1973 LECTURE
Sam Middlesex Hospital

Since 1967, the World Health Organization has been engaged in a global programme intended to eradicate smallpox. Considerable progress has been made - to the extent that it is our hope and expectation that we may record the last cases within the next few years.

But eradication is still in the future and we have to look back less than 12 months to observe in Yugoslavia the largest single outbreak of smallpox in Europe since the second World War. With smallpox incidence decreasing and the extent of the infected areas similarly, the probability is becoming less that any given traveller will contract the disease. However, the number of travellers and the facility of travel are rapidly increasing. I sense also in my travels that many more visitors to the endemic areas are less likely to remain at the tourist meccas and the Intercontinental style hotels and are more likely to travel widely throughout the country, obtaining bread and board in all sorts of probable and improbable places. This demonstrably increases the risks of coming into contact with cases of smallpox since this disease, like so many others, is a disease of the less literate and the poor - a disease primarily of the city slums and rural populations.

Today, therefore, it seemed most worthwhile to discuss with you pertinent common patterns associated with smallpox importations into Europe as they provide an insight into what might be expected in the future. The events and problems associated with the recent outbreak in Yugoslavia are of special interest in this regard. Finally, I should like to summarize briefly what is happening on the global scene for the relative success, or lack thereof, of the smallpox eradication programme governs, to a large extent, whether or not smallpox may be again introduced into England.

Since 1961, smallpox has been introduced into countries of Europe on 30 spearate occasions (1). It should be noted that the United Kingdom leads all others as the principal importer of the disease. The last introduction occurred in February 1968. Since that time, in Europe, one case has been imported into Belgium

in 1968 from Zaire; an outbreak of 20 cases occurred in 1970 in Germany, imported by a German hippie

returning from Pakistan; one fatal case occurred that same year in Denmark in a medical student returning from Afghanistan - and he subsequently infected one person from Norway; and finally, in 1972, a Yugoslav pilgrim initiated an outbreak of 175 cases and one additional case occurred in Germany as a result of infection from this source. The number of importations during the past five years is not large but the chaos which can be engendered by even a single case can be considerable.

Most outbreaks occur during the period December to May (2)

Note - (1) 20 of 28 (2 omitted because of incomplete data)

Peak season for smallpox in the northern hemisphere with which most communication occurs and from which 22 of the outbreaks originated

(2) Frequency of spread of those occurring in December - May period.

Why this season - (1) crowding (2) aerosol persistence

The obvious lesson from this is the need to maintain a particularly high level of suspicion during the December - May period.

Over two-thirds of those who have introduced the disease into the respective countries have been residents of the country in question, returning from visits abroad. Such has been the case for all but one of the importations of the past five years. In all discussions about preventing smallpox importations, there is always much ado about forged vaccination certificates given to travellers from Asia and African countries and indeed this practice is not unknown. Mack, however, in a review of 49 outbreaks which have occurred as a result of importations into Europe during the past 20 years found only four instances in which the person importing the disease had a forged or out-of-date certificate or none at all. Of the four individuals concerned, three were from Europe and one from the United States. The problem of proper vaccination of travellers obviously begins at home although obviously it is far easier to recommend reform to those in other countries.

(Note in passing immunization level - WHO)

The index case, the individual who has imported the disease has been reasonably promptly identified far more frequently than is generally appreciated. Again, from Mack's review, fully two-thirds of all index cases have been correctly disagnosed within 10 days after onset - a surprising record considering that comparatively few physicians have had experience with the disease. More than anything I believe this reflects the fact that smallpox is comparatively easy to recognize and properly diagnose. This runs counter to what I find to be a prevalent misconception throughout Europe - specifically, that in a "well vaccinated" population, mamy atypical cases occur. Admittedly, cases of haemorrhagic smallpox and highly modified cases are difficult to diagnose. But these are uncommon. The thesis propounded by many that inevitably in a European population, many cases are so highly modified as to be difficult or virtually impossible to diagnose is difficult to accept. This has not been our experience among populations which I'm confident are as well as or better vaccinated than in most countries of Europe. For example, in the endemic areas of Asia or Indonesia, it is unusual now to find population groups in which less than 90% bear a scar of vaccination. Eighty-five to 90 per cent of all cases in these groups occur among those who have never been successfully vaccinated. And in such groups, at least 85% of all cases are perfectly typical clinical cases. About one per cent of the cases are haemorrhagic and diagnosis here is indeed difficult. Most of the diagnostic problems occur among those who have been identified as known contacts of cases and vaccinated late in the incubation period. Indeed, some of these patients are real diagnostic puzzles but dealt with very simply by assuming that a rash in any close contact of a patient represents smallpox until proved otherwise. The problem in smallpox diagnosis is in the first few days of the rash and perhaps a few slides to illustrate the evolution of smallpox might be appropriate.

