The incidence of congenital syphilis in the United Kingdom: February 2010 to January 2015

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Objective
To estimate the incidence of congenital syphilis in the UK.

Design
Prospective study

Setting and population
United Kingdom

Methods
Children born between February 2010 and January 2015 with a suspected diagnosis of congenital syphilis were reported through an active surveillance system.

Main outcome measures
Number of congenital syphilis cases and incidence.

Results
For all years reported incidence was below the WHO threshold for elimination (<0.5/1000 live births). 17 cases (male=12, female=5) were identified. About 50% of infants (8/17) were born preterm (<37 weeks gestation): median birth weight 2000g (865g - 3170g). Clinical presentation varied from asymptomatic to acute disease, including severe anaemia, hepatosplenomegaly, rhinitis, thrombocytopenia, skeletal damage, and neurosyphilis. One infant was deaf and blind. Median maternal age was 20 years (17 - 31) at delivery. Where maternal stage of infection was recorded, 6/10 had primary, 3/10 secondary and 1/10 early latent syphilis. Most mothers were white (13/16). Country of birth was recorded for 12 mothers: UK (6), Eastern Europe (3), Middle East (1), and SE Asia (2). Social circumstances of mothers varied and included drug use and sex work. Some experienced difficulty accessing health care.

Conclusions
The incidence of congenital syphilis is controlled and monitored by healthcare services and related surveillance systems, and is now below the WHO elimination threshold. However, reducing the public health impact of this preventable disease in the UK is highly dependent on the successful implementation of WHO elimination standards across Europe.

Key words  Congenital syphilis, Epidemiology, Elimination, United Kingdom.
Tweetable abstract

Congenital syphilis incidence in the UK is at a very low level and well below the WHO elimination threshold.

Introduction

Alongside the re-emergence of infectious syphilis in adults at the beginning of the 21st century, there has been an increase in the number of reports of congenitally acquired syphilis. Between 2001 and 2009 around nine diagnoses of congenital syphilis were reported annually by Genitourinary Medicine (GUM) services but information from outbreak investigations and case reports suggested that congenital syphilis was more widespread1-4. Diagnoses of infectious syphilis in reproductive age women fell from 268 in 2010 to 206 in 2013 (Figure 1)5. The uptake of antenatal screening in England rose from 96.6% in 2010 to 97.9% in 20136. Despite the high antenatal screening coverage concerns were raised about the effectiveness of case management and control strategies7. This study was instigated in 2010 to estimate the incidence of congenital syphilis. The elimination of congenital syphilis from the UK was considered within the framework of the 2013 WHO guidelines for validating the elimination of mother to child transmission of syphilis8.

Methods

The methodology was based on that described by Hurtig et al. (1998) in the previous UK study of congenital syphilis undertaken between 1994 and 19979. Briefly, an initial dataset was created by combining returns made through the British Paediatric Surveillance Unit’s (BPSU) active surveillance system with laboratory reports (voluntary reporting), diagnoses reported through the GUM Clinic Activity Dataset (GUMCAD) (mandatory reporting), the national STI surveillance dataset, and ad hoc reports made by healthcare professionals10. The surveillance case definitions used during this initial data collection phase were as inclusive as possible. Paediatricians were asked to report ‘any child under the age of 24 months with a confirmed or presumptive diagnosis of congenital syphilis or acquired syphilis’ born between February 2010 and January 2015 inclusive. This definition was also used for ad hoc reports. Interrogation of Public Health England (PHE) laboratory report data was
undertaken every three months to identify children under the age of 24 months who had evidence of exposure to *Treponema pallidum*. The GUMCAD dataset was searched for diagnoses of congenital syphilis annually. All reports of suspected cases were followed up through letters, telephone calls and emails to paediatricians and microbiologists as the suspected cases were found. No limit was placed on length of time taken to capture the required information. The final surveillance dataset was created after harmonisation with data from the Surveillance of Antenatal Syphilis Screening (SASS) study which obtained data on all pregnant women testing positive for syphilis in 2010 and 2011 to evaluate the UK national antenatal syphilis screening programme.

