PREVENTION OF CONGENITAL AND PERINATAL INFECTIONS

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Perinatal and congenital infections cause morbidity and mortality throughout the world. While there are a large number of pathogens that can occasionally be harmful for the unborn child, some are of considerable public health impact, for example rubella, varicella, syphilis, hepatitis B, toxoplasmosis, or infections with cytomegalovirus (CMV) or human immunodeficiency virus (HIV). The advances in the field of clinical microbiology have increased our options in terms of preventive strategies, early diagnosis, clinical interventions and therapeutic alternatives to combat these infections.

When a considerable public health impact of a given infection is evident, preventive measures can be discussed in relation to the epidemiology, the available resources and the acceptance in the population. Information on hygienic measures and other means to avoid infection is another cornerstone in the preventive work. Immunisation before pregnancy is an option for rubella, hepatitis B and varicella. In cases where intervention to prevent damage to the unborn child is possible, large screening programmes can be organised in order to identify maternal infections that may otherwise not be recognised due to uncharacteristic or subclinical symptoms. Congenital syphilis can be prevented by antibiotic treatment in early pregnancy, transmission of HIV by antiviral treatment of mother and newborn, and transmission of hepatitis B by vaccination and immunoglobulin treatment of the newborn. Identification of a neonate with congenital CMV infection or toxoplasmosis allows treatment to reduce harm.

Lack of resources and appropriate maternal care stand in the way of efficient programmes, but there is also a need of increased knowledge. Many of these interventions could be improved not only by a better understanding of the epidemiology and the impact of the diseases as well as further research into improved diagnostics and treatments and development of vaccines, but also by distribution of information to pregnant women and health care professionals. This issue of Eurosurveillance is dedicated to infectious diseases and pregnancy and contains a number of articles highlighting different aspects of the epidemiology and control and prevention efforts for diseases such as toxoplasmosis, rubella, varicella, sexually transmitted diseases e.g. HIV and hepatitis B, and cytomegalovirus infections.

Safe vaccines against, for example, rubella, exist and are very efficient in preventing infection in the mother [1]. It is clear that congenital rubella can be eradicated by vaccination programmes, a goal that has already been reached in the Scandinavian countries and the United States (US). The combination of high uptake two-dose

childhood vaccination programmes in combination with postpartum vaccination of susceptible women has eliminated rubella within a decade [1-3]. Whatever the strategy –adherence and efficacy of the programmes will be decisive for the end result. This is clearly illustrated in an article in this issue by Pandolfi and co-workers that gives an overview of data from surveillance systems of the World Health Organization (WHO) and the European surveillance community network for vaccine-preventable infectious diseases, EUVAC-NET [4]: rubella still circulates in many parts of the world, including Europe. And not only in countries in which programmes for rubella elimination have only recently been implemented, but also in countries with a long history of vaccination with low uptake of the vaccine such as Italy. The authors review different strategies to improve the situation with the goal to achieve not only herd immunity but also protection of all women of childbearing age as long as the global circulation cannot be stopped. They further propose to include varicella vaccine in such programmes in order to prevent varicella in pregnancy, which bears a risk for foetal embryopathy and neonatal disease [5]. A vaccine against varicella has been available for a long time, and has been employed in universal childhood vaccination for example in the US since 1995 [6]. However, only few countries in Europe, e.g. Germany, have so far followed the US example. It is, however, likely that more countries will introduce this vaccine as combination vaccines become more available, which implies a considerable reduction in the costs. As the authors point out, the use of the vaccine for the prevention of adult varicella is today suboptimal. Wherever possible, the vaccine should be offered to non-pregnant women of childbearing age who do not have acceptable evidence of previous infection (susceptibility should preferentially be confirmed by immunity testing), especially women working as carers for children and adolescents, and parents of young children.

Vaccines may also be used in newborns in order to protect against maternal transmission during birth, as is the case for hepatitis B [7]. If vaccination is not possible such as for syphilis and infections with human immunodeficiency virus (HIV), transmission of the infection to the child may be prevented by antimicrobial therapy of the mother [8,9]. The cornerstone for such programmes is testing pregnant women when they have their first contact with maternity care. Surveillance of the efficiency of the preventive programmes is crucial for their success. As described by Giraudon et al., an efficient surveillance programme has been in place in London for nearly ten years, which monitors the extent of antenatal testing and the prevalence of susceptibility to HIV infection, hepatitis B, syphilis and rubella [10]. If the acceptance rate for testing is low, this will be investigated rapidly and the information used

promptly to improve the uptake. It is noteworthy that this study also investigated how children of women infected with hepatitis B are followed up by vaccination, a programme that frequently suffers from a high rate of non-adherence.

