ENCYCLOPEDIA
on Early Childhood
Development

Immunization: Comments on Scheifele, Law and Smith

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April 2013

Introduction

The four linked papers by Scheifele (two papers),[1,2] Law,[3] and Smith[4] provide an overview of the neurological aspects of vaccination and vaccine safety from three internationally-recognized authors with a strong clinical and academic background and who bring extensive experience not only in pediatrics and immunization but also importantly in the investigation and monitoring of the safety of vaccines.

Although those four papers focus only on the neurological aspect of the risks and benefits of vaccines, this narrow focus is quite appropriate and allows the authors to be more specific about their presentation of the evidence than if they were covering a wider set of aspects. Preventing neurological complications of vaccine preventable diseases and neurological risks of vaccines is indeed among the most important considerations in the choice of vaccines, and most of the lessons derived from these papers are relevant to the wider picture. The papers bring together a number of facts and considerations that may not be obvious or easily accessible to those clinicians who advise parents and those who may be confronted with managing neurologic events following immunizations, nor to parents themselves who are concerned with making the best choices for their children's health. Although the focus of the authors is slightly more

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relevant to a North American audience, there is no doubt that the content of the papers is relevant globally.

In times of high disease prevalence, fear of diseases prevails. As vaccine-preventable diseases become controlled through extensive vaccination, fears over the safety of vaccines surpass the fears of the diseases that vaccines are intended to prevent. A series of articles focusing on the risks in absence of vaccination and risks of vaccines is therefore important and perfectly timed in the context of both stalling vaccination coverage at the global level[5] and endorsement of the Global Vaccine Action Plan of the Decade of Vaccine at the May 2012 World Health Assembly.[6,7] One of the essential recommended actions to achieve the second strategic objective of the Global Vaccine Action Plan (i.e., "individuals and communities understand the value of vaccines and demand immunization as both their right and responsibility.") is to engage in a dialogue with those individuals and communities that transmit information and respond to people's concerns and fears. Continuously informing and updating the knowledge base of physicians and health care personnel on immunization is essential to these efforts.

Research and Conclusions

"Childhood immunization and brain health" by David Scheifele[1] provides an excellent overview of a long list of the most common neurological complications and their potential dramatic consequences both for the affected children and their families. Those conditions are potentially avoidable with routine childhood immunizations. The author rightly recognizes that not all of the vaccines described are used in all countries, however, and that disease risks vary with geography and population health.

Scheifele also highlights the dramatic impact that vaccination programs have had or could have and gives a fair view of the limits of the effectiveness and/or protection afforded by some vaccines (e.g., the fact that some of the serogroups of meningococcal meningitis are not yet vaccine preventable).[8-11] From a global perspective, one could have added that the African region celebrated the vaccination of 100 million persons against meningococcal meningitis A in the so-called meningitis belt with a custom-designed conjugate vaccine.[5] Not a single case of meningococcal meningitis A was reported in vaccinated individuals. The elimination of rubella and congenital rubella syndrome from the region of the Americas and its dreadful neurological consequences is also worth flagging as a major achievement.[5]

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In contrast “Neurological adverse events after vaccinations” by Barbara Law[3] presents the comparatively short list of neurologic events proven to be or possibly caused by vaccines. It highlights that fortunately the only neurologic reactions that occur with any, albeit rare, frequency are febrile seizures. The article also covers how vaccines are assessed before and after a product is marketed and some of the special challenges related to monitoring the safety of vaccines during early childhood, and particularly that of determining whether or not an event observed after vaccination is caused by the administration of the vaccine. This determination is rather difficult in view of the large number of vaccine doses administered at an age when health problems first appear. Law also refers to several useful websites and the Vaccine Safety Net, a network of websites that provide information on vaccine safety and that adhere to good information practices, which can help practitioners and parents access trustworthy information.[12-15]

Drawing on the most publicized example of a false allegation, the third paper, “Autism and MMR association debunked” by Michael Smith,[4] clearly makes the case that MMR vaccine does not cause autism and highlights the dramatic negative consequences that such unfounded allegations and inappropriate communications have had and may continue to have in the future. Not only did this situation cause serious concern and inappropriate fear of vaccination but it also took enormous resources away that could instead have been used to investigate other vaccine safety concerns.