Diagnoses of congenital syphilis were classified using the criteria given in the US Centers for Disease Control and Prevention *Morbidity and Mortality Weekly Report* (1997) (Table 1). These criteria are in line with the WHO definition of congenital syphilis in its guidelines for the elimination of mother-to-child transmission of syphilis. Reports from the different surveillance sources were de-duplicated and the remaining followed-up using a questionnaire. Data were collected on infant and maternal demographic characteristics including ethnicity and country of birth, clinical presentation, health services attended, stage of infection (mother only), microbiological results, treatment and clinical management. Gestational age was calculated using the date of the last menstrual period. Follow-up was not attempted beyond that required to establish a positive or negative diagnosis of congenital syphilis in the infant. No estimate of fetal loss was made. For the purposes of this paper confirmed, presumptive and possible diagnoses (Table 1) were considered to be cases of congenital syphilis. Negative diagnoses were based on microbiological and clinical evidence.

During this study, faulty batches of a syphilis laboratory test which carried an increased risk of false positive results were identified. The IgM test results for the congenital syphilis cases identified when this batch was in use were verified by PHE Microbiology Services.
The numerator for the calculation of the annual incidence of congenital syphilis in the UK was the number of cases detected through the surveillance system described here; the denominator consisted of the number of estimated live births in the UK during the time period covered by this study (Official Statistics). Further information on the populations from which the cases were drawn was not collected and was not available from official demographic datasets. Findings from this and other published investigations were compared against the incidence and process targets given in the WHO framework for the elimination of mother-to-child transmission of syphilis to assess whether congenital syphilis incidence within the UK had reached elimination.

Results

A total of 175 reports were received and investigated between February 2010 and January 2015 inclusive, around 35 per annum. Information was derived from laboratory reports (113), BPSU returns (62), GUM clinics (0), the SASS Survey (3) and ad hoc reports (1) (four reports were derived from more than one information source). Seventeen reports were classified as cases (3 confirmed, 13 presumptive, one possible). The remaining 158 reports were subsequently classified as negative. Although a similar number of reports were identified and investigated in each of the five years, 10 of the 17 cases were born in 2010 (Figure 2). About 50% of the cases (8/17) were born preterm at <37 weeks gestation, these infants having a median birth weight of 2000g (range: 865g to 3170g). No multiple births were reported.

Clinical presentation of the 17 cases (12 male, 5 female) varied from asymptomatic (7/17) to acute, with symptoms including severe anaemia, hepatosplenomegaly, rhinitis, oedema, thrombocytopenia, skeletal damage and neurosyphilis. One infant was deaf and blind. One case was an intrauterine death (second trimester). A stillbirth (34 weeks) was also investigated but although the mother had serological evidence of syphilis infection no evidence of congenital syphilis was seen in the infant. The cause of death was fetal
thrombotic vasculopathy. Four of the 16 surviving children were reported to have been taken into the care of social services.

Two mothers were diagnosed between 20 and 30 weeks gestation and two just over a month before they gave birth. Three mothers were diagnosed in the last month of pregnancy (includes one concealed pregnancy), five at delivery and five after delivery. Median maternal age at delivery was 20 (range: 17 to 31). Of the 16 mothers for whom ethnicity was recorded 13 were white. Country of birth was only available for 12/17 women: six were born in the UK, four of the 12 in Eastern Europe and the Middle East, and two in South East Asia.

Although reports were received from all parts of the UK, cases were only seen in England. Individual cases were seen in all English regions. A geographic cluster consisting of a number of suspected reports of congenital syphilis, including one which was subsequently defined as a case, was identified in a group of Eastern European migrants. This highly unusual incident was managed by a local outbreak control team.

Stage of infection was recorded for 10 mothers, six of whom presented with primary syphilis, three with secondary and one with early latent syphilis. All mothers diagnosed with syphilis were managed according to British Association of Sexual Health and HIV Guidelines and many were the subject of further investigations by local Health Protection Units. The social circumstances of mothers varied and included injecting drug use, sex work and imprisonment, and some had experienced difficulty accessing healthcare due to cultural barriers.

Comparability with WHO elimination guidelines

For each year studied the incidence of congenital syphilis was well below the WHO threshold of <0.5/1000 live births (Table 2): 0.0149/1000 births (2010), 0.0025/1000 (2011), 0.0026/1000 (2013) and 0.0013/1000 (2014).

