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PATTERN OF TRANSMISSION
RELATIVE SIGNIFICANCE OF CASES OF VARYING SEVERITY

by

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INTRODUCTION

The pattern of smallpox transmission depends significantly upon the immunity status of the exposed host. However, in addition to the several factors pertaining to the host and the environment, some factors pertaining to the infecting source itself may determine the transmission pattern, one of them being the severity of the disease in the infecting case.

Although all cases of smallpox are potentially infectious from the first day of fever until the last scab falls off, they may not have the same capacity to infect others throughout the course of the disease. Similarly, several materials, like the nasopharyngeal droplets, the saliva, sputum, tear the material from the lesions; the scabs, the urine, etc. of the patients contain virus and so are potentially infectious but it is doubtful whether all play a role in transmission of disease. Practical experience shows that the "infectivity" of a case (capacity to infect) is different from the case "being infectious".

Rao et al. (1967)[1] in their studies on intra-familial transmission have found that nearly 82% of the first generation of cases became infected from the index or source case during the first six days of the disease, especially during the fourth to sixth day. There was no contact who became infected after the thirteenth day of disease in the index case. Although this, of course, does not mean that cases of smallpox are not infective in the later stages, it is notable in these studies that transmission did not take place late in the course of the disease and, in fact, transmission was maximum during the first six days.

There is some virological evidence to support this epidemiological observation. Downie et al. (1961)[2] were able to isolate virus from throat washings from patients suffering from smallpox only from the third to the thirteenth day of disease with maximum isolates being obtained between the sixth and ninth days. They also found (1965)[3] that the circumoral skin swabs of patients and swabs taken from pillow covers used by patients yielded ample virus as early as the fifth day. These findings indicate again that variola virus is voided quite early in the course of the disease by way of the respiratory tract and suggest that transmission of infection may occur predominantly by this route.

Though maximum infectivity is during the first week of disease, all cases may not be equally infective.

The relative likelihood of transmission from a case probably depends upon several factors:

(i) the ambulatory nature of the case;
(ii) the severity of the mucous lesions in the mouth and nose;
(iii) the stage of the disease at which the case is isolated or dies.

A patient who is so sick that he cannot move out of the bed can naturally infect only those who actually come near him, whereas an ambulatory case who moves about freely contacts more potentially susceptible persons.

Since it has been found that cases of smallpox are mostly infective in the first week of the disease and since it is probable that virus excreted by the respiratory route is principally responsible for transmission, it stands to reason that the infectivity of a case depends upon the degree of severity of the enanthem a patient has, on the lips, tongue, etc., since it is such patients who void large amounts of virus in the saliva, nasopharyngeal droplets and discharges.

Since there is some epidemiological and virological evidence to show that cases of smallpox are mostly infective after the fourth or fifth day, it is possible that cases that are isolated or dead before that time may not transmit infection to home contacts to a great extent.

To provide information regarding the influence of the severity of a case on transmission, some of the relevant data which we have collected from our studies on the intra-familial transmission in families of 254 index cases are quoted here. The author's classification of the clinical varieties of smallpox is described in another paper (4.1 "The classification and frequency of the principal types of variola major"). As per this classification, the varieties are discussed in descending order of severity, "haemorrhagic", "flat", "ordinary", and "modified".

There were nine (3.5%) cases which belonged to the most severe variety, "haemorrhagic". They had 49 exposed contacts, two of whom were unvaccinated, but there was no transmission of disease to any of the contacts whether vaccinated or unvaccinated.

Six cases (2.4%) were of the "flat" variety. They had 33 contacts, one of whom was unvaccinated. The contact transmission rate was 3.0% (one case).

Two hundred and nineteen (86.2%) were of the "ordinary" variety. They had 1099 contacts, 8.6% of whom were unvaccinated. The contact transmission rate was 4.6%.

The remaining 20 (7.9%) belonged to the mildest variety, "modified". They had 68 contacts, five of whom were unvaccinated. The contact transmission rate was 1.7%.

Notably cases of the severest and mildest types resulted in the least transmission of disease. Does this mean that transmission does not depend upon severity? Probably not, for other factors, as described also bear on the probability of transmission taking place.

The "haemorrhagic" cases normally are so sick that they cannot move out of bed; they do not develop an enanthem before they die; and they are removed to the hospital much earlier in the course of the disease because of haemorrhages.

In the instance of "modified" cases, which are most ambulatory and stay longest in the home, transmission is minimal, probably because very few have an enanthem.

Cases of the "flat" variety have a severe enanthem and most remain at home for a week, but they are so severely sick that they are not ambulatory. This may account for a lower transmission rate than for "ordinary" cases.