The final paper of the series, “What Else Could It Be? When neurologic disorders follow immunization,” again authored by Scheifele,[2] reviews the etiologies of neurological events that follow immunization, with emphasis on Dravet syndrome and sodium channel mutations.[16-19] Scheifele stresses that the most alarming situation for parents and health professionals is the occurrence after vaccination of acute encephalopathy that results in persistent seizures and developmental delay or reversal. This rare situation typically follows one of the first vaccinations in early infancy. Since those vaccinations contain pertussis vaccine, the syndrome was labeled “pertussis vaccine encephalopathy,” although there was no direct evidence that the vaccine was the cause. Scheifele rightly stresses that when brain disorders such as seizures or encephalopathy occur after an immunization, people (including many physicians) have a strong natural tendency to blame the vaccine. Without an obvious alternative cause such as trauma or intercurrent infection, immunization may be considered guilty by default. Scheifele indicates how in recent years increasingly sophisticated diagnostic tools have revealed a substantial number of alternative causes that may not be evident unless looked for and that, in fact, alternative causes

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exist for almost all of the severe neurologic disorders that follow infant vaccinations, including Dravet syndrome. Thorough investigation and correct diagnosis will reassure the family as to the true cause, remove the blame for having vaccinated the child, direct appropriate treatment and allow realistic planning for prognosis.

However, what the article does not say is that the saga of pertussis and encephalopathy has much in common with that of MMR and autism. The National Childhood Encephalopathy Study in the U.K. long ago concluded that a potential rare association existed between encephalopathy and administration of whole cell pertussis vaccine. Although upon reanalysis it was shown that there was actually no association between pertussis vaccine and encephalopathy,[20] the two continued to be linked for many years including in pediatric textbooks that were not updated or as informed as they should have been. Since textbooks are supposed to represent medical truth, many cases of encephalopathy detected post-vaccination were unfortunately too quickly labeled post-pertussis encephalopathy and deprived of proper investigation and, even more tragically, of the appropriate treatment. In 1999 a cluster of deaths occurring among infants 2 months of age post vaccination was reported in Egypt.[21] A thorough international investigation revealed that the deaths were not due to the vaccine itself but to the application at the injection site of methanol impregnated compresses. Unfortunately clinicians labeled the deaths as post-immunization encephalopathy and fell short of ensuring the proper clinical investigations. As a result children died for not receiving the appropriate antidote that would have saved them.

Yet Dravet syndrome and its potential to be confused for a vaccine-related condition is not well known and by publicizing this potential confusion, Scheifele and the Encyclopedia lead the way forward.

Implications

It is essential that vaccinators and other health care providers give accurate information regarding common and rare vaccine side effects along with advice on what to do should an adverse event occur. It is equally important that parents and physicians alike be reminded of the dramatic consequences of vaccine-preventable diseases that would occur without vaccination. In a population with high vaccine coverage, disease risks are not equally distributed and they remain high for those not vaccinated. This was illustrated recently with the occurrence of serious cases of measles and related neurological complications in France and other European countries.[22]

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This series of papers makes the case for early and timely vaccination of infants and vaccination of the mother prior to or during pregnancy in order to prevent the serious neurological complications of vaccine preventable diseases.

All those concerned with immunization and medical care of young children should remain vigilant to the possibility of adverse events following immunization and not only report them but also investigate them thoroughly to ensure that immunization programs remain as safe as possible and to ensure appropriate diagnosis and treatment. There are new possibilities to discriminate vaccine from non-vaccine related causes of neurological disorders and it is essential that one uses those possibilities to the extent possible particularly in countries where such diagnostic tools are readily available.

Following a legitimate suspicion and hypothesis that a medical condition might be caused by a vaccine, there is a need for prompt scientific investigations. The work by far does not stop with the conclusion of this investigation. It needs to go on to ensure that these conclusions are promptly and widely communicated to all who should know. There is a duty for pediatric textbooks to be up-to-date on vaccine safety issues. When updated versions cannot be produced quickly enough, critical information should be proactively disseminated to readers relying on those textbooks as a credible source of information. In view of the body of evidence and speed with which research can generate valuable information, there is also a duty for health providers to proactively and regularly update and inform themselves. Hopefully all modern textbooks will be accompanied by necessary brief web updates. Readers are encouraged to regularly access the WHO website and Vaccine Safety Net for regular updates reflected through vaccine position papers or statements from the Global Advisory Committee on Vaccine Safety.[23-24]

In view to contribute information into the potential association or lack of between various pediatric conditions and various immunizations, and considering the paucity of such systems around the world, it is a Canadian duty to maintain the Canadian vaccine safety surveillance network of pediatric hospitals first for the sake of Canadian children but beyond as an essential element of the global investigative capacity.[25]

The author is a World Health Organization staff member. The opinions expressed in this article are those of the author and do not necessarily represent the decisions, official policy or opinions of the World Health Organization.

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