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Hand–genital transmission of genital warts? An analysis of prevalence data

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SUMMARY

The role of hand–genital transmission in the aetiology of genital warts is unclear. However this route is suggested by a number of observations including the relatively high proportion of genital warts in children which contain HPV types 1–4 (15% for children and 2% for adults). We compared two transmission models; one which assumes that hand–genital transmission occurs and one that it does not, and determined the conditions in which each model can reflect the available prevalence data. Hand–genital transmission provides a simple explanation of the observed differences in the proportions of genital warts containing HPV types 1–4 and 6/11 in children and adults. If hand–genital transmission does not occur, the observed difference could only be explained by an eightfold greater probability of transmission to children of types 1–4 than types 6/11, or by an eightfold greater duration of infection with types 1–4. Our findings provide support for the view that genital warts may be transmitted by hand–genital contact.

INTRODUCTION

Earlier this century genital warts were believed to be transmitted by hand–genital contact rather than by sexual intercourse. However, in 1954, sexual transmission was demonstrated by Barrett and colleagues who noted that genital warts had developed in the wives of returned service men who themselves were affected with the same condition [1]. A later study by Oriel documented a mean incubation of 2·8 months for this condition [2]. The transmission of genital warts in children is less clear. Some believe this condition in children is virtually pathognomonic of sexual abuse [3, 4], while others disagree [5]. To clarify this, the proportion of children with genital warts who have documented sexual abuse has been estimated, but varies greatly from a low of 11% ($n = 73$) in one study to 91% ($n = 11$) in another [6, 7].

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Determining the HPV type of genital warts is another approach that was initially hoped to provide more objective information about their aetiology in children, because of the observation in adults that most genital warts contain HPV types 6/11 (and less commonly types 16 and 18) while warts on the hands contain HPV types 1–4 [8, 9]. If genital warts in children are caused solely by sexual abuse, the same HPV types should be found in genital warts in children and adults.

Studies suggest that the HPV types 1–4 make a significant contribution to genital warts in children but not in adults. In this paper we compare two transmission models; one which assumes hand–genital transmission occurs and one assuming it does not. The objective was to determine the conditions in which each model can reflect the observed proportions of genital warts due to HPV types 1–4 and 6/11.

METHODS

Simple model for endemic STDs

In a population of N sexually active persons, suppose that Y individuals are infected with a sexually transmitted disease. The remaining $X\,(=N-Y)$ individuals in the population are susceptible to the disease and, if they are a sexual partner of an infected person, may be infected with a probability p. Infected individuals recover (or are cured) at a rate v and are then susceptible to further infection. To achieve the simplest model, it is assumed that each individual has c partners per unit time.

If the disease is at an endemic equilibrium, the prevalence of disease is constant over time. The number of persons recovering from infection over a period of time is therefore equal to the number of new infections in that time. Hence

$$vY = Xpc\frac{Y}{N}.$$

This equation has the solutions

$$y = 0 \quad \text{and} \quad y = 1-\frac{v}{pc},$$

where $y\,(=Y/N)$ denotes the prevalence of infection. The prevalence at the endemic equilibrium is determined by the recovery rate (duration of infection), the number of partners, and the per partner transmission probability. The endemic state only exists if $pc > v$; if $pc \leqslant v$ the disease cannot persist in the population [10].

This simple, homogeneous model does not explore the great heterogeneity that exists in sexual behaviour. In any real population some individuals will have many partners, others relatively few. Diseases may persist mainly in core groups consisting of individuals who have a large number of partners. Some authors have defined an 'effective rate of partner change' to derive a value of c that takes some account of this phenomenon [10]. Other studies have produced more complex models in an attempt to describe in detail the interactions between subgroups of populations [11, 12], but such details are not fundamental to the arguments presented here.

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Table 1. *Number of genital warts due to different HPV types in children and adults: collation of published data*

	Children	Adults
HPV types 1–4	27	2
HPV types 6/11	104	60
Other HPV types	12	1
HPV negative	41	18
Total	184	81
References	6, 7, 9, 14–24	8

Assumptions. For the purposes of this study, HPV types 1–4 are considered as a single infection, and types 6 and 11 as another single infection which circulates independently in the same population. HPV causes both hand and genital warts; scenarios are investigated in which hand–genital transmission does and does not occur. The population is divided into adults, who may be sexually active, and children whose only sexual contact is through sexual abuse.

Notation. We denote the prevalence of genital warts in the adult and child populations by A and C respectively, with subscripts *1* and *6* to indicate types 1–4 and 6/11 respectively.

Reported prevalence

Accurate information on the proportion of individuals with genital or hand warts or the proportion infected with various HPV types is not available. Estimates of these have been drawn from available published information or from personal communication with experts in the field.