Considering deaths, the infection rate among contacts of patients who died was slightly more than among contacts of survivors, the rates being 5.2 and 3.8%. However, a similar relationship with respect to variety and transmission rate was observed among those who died as among those who survived. Eight of nine fatal haemorrhagic cases resulted in no transmission; among contacts of six fatal "flat" cases, less transmission occurred than among contacts of "ordinary" cases.

Studies were also carried out to determine whether deaths occurring at home differed from deaths occurring at the hospital in their capacity to transmit infection.

Seven of eight deaths due to "haemorrhagic" smallpox occurred in the hospital and there was no transmission to contacts of those who died in the hospital or at home; five of six "flat" cases died in the hospital and there was no transmission to the 26 contacts of these cases, whereas one of seven vaccinated contacts of the case who died at home developed smallpox. In the case of the "ordinary" variety there were 35 deaths in the hospital as against 16 at home. 11.4% of the families of patients who died in the hospital experienced further transmission as against 43.7% of the families of patients who died at home. Only 2.3% of contacts of hospital deaths developed the disease as against 13.7% of contacts of home deaths. There were no cases of smallpox in the vaccinated contacts (0/168) of hospital deaths whereas 5.8% (5/86) of the vaccinated contacts of house deaths developed the disease; four of nine unvaccinated contacts of hospital deaths developed the disease, as against eight of nine of the house deaths. Thus one finds that deaths occurring at home result in more frequent transmission of infection to contacts than deaths occurring in the hospital. It seems conceivable that fear, strain and stress as a result of the calamity at home may cause hormonal disturbances which may predispose to infection.

In brief, it would appear that there are several factors of importance besides severity of the index case that may determine the frequency of transmission, viz, the ambulatory nature of the case, the degree of severity of the enanthem, the stage at which the case is isolated or dies, and the clinical outcome of the case, be this survival or death, or in the case of the latter, whether death has occurred at home or in the hospital. Therefore, no generalization is possible with respect to the severity of the case and the frequency of transmission.

Importance of infected houses

Since the variola virus is viable for a considerable time outside the host, it is possible for infected fomites to serve as reservoirs of infection in the absence of patients. The room occupied by a smallpox case is potentially infectious since the virus can persist if proper disinfection is not done. Several instances have been reported in which the infected room was incriminated as the source of infection for cases. Dixon (1962)[4] described how a nurse contracted smallpox in Tripoli "after cleaning out the room and removing the bedding following a very perfunctory disinfection three days earlier". He also noted an outbreak of smallpox at Hendon (1923) in which two persons who subsequently occupied the same hotel room as a case developed smallpox. In both these instances it appeared that the bed linen was the responsible fomite.

A patient's room is normally contaminated with virus discharged by the patient through the nasopharyngeal secretions and scabs. The nasopharyngeal droplets may lose their moisture envelope and float in the air in the room as droplet nuclei finally settling on the floor as infective dust. Nasopharyngeal discharges will contaminate the patient's clothing and bed linen. Shaking the clothing or bed linen or dry sweeping the floor will raise large clouds of infective particles. Although contamination of the environment certainly occurs, is it important as a medium of transmission and, if so, for how long a time? There are no certain answers to these questions.

It is worth recalling the observations made by Downie et al. (1965)[3] "the frequent failure to find virus in the air samples collected in the impinger was rather surprising. Even the air samples taken with the impinger held near the mouth of the patient, who had obvious mouth lesions and who talked, coughed, during the period of collection, were negative". However, they observed that settling plates, circumoral skin swabs and pillow cover swabs were positive. The impinger used has shown to be effective in recovering the vaccinia in one micron aerosols in a cloud chamber. They concluded that "our results indicate that very little virus is discharged from the mouth of the patient in droplets or droplet nuclei of this order of size when he is breathing, talking or coughing".

The fact that settling plates were invariably positive when impingers failed to recover the virus is an indication that virus is voided through the mouth and nose, but not in such small sized particles that they can be collected by the impingers. Hence a patient is not likely to contaminate the air in the room with the virus directly but instead contaminates the clothes and bed linen. It is possible, of course, that the air in the room may become infected later from the virus containing dust which settled on the ground or the linen.

If, as soon as a case is removed from a room, all the linen is carefully soaked in oil or water and the room is washed thoroughly with a disinfectant and opened to fresh air for 24 to 48 hours, the chances of such a room acting as a source of infection are negligible. Employing such a procedure, we experienced no cases of cross-infection amongst patients occupying a ward previously occupied by smallpox cases.

It is possible that the tropical climate and fresh winds may have played a role in reducing the quantity of virus in these wards but the use of a copious amount of water is probably most important.