3
4 day 1
5 day 2
6 day 3
7 day 4

8 day 5
9 day 7
10 day 9
11 day 12

Note - important in diagnosis

- time
- character of rash
12 - distribution (slide 32)

Once the disease has been introduced into a country, how does it spread? Consistently in Europe and no less in Yugoslavia, the principal place of transmission of infection has been the hospital - fully half of all cases occurring in the course of European outbreaks during the past decade have been among medical staff, patients and visitors. Admittedly, little could have been done to prevent some of these cases, admitted after erroneous diagnosis. But is there any reason for physicians, nurses, ward attendants, etc. to develop smallpox? And once the diagnosis is made, adequate preventive measures should immediately be taken. A number of cases and deaths have occurred among contacts not vaccinated or otherwise protected because of pregnancy, congestive heart failure, etc., by physicians who have continued to observe the niceties of contra-indications appropriate to a non-endemic area at no riskforgetting that, under circumstances of an outbreak, the risk of smallpox outweighs the small risk of complications. The extreme case of conservatism was epitomized several years ago by a District Health Officer in England who refused to vaccinate healthy household contacts of a case because of the possible risks of vaccination!

I have touched on only a few of the many characteristics of importations but these, I believe, are the key ones so far as the clinician is concerned.

1. The need to be particularly alert during the December - May period
2. The need to assure that persons travelling abroad are successfully vaccinated
3. The need for vaccination of hospital personnel
4. The fact that smallpox is not such a difficult disease to recognize.

I have said nothing of isolation and control procedures; the role of vaccinia immune globuline; etc. - and for good reason. Once a case is suspected, there should be available a small, well-trained and experienced team familiar with all these nuances and prepared immediately to take the necessary measures, conduct the appropriate investigations and provide the necessary advice and direction.

The need for such arrangements was only too well-demonstrated in Yugoslavia last year. In January, 1972, a Yugoslav pilgrim journeyed by bus to Mecca and then to Iraq in company with 25 others. All had been vaccinated in Yugoslavia in November.

~~leaving Yugoslavia.~~ Subsequent to the event, however, serological studies revealed that not more than 3 of the 26 were successfully vaccinated. Smallpox was present at that time in Iraq and it was here he became infected. He returned to the rural Moslem area of Kosovo bearing, so we were told, over 200 kilograms of gifts. Shortly after arrival he developed a rash and fever but did not seek medical attention. The illness apparently was modified as a result of much earlier vaccination. During this time he received a great many friends, embracing each as is the custom. Among those who visited him seven persons became infected as well as four others who were in contact with him in a bus on 21 February and perhaps in a cafe in a nearby city.

Cases from this second generation were first diagnosed on 18 March, contacts were isolated and vaccination was begun. Special problems occurred, however, as the people of Kosovo are a rural people and, as rural people, both secretive and suspicious. That they also spoke Albanian, which was unknown to many of the epidemiologists involved, further complicated the matter. The disease spread as cases were hidden from the authorities and information about contacts was suppressed. The traditional custom of friends visiting those who were ill, whatever the disease, amplified the problem. Because of these problems, mass vaccination was begun but, unfortunately, with liquid vaccine whose stability is notoriously poor and with many vaccinators not well-trained in the technique.

