diagnostiques a diminué. Les tests IgM peuvent aussi donner des résultats faussement positifs lorsqu'on teste des cas suspects de rougeole avec exanthème provoqués par des virus tels que le parvovirus B19, le virus de la rubéole et le virus de l'herpès humain type 6, entre autres. De plus, comme les pays entretiennent un haut niveau d'activité vaccinale et une surveillance accrue des cas d'éruptions et de fièvre, la notification de cas de maladies éruptives fébriles chez des personnes récemment vaccinées est prévisible. Les responsables des programmes d'élimination de la rougeole doivent donc être préparés à revoir l'interprétation de résultats positifs lors de tests de recherche des IgM antirougeoleuses lorsque les données cliniques et épidémiologiques tendent à indiquer qu'il ne s'agit pas d'un cas de rougeole. L'interprétation des tests positifs pour les IgM dans d'autres circonstances et la définition d'une maladie éruptive liée au vaccin là où la transmission de la rougeole est très faible voire nulle sont examinées.

Resumen

Confirmación de laboratorio de los casos sospechosos de sarampión en los entornos de baja transmisión de la enfermedad: conclusiones de la experiencia en las Américas

Las Américas se han fijado la meta de interrumpir la transmisión autóctona del sarampión mediante una estrategia desarrollada por la Organización Panamericana de la Salud (OPS). La estrategia incluye recomendaciones para emprender actividades de vacunación encaminadas a lograr y mantener una inmunidad alta en la población y se complementa con sistemas sensibles de vigilancia epidemiológica concebidos para vigilar las enfermedades caracterizadas por la presencia de exantema febril y para garantizar una vigilancia virológica y serológica eficaz. Un componente clave para el éxito del programa ha sido una red de 22 laboratorios nacionales, incluidos centros de referencia. Actualmente se están empleando en toda la región kits comerciales de inmunoensayo enzimático indirecto para los anticuerpos IgM (inmunoglobulinas M). Sin embargo, como hay pocos o ningún caso real de sarampión en la región, el valor predictivo positivo de estas pruebas diagnósticas ha disminuido. Pueden producirse también falsos positivos en las pruebas de IgM al someter a ellas a los casos sospechosos de sarampión con exantemas causados por parvovirus B19, rubéola y herpesvirus 6 humano, entre otros. Además, cuando los países aseguran unos niveles altos de vacunación y una mayor vigilancia de las erupciones cutáneas y la fiebre, puede preverse que se notificarán erupciones febriles en las personas recientemente vacunadas. Por lo tanto, los gestores del programa de eliminación del sarampión deben estar preparados para interpretar cual quier resultado positivo de las pruebas de laboratorio para la IgM del sarampión en un contexto de datos clínicos y epidemiológicos que lleven a pensar que no se trata de un caso de sarampión. Se examina la manera de interpretar una prueba positiva de IgM en diferentes circunstancias y la definición de enfermedad eruptiva asociada a la vacuna en un entorno de transmisión muy reducida o inexistente del sarampión.

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ملخص

التأكيد المختبري لحالات الحصبة المشتبه بها في المواقع ذات الانتقال المنخفض للحصبة: حصائل التجربة في البلدان الأمريكية

نتائج إيجابية كاذبة لاختبار الغلوبولين المناعيM ، نتيجة لاختبار حالات الحصبة المشتبه بها عن طريق الطفح الظاهر الناجم عن الفيروسة الصغيرة B19 ، أو الحصبة الألمانية، أو الفيروسة الهربسية، أو غيرها. وإن محافظة البلدان على مستويات عالية من أنشطة التلقيح والترصُّد للطفح والحُمَّى، يمكن معه توقع التبليغ عن مرض الطفح الحُمَّوي بين الأشخاص الملقحين حديثاً. ومن ثم، ينبغي أن يكون مديرو برنامج التخلّص من الحصبة على استعداد لتفسير أية نتيجة إيجابية للاختبار المختبري للغلوبولين المناعي M للحصبة، إذا ما أشارت المعطيات السريرية والإبيدميولوجية (الوبائية) إلى أن الحالة ليست حصبة. ويتم في هذه الدراسة مناقشة تفسير اختبار الغلوبولين المناعي M الإيجابي في ظروف مختلفة، ومناقشة تعريف المرض الطفحي الناجم عن اللقاحات، وذلك في المواقع ذات السريان الشديد الانخفاض أو المنعدم للحصبة.

الملخص: حدَّدت البلدان الأمريكية مرمى وقف سريان الحصبة داخل البلدان، عن طريق تنفيذ استراتيجية أَعَدَّتها منظمة الصحة للبلدان الأمريكية. وتوصي هذه الاستراتيجية بتنفيذ أنشطة تلقيح تستهدف تحقيق تغطية تمنيعة عالية ومستديمة بين السكان، تكمِّلها نُظُم ترصُّد إبيدميولوجي (وبائي) حسَّاس لرصد الأمراض التي تتميَّز بالطفح الحُمَّوي، مع القيام بترصُّد فيروسي ومصلي فعَّال. ويتوقف نجاح البرنامج على مكوِّن رئيسي، هو وجود شبكة مختبرات تتكوَّن من 22 مختبراً وطنياً، من بينها المختبرات المركزية المرجعية. وتُستخدم حالياً في جميع بلدان الإقليم الأمريكي العتائد المتاحة تجارياً للازمة للمقايسات المناعية الإنزيمية غير المباشرة لأضداد الغلوبولين المناعي M. ولكن نظراً لوجود حالات قليلة للحصبة، أو انعدامها تماماً، في الإقليم، فقد انخفضت القيمة التنبؤية الإيجابية لهذه الاختبارات التشخيصية. وقد يتم الحصول على

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