Importance of air-borne infection over long distances

As noted, the failure to isolate virus from air sampled near patients indicates that the air is not directly infected by the patient through the nasopharyngeal droplets or droplet nuclei but rather that contamination occurs through the infective dust from the floor or infected linen.

Whether air so infected can carry the infection over long distances has been a controversial subject for decades. In the late nineteenth century it was believed that prevailing winds could carry the virus up to a distance of a mile; circumstantial evidence was offered in support of this view.

Several aspects of this question must be considered. Does the air in a smallpox ward or hospital become sufficiently contaminated with virus to infect persons and can the virus be carried over long distances in a concentration adequate to infect? No systematic work has been done which provide specific answers to these questions. However, there is some indirect and circumstantial evidence.

Meiklejohn et al. (1961)[5] failed to detect virus in air sampled in acute and convalescent smallpox wards at the Infectious Disease Hospital, Madras. We thought there might be something wrong with our technique or the impinger. However, using experimental aerosols, the technique was found to be quite good for detecting vaccinia virus. Yet only in one of 38 samples was virus detected. The authors concluded that "it is possible that the virus excreted in saliva or scabs is not efficiently detected by these methods. It is also likely that the very considerable air movement through the open type of wards at the hospital produced rapid dilution of the excreted virus".

Subsequent work done by us (Downie et al., 1965)[3] showed that even with an improved technique and using a liquid impinger, virus could not be detected in large quantities from air even at short distances from the patient. Even when dust was raised from the floor the detection of virus in the air of the open wards was not increased. It would seem doubtful therefore whether air can carry the infection over long distances and infect persons.

In support of this view, I would like to mention three observations from my experience.

Fig. 1 shows the disposition of the wards at the Infectious Diseases Hospital, Madras. Wards 1, 2 and 3 were almost always occupied by smallpox cases. Wards 10 to 13 are always occupied by cases of measles and chicken-pox. Vaccination of all cases is done usually on all cases except those of smallpox, within 24 to 72 hours after their admission depending upon the time of admission and the condition of the patient on admission. Seventy to 80% of all these vaccinations were successful showing that their immunity status against smallpox

was not very high. Further, wards 10 to 13 are not barricaded from the smallpox wards and it is not uncommon to find the patients from these wards spending most afternoons on the corridor connecting wards 2 and 3 and the open space between wards 3, 10 and 11. During the six years from 1961 to 1966 we admitted 11 961 cases of smallpox, 22 702 of chicken-pox, and 8825 of measles. There were only seven cases who became infected presumably while in the hospital and were readmitted for smallpox. All of these patients escaped vaccination during their stay in the hospital. Knowing as we do that vaccination after exposure has limited value in protection and in spite of the fact that there was less than 20 yards between the smallpox wards and the other wards and in spite of the fact that non-smallpox cases used the corridors leading to the smallpox wards for resting, the instances of cross-infection were very few indeed. This suggests that either the air was not heavily contaminated or that it could not carry infection this short distance.

Around the hospital there are nearly 500 huts abutting the compound wall. In no epidemic was there any greater incidence of smallpox amongst these slum dwellers near the hospital than in other areas; the vaccination success rate was in no way different here than in other areas.

There are some additional pertinent observations regarding transmission rates in familial contacts and extra-familial contacts in infected households. In studies in Madras, 115 out of 254 families studied were living in a common household with other families. Those 115 households contained 548 families with an average of 4.6 families per household. The average number of persons living in each household was 21.7. The average size of the infected family was 5.9 and that of the other families exposed was 5.2. Most of the houses have a single common entrance and the majority, a common closet and bath. The typical dwelling consists of a central open courtyard around which are rooms with open corridors connecting all entrances into the rooms. The corridors and open courtyard are used for sleeping at night. Clothes are washed either in the bathrooms or at the tap or well if one is available. The transmission rates for familial contacts of the index case and the rates amongst extra-familial contacts in this household complex are shown in Table 1. The extra familial transmission rates are considerably lower than the intra-familial rates. In the unvaccinated extra-familial contacts the transmission rate is 16 times lower than that in familial contacts and in the vaccinated contacts three times less. If the air were heavily laden with virus and able to carry infection over long distances, one would not expect to see such significant differences.

Thus, in Madras at least, air-borne transmission of smallpox does not seem to be significant.