A more cumbersome strategy has to be adopted if treatment needs to be given to the mother within a short interval after contracting the infection, in order to prevent permanent damage of the child. This is the case with *Toxoplasma gondii* infections, and seronegative women, who may be exposed any time, have to be screened at monthly intervals starting at the latest in the 12th week of pregnancy [11]. C. Cornu et al. studied factors influencing adherence to such a programme in the French Rhone-Alps region [12]. The authors conclude that there are gaps in the adherence to the screening schedule, regarding the adequate time of first visit, intervals between visits and numbers of subsequent visits for sampling. They suggest that simplification of the logistics of the procedure (prescription, reimbursement) might improve adherence, but also point out that special attention needs to be paid to the background of the women who are not able to follow the schedule.

A study from Greece by I. Elefsiniotis et al. highlights the, often significant, differences in the epidemiology of hepatitis B that exist between immigrants and indigenous inhabitants [13]. The very high rate of hepatitis B in immigrants from Albania illustrates the well-known fact that special attention has to be taken to include immigrants and refugees in ongoing public health programmes.

Other populations who need special attention and care are drug users who are at high risk of contracting blood borne and sexually transmitted disease. These aspects and the need for social and psychiatric support is well summarised in the review from Lisbon by V.A. Gyarmathy and co-workers [14].

The present status and knowledge of congenital CMV is the topic of three more papers in this issue of Eurosurveillance. The fact that CMV infections are without symptoms in pregnant women and in most of the congenitally infected neonates, has made the exploration of the topic cumbersome, but much information has been gained from large prospective studies (see the review by Ludwig and Hengel [15]). Previously, retrospective diagnosis of congenital CMV at the time of the appearance of late sequelae had not been possible as differentiation between congenital and the very frequent early postnatal infection could not be done. However, advances in molecular diagnostics now allow a retrospective diagnosis, provided that dried blood spots from metabolic testing are preserved, which at the same time provide an easier approach to epidemiological investigations, as exemplified by P. Paixão et al. [16].

The epidemiology of CMV varies widely in different populations but, wherever tested to date, congenital CMV is a major cause (20-25 %) of severe neurologic deafness, often with delayed onset. Severe neurologic disability and ocular problems may also occur. The present knowledge on congenital CMV infection is summarised in the review by A. Ludwig and H. Hengel [15] and the report by A. Vossen et al. [17] from the International Conference on Congenital CMV, held at the Centers for Disease Control and Prevention (CDC) in Atlanta in November 2008.

A first-grade conference on this topic being held at the US CDC underlines the great efforts directed to the prevention of congenital

CMV in the US. The development of a CMV vaccine is considered a first priority, followed by seroepidemiology in different populations and mapping of the extent of congenital CMV among deaf children, pathophysiology and many other aspects.

In Europe, a screening programme to identify primary CMV infection in pregnancy has been in place for some years in Italy, now withdrawn but considerable voluntary testing is still ongoing, and valuable experience has been gained [18-19]. Several other projects are ongoing or starting (e.g. in Belgium, France, Germany, Sweden, the United Kingdom and several other European countries). Controlled studies are being initiated on the effectiveness of immunotherapy in preventing or alleviating foetal damage and on antiviral therapy for the treatment of children with symptoms affecting the central nervous system [20].

There is also a role for hygienic measures in avoiding transmission of CMV, a ubiquitous infection among young children. The European Congenital CMV Initiative (ECCI), a collaborative organisation of European CMV researchers from many disciplines, initiated by G.M. Revello, T. Lazarotto and M. Barbi is now distributing information to the public and to health professionals through the London-based website (www.ecci.ac.uk). The website also contains a case register. Further information is available at the website of the US CDC (www.cdc.gov/cmvm) as well as on a national basis on a Swedish website on congenital-perinatal infection (www.infpreg.se). As it is apparent that the public health impact of congenital CMV damage is considerable, more resources are now needed in Europe as in the US in order to make further progress in prevention. The strength of a European collaboration has previously been well illustrated in the European Union collaborative study of mother-to-child transmission of HIV, hepatitis C and toxoplasmosis [21-23].

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