Genital warts. The prevalence of genital warts in the general adult population (20–40 years of age) is about 1% [13]. In a study of 81 cases, 2% were found to contain HPV types 1–4, while 74% contained HPV types 6/11; the remaining 24% either contained other HPV types or were negative (Table 1) [8]. These figures concur with observations made by zur Hausen (personal communication). Hence we take

$$\frac{A_1}{A_6} = \frac{2}{60}.$$

The prevalence of genital warts in children is not known, but the HPV type in genital warts from 184 children have been analysed in studies published to date. These results are collated in Table 1: 57% contained HPV 6 or 11, 15% HPV 1–4, while the remaining 28% were either negative or contained other types [6, 7, 9, 14–24]. There was however considerable variation in the proportion of warts containing HPV types 1–4 in each study. Of the larger studies, one reported HPV 2 in only 1 (4%) of 25 genital warts while another found 6 (35%) of 17 genital warts contained HPV 2 [14, 15]. This variation may indicate a biased referral or reporting pattern.

Using all the cases from previous studies, the ratio of types 1–4 to 6/11 in genital warts in children is

$$\frac{C_1}{C_6} = \frac{27}{104}.$$

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Hand warts. The reported prevalence of hand warts in children and adults varies from 3·5 to 9·9% [25, 26]. We were unable to locate publications reporting HPV types 6/11 in common warts from non-immunosuppressed individuals and nor has zur Hausen identified them from 2000 warts from non-genital sites (personal communication). Therefore we will assume that all hand warts are due to types 1–4 [8, 9].

RESULTS

Scenario 1. No hand–genital transmission occurs

If no hand–genital transmission occurs then genital warts caused by types 1–4 and 6/11 can be considered as two independent STD circulating in the same population. The simple model explained earlier does not capture the detailed heterogeneity of the contacts within the population. However, the principle established is that the endemic prevalence depends on the 'effective' number of partners, the transmission probability, and the duration of infection. Two diseases circulating in the same population encounter exactly the same patterns of sexual behaviour and partnership formation. Therefore, in the absence of competition between these diseases, differences in the endemic prevalence must be due to differences in the duration of infection or differences in the probability of transmission from an infected person to his/her partners, i.e. $A_1 < A_6$ implies that

$$\frac{p_1}{v_1} < \frac{p_6}{v_6}. \tag{1}$$

The non-linear relationship means that small differences in these parameters can cause large differences in the endemic prevalence.

If genital warts are caused solely by genital–genital contact then genital warts in children (assumed not to be sexually active) must be caused by sexual abuse from an infected adult. Committing sexual abuse is assumed to be independent of infection with genital warts. Thus the incidence of genital warts in children is proportional to the prevalence of genital warts in adults, since no transmission occurs between children. The prevalence of genital warts in children is determined by the equilibrium between recoveries and new cases:

$$v'C = ap'A,$$

where a is the incidence of sexual abuse (average number of abusers per child per unit time), p' is the probability of transmission to children through sexual abuse, and $1/v'$ is the average duration of infection in children. So the relative prevalence of types 1–4 and 6/11 is given by

$$\frac{C_1}{C_6} = \frac{p'_1}{p'_6}\frac{v'_6}{v'_1}\frac{A_1}{A_6}. \tag{2}$$

We have demonstrated (equation (1)) that, in order to explain the observed differences in prevalence in adults

$$\frac{p_1}{p_6}\frac{v_6}{v_1} < 1.$$

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If the ratio of the probabilities of transmission of types 1–4 and 6/11 to children is the same as for transmission to adults (i.e. $p'_1/p'_6 = p_1/p_6$), and the ratio of durations of infection by types 1–4 and 6/11 in children is the same as in adults (i.e. $v'_1/v'_6 = v_1/v_6$) then (from equation (2))

$$\frac{C_1}{C_6} < \frac{A_1}{A_6},$$

i.e. types 1–4 would account for an even smaller proportion of genital warts in children than in adults. This is not consistent with observations. If genital warts are caused solely by genital–genital contact then

$$\frac{p'_1}{p'_6}\frac{v'_6}{v'_1} = \frac{C_1}{C_6}\frac{A_6}{A_1} = \frac{27}{104}\frac{60}{2} = 7{\cdot}8 \quad 95\%\ \text{CI}: (1{\cdot}83, 69{\cdot}4).$$

That is, either: (*a*) the probability of transmission of genital warts to children through sexual abuse is approximately eight times greater for types 1–4 than types 6/11; or (*b*) the duration of infection in children is approximately eight times greater for types 1–4 than types 6/11; or (*c*) a suitable combination of these factors produces the same effect.

Scenario 2. Hand–genital transmission occurs

No hand warts caused by types 6/11 have been observed, so these types are assumed only to cause genital warts. The prevalence of hand warts caused by types 1–4 is approximately 5% in both adults and children. It is likely that almost all hand warts are caused by hand–hand transmission. In this scenario we assumed that hand–genital transmission can occur, and investigate the proportion of type 1–4 genital warts that might be transmitted by this route. Hand–genital transmission may occur from warts on an individual's own hands or from warts on the hands of a carer or sexual partner.