Other modes of transmission

There is adequate documentary evidence in the literature to indicate that infected materials like clothing, rags, bed linen and even cotton may be the source of infection. As noted, laboratory findings also show that bed linen is infected by patients from the fifth day of disease and perhaps earlier and large quantities of virus may be isolated from infected linen. Studies were undertaken in Madras to determine how long this virus remains viable under conditions similar to those prevailing in houses in endemic areas. This work is still in progress. Pillow covers used by smallpox cases admitted before the fifth or sixth day of disease were kept unchanged for five days. At the end of this period, these covers were swabbed for culture of virus and carefully folded in such a way that the exposed portion was turned inside. They were kept in an empty shed in an open enclosure on a raised platform. The shed is locked but the windows are kept open. The shed has an asbestos cement roof. The linen is never agitated or removed, but every month one square inch is cut from the exposed portion. This is soaked and agitated in broth and inoculated into eggs. The preliminary results show that virus can be isolated up to a maximum of 45 days from the date of collection. The conditions of storage in this shed are not completely identical with conditions prevailing in many of the houses where linen may be kept bundled up in an ill-ventilated room or a thatched hut, whereas in this instance, the shed is well-ventilated and the roofing is asbestos cement which radiates considerable heat. The viability

might be expected to be greater in the ill-ventilated houses. In general, however, the linen used by smallpox patients in the home is washed without special intervention by the health authorities. One piece of linen that is not usually washed is the blanket or the rug (usually woollen) used by the patient in the early stage of the disease. In the later stage of the disease, a smallpox patient cannot tolerate such a heavy and uncomfortable blanket. Such blankets may contain considerable virus voided at a stage when the family does not know that the patient is suffering from smallpox. These blankets are simply folded and thus may act as a source of infection for a considerable time. We do not know how frequently this kind of transmission occurs in endemic areas.

Work is in progress to determine if simple exposure of the infected linen to the hot tropical sun may destroy virus, and whether there is any difference in viability between the respiratory virus and the scab virus under these conditions.

Amongst the other possible reservoirs of infection are the corpses of smallpox cases. We have observed no instance in which a grave digger, who buries these dead, has developed smallpox nor have any of our mortuary attendants developed smallpox. The linen or shroud covering the dead may be infectious just as the bed linen but mere handling of the body is not likely to transmit the disease. We do not know how long the virus is viable in the body following burial. Whether there is any danger in exhuming the bodies of smallpox cases within a certain period, we have no knowledge. In this field, work is also being done.

Lastly, the possibility must be considered as to whether insects, birds or animals might carry infection over distances. Flies sitting on smallpox patients are found to carry the virus on their wings and legs but whether they are subsequently responsible for transmission of infection is doubtful. However, Dixon describes one case in the Tripoli epidemic attributed to flies. Unless the infected fly actually deposits the virus on the nasal mucous membrane, there would appear to be little likelihood of the fly serving as a mechanical vector. We are presently endeavouring to determine whether mosquitos and bed-bugs can be infected with virus and whether they can transmit the infection. Even if they can be infected, the role of these insects in transmission would appear remote. In the case of these two arthropods, they would have to be infected when the patient was in the viremic stage, which is very transient, except in the haemorrhagic variety. If the virus multiplied in their body, they could transmit the infection only by inoculation through the skin, in which case the majority of smallpox cases should present the local variolar lesions at least seven to 10 days before the onset of fever, which is very rare.

Amongst the birds, the crow and the sparrow eat smallpox scabs. Although they do not, of course, develop smallpox, the question as to what happens to the virus may be important. Is it destroyed in the gut or is it excreted in their faeces? If the virus is excreted in the faeces, it may perhaps explain the mysterious spread of infection over long distances. Studies of this problem are contemplated.

Amongst the animals, dogs and cats also eat the scabs of smallpox. It is also likely that these animals, if permitted in smallpox wards, might carry virus mechanically on their furs. The likelihood that these animals might act as disseminators of infection is problematical.

In transmission of disease beyond the infected family, there are several possible routes besides that of direct contact or contact with infected linen but they are all remote possibilities. Only circumstantial evidence indicates the possibility of such modes of transmission. Perhaps the same statement cannot be categorically made in the case of the non-endemic countries.

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TABLE 1. TRANSMISSION RATES IN HOUSEHOLD COMPLEXES

	Familial contacts	Extra-familial contacts in household complex
No. of families exposed	119	433
No. of families experiencing secondary cases	13 (10.9%)	4 (0.9%)
No. of contacts	581	1 841
No. who developed smallpox	15 (2.6%)	6 (0.3%)
No. of vaccinated contacts	549	1 758
No. who developed smallpox	4 (0.7%)	4 (0.2%)
No. of unvaccinated contacts	32	83
No. who developed smallpox	11 (34.4%)	2 (2.4%)

FIG. 1. PARTIAL SCHEMATIC
INFECTIOUS DISEASES HOSPITAL, MADRAS