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Congenital syphilis: A continuing but neglected problem

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Summary Congenital syphilis was rare in most affluent countries but there has been a slight resurgence recently in several European countries. In large parts of the world and particularly sub-Saharan Africa congenital syphilis is a significant public health problem. The cornerstone of congenital syphilis control is antenatal screening and treatment of mothers with penicillin, which is a cost-effective intervention. In affluent countries it should be strengthened among those at high risk. Clinicians should be more vigilant for the possibility of babies being born with congenital syphilis, which is often asymptomatic. In developing countries not only does antenatal care screening need to be strengthened by implementing point-of-care decentralised screening and treatment but alternative innovative approaches to controlling congenital syphilis should be explored. There is an urgent need for international health agencies to support focused approaches to tackling the tragedy of continuing congenital syphilis. This could be a part of a pro-poor strategy to meet the Millennium Development Goals.

Introduction

In much of the world congenital syphilis continues to present a significant public health problem. Untreated syphilis among pregnant women can profoundly affect pregnancy outcome. Syphilis is neither a new disease nor a newly-recognised one and humans are the sole natural host.[1,2] Many of the basic facts and characteristics of congenital involvement have been described for well over 100 years.

With the advent of penicillin in the 1940s and the establishment of its effectiveness in treating syphilis, antenatal syphilis screening services were introduced as part of national programmes for controlling congenital syphilis.[3] To a great extent these programmes were responsible for almost eliminating congenital syphilis in more affluent countries and, until recently, it was considered a disease of the past. In poorer areas of the world congenital syphilis has persisted.[4]

Although there have been marked advances in other biomedical fields the tools for the management and control of syphilis have changed little over the past 60 or so years.[5] Recently more attention has been given to congenital

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syphilis and there are indications that this is beginning to lead to some concerted action to tackle syphilis and, in particular, congenital syphilis.[6] This chapter will give an overview of the situation regarding congenital syphilis, recent developments and continuing challenges.

Congenital syphilis: epidemiology and burden of disease

Congenital syphilis in different regions of the world reflects that of syphilis more generally.[5] The World Health Organisation (WHO) estimates that 12 million people are infected with syphilis each year and more than 90% of infections occur in developing countries.[7]

In Western Europe the disease became very uncommon until recently, largely through effective treatment at genitourinary clinics with efficient partner tracing and treatment. In North America syphilis rates have historically been higher than in Western Europe.[2,8] In 1999 the United States of America agreed a national plan to eliminate syphilis from the country[9] and some progress has been made.[10] However in the last few years the number of cases of primary and secondary syphilis has increased in the United States[11] and in many European countries.[12–14]

In high-income countries, until recently, very few babies were born with congenital syphilis but there has been a slight resurgence over the past decade.[12,13] In the United Kingdom the reported number of babies with syphilis increased from two in 1996 to 14 in 2005[15] (a rate of 1.9 per 100,000 births) and 'anecdotal reports suggest that many more cases of congenital syphilis have been seen than have been reported…and if control strategies are not improved an increasing number of cases will emerge as the (syphilis) epidemic progresses'.[13]

In the USA there has been a consistent fall in the number of babies born with syphilis from a high in 1991 of 4410 to 353 in 2004 (a rate of 8.8 cases per 100,000 livebirths).[16] Congenital syphilis was very rare before 1990 in Eastern Europe and the former Soviet Union, but the number of babies born with syphilis in the Russian Federation increased from 29 in 1991 to 743 in 1999, a rise from 0.9 to 8.5 cases per 100,000 live births.[17,18]

In much of the developing world the prevalence of syphilis among pregnant women and the consequent congenital syphilis has continued to be an often unappreciated but significant public health problem.[6] Rates vary greatly with, for example, the reported prevalence in Asia of syphilis among pregnant women being generally below 5%,[7,19–21] while in Latin America and the Caribbean rates tend to be higher at between 5% and 10%.[3,22]

In sub-Saharan Africa syphilis is common among women in the fertile age group, with recent national surveys reporting rates ranging from 3.1% in Uganda[23] to 4.2% in Madagascar,[24] 6.6% in Ghana[25] and 8.3% in Zambia.[26] Among pregnant women prevalence is frequently around 10% and rates as high as 17% have been reported.[27] Re-infection with syphilis during pregnancy is also common with reports suggesting it occurs in about 10% of infected women.[28]

Syphilis promotes transmission of human immunodeficiency virus (HIV)[29,30] and susceptibility to infection by either is probably increased during pregnancy.[31,32] This makes the implications of the HIV epidemic in sub-Saharan Africa on existing endemic syphilis particularly tragic. However, paradoxically in most countries more attention has been given to screening for HIV for which, at present, no cure is available. This has led to the situation where people are 'avoiding HIV and dying of syphilis'.[33]

About a million pregnancies globally are annually adversely affected by syphilis (about 270,000 babies are born with congenital syphilis, 460,000 pregnancies end in abortion or perinatal death and 270,000 babies are born prematurely or with low birthweight).[4,34,35] This is higher than for other major neonatal infections including HIV infection and tetanus. In sub-Saharan Africa it is estimated that about a third of stillbirths are caused by infection with syphilis, a similar percentage to that estimated by Osler in 1917 to be the then situation in the USA.[36]

A considerable burden is placed on the already limited health services in many developing countries with around 5% of babies being born with congenital syphilis.[22,37] Babies with congenital syphilis are more likely to be admitted to a neonatal intensive care unit (NICU), stay longer in hospital and receive care which is more than three times higher than the cost of that for an infant without the disease.[38,39] In one large South African referral hospital, on average one NICU bed out of a total of 12 is occupied by a baby with syphilis.[40]

The organism—microbiology

Syphilis is caused by *Treponema pallidum* but little is known about its mechanism of action or what determines virulence of infection.[1] Treponemes are macroaerophilic gram-negative bacteria that are 6–20 μm long and 0.1–0.5 μm in diameter.[2] The genome was sequenced in 1998 and the outer membrane is mostly lipid and contains little protein creating challenges for the development of accurate diagnostic tests and effective vaccines.[8,41]

Maternal syphilis

Frequently women infected with syphilis are unaware of this. The painless genital sores (or chancres) of primary syphilis often go unnoticed and many women do not seek care. This is followed several weeks or months later by widespread cutaneous, mucosal and sometimes systemic indications of the dissemination of the spirochetes of secondary syphilis. Syphilis is most contagious at this stage, which can last up to a year. Again treatment might not be sought nor be accessible and even without treatment both primary and secondary lesions resolve and the infection enters a 'latent' stage. During this phase there are no clinical manifestations but, as during the primary and secondary stages, the infection can still be passed to babies born to infected mothers.

Congenital syphilis—clinical features

The consequences of infection with syphilis on affected babies are profound. Congenital syphilis is a multiorgan infection that may cause neurological or skeletal disabilities or death in the fetus or newborn. However, when