Discussion

Main findings
The WHO seeks to eliminate congenital syphilis using a three step strategy; universal access to antenatal care, including screening for syphilis, access to care in early pregnancy, and on-site testing and treatment supported by clearly structured healthcare pathways\(^7\). In the UK, this well established strategy is supported by open access, free and confidential GUM services, including partner notification, a combination of interventions that has kept incidence below the WHO elimination threshold. These interventions have been successful in achieving the WHO Europe targets for the elimination of congenital syphilis (Table 2).

At the nadir of the syphilis epidemic in the mid-1990s Hurtig et al. identified nine presumptive and eight possible cases of congenital syphilis which represented an incidence of 0.006/1000 live births, findings that were sufficient to ensure that antenatal screening was retained into the 21st century\(^9,18\). Although incidence was less than half that reported by Hurtig et al. from 2011 to 2014 our study indicated that congenital syphilis continues to present a complex clinical, social and public health problem in the UK. For example, several of the mothers had experienced difficulties accessing healthcare and consequently most children diagnosed with congenital syphilis were born to women who presented to antenatal services close to delivery. Another example of the difficult social circumstances of some of the families involved was that several children were taken into the care of social services. Although some congenital syphilis cases were asymptomatic, clinical presentation varied substantially and in some cases was life threatening. In contrast Hurtig et al. only reported clinical abnormalities in three of their 17 cases: two had signs on x ray, one osteochondritis of the skull, and the third had hepatosplenomegaly, rhinitis, oedema and thrombocytopenia.

**Strengths and limitations**

The characteristics of surveillance systems vary in relation to their purpose. Here data were drawn from a number of systems. Whilst this was a strength of the investigation in that it allowed as many suspected cases as possible to be captured it also resulted in the collection of several overlapping datasets. For example, the laboratory data did not correspond exactly with the BPSU reports because the laboratory report system relies on voluntary reporting as
does the referral of samples for confirmatory testing. Suspected cases reported by more
than one source were de-duplicated prior to analysis.

The small number of detected cases presented a number of challenges: in particular
providing a detailed insight into the epidemiology of this rare disease whilst preserving
patient confidentiality. Consequently cross tabulations have not been shown and no
information has been presented that could identify individuals.

**Interpretation**

The past decade has seen increased population movement across the European Union. In
this study several of the mothers of children with congenital syphilis were born in Eastern
Europe and the Middle East whereas none of the cases described by Hurtig *et al.* twenty
years earlier were linked to these regions. Historically Eastern Europe has experienced a
high rate of infectious syphilis diagnoses amongst women of reproductive age and this was
reflected in the findings of this study including the outbreak control team investigation of the
cluster. Social marginalisation of such migrants has also been suggested as a factor that has
contributed to a resurgence of congenital syphilis in Italy. Unfortunately it is difficult to
compare trends in incidence and screening coverage between European countries because
of variations in methodology. Antenatal screening coverage is below the WHO target
across Eastern Europe and, for some minority groups living in marginalised settlements,
access to antenatal care and sexual health services is limited.

The WHO target seeks to support the elimination of mother-to-child transmission of syphilis
worldwide. This encompasses a wide variety of healthcare systems that seek to control
distinctly different epidemics. It is for individual countries to use the information from the
impact and process indicators to refine local control strategies even if the target has been
met. For example, the presence of diagnoses of congenital syphilis within the UK indicates
gaps in coverage of the antenatal care delivery systems and syphilis intervention strategies
aimed at adults. Identifying women at high risk of infection and encouraging them to attend
clinical services in early pregnancy is challenging. Local, proactive multi-agency interventions aimed at improving service access for women, their children and sexual partners in communities that have low rates of general practice registration and antenatal care attendance could play a vital role in increasing engagement with healthcare services. Clinicians also need to develop ways of identifying vulnerable women who may present late for antenatal care and who are at risk of missing out on appropriate interventions.

**Conclusion**

Congenital syphilis in the UK continues to be contained by maintaining high quality healthcare services including antenatal screening, and related surveillance systems. A possible reduction in incidence since 2010 may suggest that vulnerable groups are engaging with health services. Achieving further reductions is highly dependent on the successful implementation and maintenance of WHO standards for the elimination of mother to child transmission of syphilis across Europe.

**Disclosure of interests**

The authors declare no financial, personal or professional competing interests related to the work detailed in this manuscript, nor do any of the authors maintain a financial stake in any product, device or drug cited in this report. The ICMJE disclosure forms are available as online supporting information.