Let α denote the number of cases of genital warts types 1–4 in children caused by hand–genital transmission for every case caused by genital–genital transmission. Then

$$\frac{C_1}{C_6} = (1+\alpha)\frac{p'_1}{p'_6}\frac{v'_6}{v'_1}\frac{A_1}{A_6}.$$

If the transmission probability and duration of infection of the types do not differ between children and adults, then

$$\frac{p'_1 v'_6}{p'_6 v'_1} < 1,$$

and so

$$\alpha > \frac{C_1}{C_6}\frac{A_6}{A_1} - 1.$$

Using the observed prevalences leads to

$$\alpha > 7.$$

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This suggests that for every case of type 1–4 genital warts in children caused by sexual abuse, at least seven are caused by hand–genital contact.

DISCUSSION

Hand–genital transmission provides a simple explanation of the observed differences in the proportions of genital warts containing HPV types 1–4 and 6/11 in children and adults. More than 85% of the genital warts caused by types 1–4 may be transmitted by the hand–genital route. If hand–genital transmission does not occur, the observed difference could only be explained by an eightfold greater probability of transmission to children of types 1–4 than types 6/11, by an eightfold greater duration of infection with types 1–4, or by a combination of these factors.

There is no evidence or reasons to believe that the duration of infection with genital warts differs between HPV types. This suggests that the differences observed in the prevalence of genital warts caused by types 1–4 and 6/11 in adults are due to differences in the transmission probability, i.e. types 1–4 are less transmissible through genital–genital contact than types 6/11. If hand–genital transmission of genital warts does not occur the observed prevalences in children could only be explained if this relationship were reversed for transmission to children, so that the probability of the transmission of genital warts from an infected adult to an abused child were at least eight times higher for types 1–4 than types 6/11. Differences in transmission probability may be due to differences in the susceptibility of genital epithelium to different HPV types. However it appears unlikely that the genital epithelium of a child is more susceptible to infection with types 1–4 if the reverse is true in adults. It is not possible to extend this argument until further information is available.

The hypothesis that hand–genital contact can transmit warts from hands to genitals is supported by circumstantial evidence. First, children with genital warts containing HPV types 1–4 are often found to have warts elsewhere, or if they are not, a family member (mostly their mother) has them. In the study by Padel and colleagues for example, three of six children with genital warts due to HPV types 1–4 had warts elsewhere [14]. Two of the three who did not have warts elsewhere, had mothers with hand warts. There are also reports where HPV 2 was isolated from warts on both the genitals and the hands in the same individual [23].

The proportion of genital warts containing specific HPV types in children and adults is poorly documented. In children, this information comes from small published series, from different centres. Taken together, the overall proportion of genital warts containing HPV types 1–4 was 15%, although this varied considerably from 0 to 35% in different studies [6–9, 14–24]. These differences could be explained by random error or alternatively by a biased referral pattern. If for example, the children in one study contained a different proportion of sexually abused children, then the proportion of genital warts due to types 1–4 would vary accordingly. Two studies support this inference, with highest proportion of sexually abused children (60% and 40%) reporting the lowest proportion of HPV types 1–4 (0% and 4%) [15, 16]. In adults, the only recent

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article to have estimated the proportion of genital warts containing types 1–4 suggested the proportion was about 2% [8], and this concurs with zur Hausen (personal communication). In the absence of further information we have used this estimate.

Other possible routes of transmission have not been included in our models. Intrapartum transmission, for example, has been suggested by a number of observations including the case report of an infant with genital warts present at the time of delivery [27]. The effect of including intrapartum transmission into our models would be to increase the differences in transmissibility required to explain the observed prevalences, because most maternal genital warts contain HPV types 6/11. However, intrapartum transmission is only likely to be important for children of under 2 years of age (towards the upper limit of the incubation period).

The prevalence of hand warts (caused by HPV types 1–4) in children and adults is approximately 5%, many times greater than the prevalence of type 1–4 genital warts. Most transmission of HPV types 1–4 is therefore by hand–hand contact; genital warts play only a small role in maintaining transmission of types 1–4. Indeed, it is possible that the transmissibility of type 1–4 genital warts is below the threshold for them to remain endemic solely through genital–genital transmission, and that the majority of type 1–4 genital warts in adults are caused by hand–genital transmission. If most type 1–4 genital warts result from self infection in individuals with hand warts, it might be reasonable to expect prevalence in children to be similar to that in adults, i.e. approximately 1 in 4000.

While we suggest that hand–genital contact may be responsible for most genital warts which contain HPV types 1–4 in children, we do not mean to imply that sexual abuse is responsible for all genital warts in children which contain HPV types 6/11. Nor do we suggest that genital warts containing HPV types 1–4 rule out sexual abuse, as this may take the form of digital contact. Notwithstanding these reservations, the HPV type found in genital warts from children may be useful in determining the route of transmission. One study supported this suggestion and reported that children with evidence of sexual abuse were more likely to have HPV types 6/11, 16/18 and 31 than those without evidence of sexual abuse [28].

The transmission of genital warts in children is poorly understood, in part because this condition is rare and likely to be under reported, but also because of the difficulties of investigating a condition with such significant social and legal implications. The models used in this study are based on a number of assumptions and are applied to imprecise prevalence data. Whilst our study suggests that hand–genital transmission may transmit genital warts, additional research that defines the prevalences more clearly will allow the transmission of this condition to be better understood.

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