Assessment of screening for cytomegalovirus (CMV) infection in pregnant women in France

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Aim

To assess the benefit of serological screening for cytomegalovirus (CMV) infection in pregnant women in France.

Results and conclusions

(i) *Natural history of the disease*. This is not fully understood. A pregnant woman may become infected with CMV as a result of primary or secondary infection (reinfection or viral reactivation). The disease is not always transmitted to the child. However, if this does occur, the newborn may or may not be symptomatic, and sequelae may appear months or years later. There is little data on the frequency and severity of fetal infection following secondary maternal infection.

(ii) *Epidemiological data*. Approximately 50% of pregnant women in France are sero-negative and 0.6 -1.4% have a primary infection. The transmission rate from mother to fetus is about 47% for primary infection; the estimated prevalence among neonates is 0.5%. There is little data on (a) the incidence of secondary infection, (b) the rate and severity of sequelae, particularly long-term sequelae, in infected neonates who are asymptomatic at birth.

(iii) *Risk factors*. Identified risk factors are not specific, i.e. first pregnancy in a young and/or unmarried mother, low socio-economic level. Creche and nursery staff are thought to have a higher risk of seroconversion and therefore a higher seroprevalence, but the profession itself is not an established risk factor for congenital infection.

(iv) *Diagnostic tests*. ELISA tests for anti-CMV IgG and IgM are available but their performance is hard to assess in the absence of a reference test. They determine the serological status of a pregnant woman or support a diagnosis of recent maternal infection. The tests are simple and noninvasive for the mother but can be difficult to interpret. In particular, secondary infection is difficult, even impossible, to diagnose.

(v) *Treatment*. There is no preventive or curative treatment for CMV infection. In France, lifestyle measures are recommended but their efficacy and feasibility have not been assessed. There is no consensus on how to manage recent maternal infection (ultrasound monitoring alone or combined with amniocentesis). It is difficult to give any prognosis for the fetus and, at present (2004), the only possible intervention to reduce the prevalence of severe infection and sequelae in children is medical termination of pregnancy. If a screening test has been performed, diagnosis of seroconversion implies specialist management in a multidisciplinary centre for prenatal diagnosis.

(vi) *Mass screening*. Introduction of mass screening would require a study of feasibility, acceptability, and the benefit/risk ratio. Data for building an accurate model are lacking. Serological screening could cause significant anxiety and increased amniocentesis (0.5-1% risk of miscarriage). There are ethical issues (termination of pregnancy of a potentially healthy child) and legal issues which need to be examined.

(vii) *Conclusions*. Mass serological screening for CMV infection is not justified because (a) there is no treatment, (b) the epidemiological data are incomplete, (c) it is difficult to establish any prognosis, (d) there is no consensus on management and (e) there are potential harmful consequences (anxiety, iatrogenic miscarriage, medical termination of pregnancy). For the same reasons, screening prior to conception or targeted screening of a risk population (yet to be defined) is not appropriate. Pregnant women should be given information about standard lifestyle measures. These conclusions will need to be reviewed when effective antiviral treatment or valid and reliable prognostic markers of fetal infection have become available.

Methods
The assessment was based on WHO criteria. A systematic review of the literature was carried out by the *Institut de Santé Publique d'Epidémiologie et de Développement* at Bordeaux University 2. The Medline, Embase and Pascal databases, useful websites and the grey literature were searched between 1975 and 2004. Studies were selected according to their level of evidence and quality of design. The report was submitted to a working group of 17 experts and to a multidisciplinary peer review group of 29 experts recruited from the relevant learned societies.

Looking ahead
The working group emphasized the need to

(i) produce guidelines on what to do when seroconversion is diagnosed in a pregnant woman (management) and when fetal infection is diagnosed (assessment of prognosis);
(ii) assess the lifestyle measures recommended by the *Conseil Supérieur d'Hygiène Publique*;
(iii) carry out clinical trials establishing (a) the rate of occurrence and the factors suggestive of long-term problems and sequelae, (c) the risk of transmission and sequelae in secondary infection, and (d) the safety and efficacy of new antiviral therapies.

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