**Contribution to authorship**

IS instigated the study with BE and developed the methodology with PT, BG, HL and CI. IS, PT and CL harmonised the dataset against the SASS dataset. BG, CI and HF advised on the case definition, microbiological diagnosis and the final diagnosis attributed to each report. All authors contributed to drafting and revising the manuscript.

**Details of ethics approval**

The Central London research ethics committee granted ethical approval for the study (REC reference 09/H0718/44) on 7 October 2009.
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References


12 CDC. Case definitions for infectious conditions under public health surveillance. Recommendation and reports RR-10. *MMWR* 1997;46.


Figure 1 Uptake of antenatal screening for syphilis and diagnoses of infectious syphilis in reproductive age women, England: 2010 to 2013

Figure 2 Congenital syphilis: confirmed, presumptive and possible cases together with negative reports by date of birth: 2010 (Feb) to 2015 (Jan)

Table 1 Summary of congenital syphilis case definitions adapted from MMWR 1997 and Hurtig et al. 19989,12

Table 2 WHO targets for validating the elimination of mother to child transmission of infectious syphilis8
**Table 1** Summary of congenital syphilis case definitions adapted from MMWR 1997 and Hurtig et al. 1998\(^9\)^12

<table>
<thead>
<tr>
<th>Definition</th>
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<tbody>
<tr>
<td>1 Confirmed(^*) (definite(^†))</td>
<td>Demonstration of <em>Treponema pallidum</em> by darkfield microscopy, fluorescent antibody, or other specific stains in specimens from lesions, placenta, umbilical cord, or autopsy material. Also included specimens shown to be positive as a result of polymerase chain reaction (PCR) testing(^††)</td>
</tr>
<tr>
<td>2 Presumptive (probable(^†))</td>
<td>(i) A condition affecting an infant whose mother had untreated or inadequately treated syphilis at delivery, regardless of signs in the infant; or &lt;br&gt; (ii) An infant or child who has a reactive treponemal test for syphilis; and any one of the following: &lt;br&gt; o a reactive fluorescent treponemal antibody absorbed—19S-IgM antibody test or IgM enzyme-linked immunosorbent &lt;br&gt; o any evidence of congenital syphilis on physical examination &lt;br&gt; o any evidence of congenital syphilis on radiographs of long bones &lt;br&gt; o a reactive cerebrospinal fluid (CSF) venereal disease research laboratory (VDRL) &lt;br&gt; o an elevated CSF cell count or protein (without other cause)</td>
</tr>
<tr>
<td>3 Possible(^**)††</td>
<td>Infants where congenital syphilis was indicated but for whom laboratory results were either not recorded or inconclusive. For example, where the result of the infant’s IgM test was positive but no corresponding information was recorded for the mother.</td>
</tr>
</tbody>
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\(^*\) Direct detection of *T. pallidum* was performed on three reports; one infant was negative, the others positive.  
\(^†\) Terminology used by Hurtig et al.\(^9\)  
\(^**\) Not included in MMWR definition but used by Hurtig et al.\(^9\)  
\(^††\) Criteria extended to include PCR diagnosis to reflect current diagnostic practice.
Table 2  WHO targets for validating the elimination of mother to child transmission of infectious syphilis

<table>
<thead>
<tr>
<th>Targets</th>
<th>Criteria met?</th>
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<tbody>
<tr>
<td>Impact</td>
<td></td>
</tr>
<tr>
<td>≤50 cases of congenital syphilis per 100 000 (0.5/1000) live births</td>
<td>Yes</td>
</tr>
<tr>
<td>Process</td>
<td></td>
</tr>
<tr>
<td>Antenatal care coverage (at least one visit) of ≥95%</td>
<td>Yes¹⁶</td>
</tr>
<tr>
<td>Coverage of syphilis testing of pregnant women of ≥95%</td>
<td>Yes⁶</td>
</tr>
<tr>
<td>Treatment of syphilis seropositive pregnant women of ≥95%</td>
<td>Yes¹¹*</td>
</tr>
</tbody>
</table>

*96.1% (516/537) of seropositive women requiring treatment in pregnancy (i.e. with active newly diagnosed infection or uncertainty about previous treatment) treated effectively (SASS study data)¹