One of the cases who acquired the disease from the first case inadvertantly compounded the problem further. This man lived some distance from Kosovo and the fact of his contact with the first case was not recognized. He developed a high fever and, on consulting a physician, was given pencillen. Subsequently when he developed a rash and became extremely toxic, he was admitted to the local hospital with the provisional diagnosis of a drug reaction. On the following day, he was transferred to a District Hospital and finally, to a dermatological ward in Belgrade. Because his condition was rapidly deteriorating, he was finally moved to a surgical intensive

care unit. Perhaps a reflection on the medical care of the modern era for within 5 days, he had been admitted to four hospitals. On the fifth day he died whereupon his body was shipped home, the case still undiagnosed. Only when his brother developed a typical smallpox illness was the correct diagnosis made. By then, cases began appearing in many areas in and around Belgrade. In all, he had infected 37 persons. The hospitals were quarantined and thousands of contacts isolated but identification of all with whom he might have come in contact in Belgrade proved impossible. Accordingly, mass vaccination was begun in Belgrade with over 300 vaccination sites manned 24 hours a day. Lines formed and continued throughout the night. Over one million persons were vaccinated within a 3 day period.

Following the index case, there were, as noted 11 cases in the first generation, 142 in the second and 21 in a third generation. The last generation of cases occurring primarily among those already in quarantine or in unrecognized infected locales in Kosovo. Four weeks elapsed between the discovery of the first case and the last.

The outbreak, as I mentioned, was the largest in Europe since World War II but, in many ways was atypical and marked by unusually unfortunate circumstances - (1) The spread of smallpox from a modified case to 11 other persons. Normally, not more than 4 or 5 usually acquire infection from a typical case and modified cases (contrary to many casual commentators) transmit the disease only one-third as frequently. The unusually large number of contacts which this man had following the pilgrimage and the customary form of embrace resulted here in unusually close contact with an extraordinarily large number of people. (2) The spread of infection in a rural less-developed area where accurate information was a problem to obtain, thus precluding the conventional approach to control in which one normally does not need to vaccinate or place under surveillance more than a few hundred persons and (3) the solicitous medical care of a modern age permitting one man to visit and

expose persons in four hospitals in five days.

A central authority, experienced in smallpox control did not exist and this led to no end of problems vis-a-vis policies of medical care, isolation and overall control measures. Many tended to observe conventional practices in regard to vaccine contraindications and a number of preventable cases occurred in consequence; hospital staffs were not properly vaccinated and cases and deaths occurred among nurses and physicians; and, finally, a reserve of good-quality freeze-dried vaccine was not available with the result that vaccine shortages occurred and many were vaccinated but unsuccessfully.

Should an introduction into Yugoslavia occur in the future, they will be found better prepared - but one must note in passing that the last outbreak occurred in Yugoslavia 42 years ago - in England, it was only five years ago. How well prepared are you today?

But it is often said that the best defence is a good offence and in regard to smallpox, this is especially true. The reduction and hopefully eventual elimination of smallpox throughout the world is obviously a surer approach than a reliance on grossly imperfect quarantine barriers.

It is of interest to note that all importations into Europe during the past 15 years have come from countries recording a rate of 3.0 cases of smallpox per 100 000 or greater. ~~One might query the recent Yugoslav experience in which infection occurred in a country reporting only 37 cases - let me only assure you that the unofficial rate did indeed exceed 3.0 per 100 000 but that now the official and unofficial reports finally correspond.~~ The global experience in regard to smallpox is thus worth examing with this in mind (13)

Note 1961 - 56 countries recorded smallpox 28 with rates >3.0

1967 - global programme of SE began

42 countries report 18 with rates >3.0

1972 - 19 countries report 4 with rates >3.0

Why this remarkable change

(1) Freeze-dried vaccine and bifurcated needle

Stability of freeze dried vaccine

10-15 per cent in 1967

> 95 per cent by 1969 - now universal in endemic areas

Vaccine produced in endemic areas plus large donations

USSR, USA, Canada, Switserland, Kenya, Belgium, Netherlands

(14) Needle introduced in 1968 - 50% vaccine need reduction

(2) Shift in strategy from mass vaccination to one emphasing epidemiological surveillance

Mass vaccination 80% - 100%

Countries > 95% - no stop

Experience non-endemic countries. Endemic countries - series of outbreaks

Thus surveillance, reporting + surveillance teams

What specifically are the results -

1967 (16)

1973 (15)

S. America (26)

Africa (17) (18)

Asia (19) smallpox confined now to northern India, western Bangladesh + one province of Pakistan.

In September 1972, final phase of programme to accelerate activity. While it is too early as yet to know precisely when a nil incidence will be reached - progress is gratifying.

Hopefully, an historic day will soon be reached when we may say 'cease vaccination and discard vaccination certificates' - for medicine, this will represent an historic milestone indeed.