I.J.M.S., Dublin
March, 1963, pp. 99-103
Printed in the Republic of Ireland

AERIAL DISINFECTION WITH HEXYL RESORCINOL IN A MONKEY HOUSE

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ON general principles the prevention of cross-infection by means of a bacterial vapour has obvious attractions although a surprisingly small amount of work appears to have been done on this subject in recent years. In laboratory tests hexyl resorcinol (1-n-hexyl-2 : 4-resorcinol) appears to have given good results capable of being transferred to the field (MacKay, 1952; Darlow, Powell, Bale and Morris, 1958) but experience in practice seems to have been conflicting (Dickson, 1953; Lidwell and Williams, 1954; Holland, 1961). There can be little doubt but that the difficulty of mounting a properly controlled field trial has been a major factor in the conflict of evidence so far presented. Ten years ago McGrath (1953) reported briefly an experience with hexyl resorcinol in the Monkey House of the Dublin Zoological Gardens, and stated that, in the four years from 1949 during which it had been in use, respiratory infection had become almost unknown and that, in particular, no case of tuberculosis had occurred in that time. This result appeared the more striking since it had been necessary to close the House for several months in 1947 due to an extensive outbreak of tuberculosis and there had been a high incidence of other respiratory infections.

In spite of the fact that tuberculosis is rare in wild monkeys not living near humans the history of monkey colonies in Zoological Gardens is a constant catalogue of losing battles against respiratory diseases and especially tuberculosis. Urbain (1941) reported that in the Zoological Gardens of the Bois de Vincennes in Paris 319 simian primates died of tuberculosis in the seven and one-half years ending in 1939. In an important study Habel (1947) recorded that in the years 1942-1944 one-third of all monkeys received at the National Institute of Health, Bethesda, died of tuberculosis. He concluded that spread was probably through the respiratory tract, that the majority of monkeys died within six months of becoming tuberculin positive, and that in *M. mulatta* monkeys there is no evidence of immunity. Hill (1952) stated that the incidence of tuberculosis in the London Zoological Gardens was increasing and later (Hill, 1957) that an epizootic in the Monkey House caused 67 deaths in 1954 and 1955. Benson, Fremming and Young (1955) reported the enforced destruction of nearly 250 *M. mulatta* monkeys within three months due to an outbreak of tuberculosis in a research colony. Forty-five of these animals—nearly half of which were tuberculin positive—were treated with streptomycyclidene isonicotinyl hydrazine sulfate with good results, but the danger of relying on treatment after infection is underlined by Habel (1947) who states that by the time these monkeys become tuberculin positive gross disease is already present.

Other respiratory infections appear to be equally prevalent if not

always so lethal and pneumonia is a major cause of death in monkey colonies, its incidence varying from time to time. Ruch (1959) has reviewed the literature on respiratory bacterial infections in monkeys demonstrating infection with Group A streptococci and pneumococci. Fegley and Sauer (1960) report on the results of mass chemotherapy in animals newly arrived in a monkey colony following on the discovery that 63 per cent. of 123 apparently healthy cynomolgus monkeys had gross lesions of pneumonia. Pneumococci, streptococci and micrococci were the pathogens most frequently isolated. The same authors (Sauer and Fegley, 1960) studied a dynamic pool of some 2,000 monkeys in the colony of a pharmaceutical firm. The average length of stay in the colony was one week—varying from one day to one year—and bronchopneumonia was either a major or a contributory cause of death in 49 per cent. of those animals which died.

It would appear that old world monkeys are not susceptible to influenza, although the position of new world species is not so clear (Ruch, 1959). There is, however, no question but that monkeys may be infected with many other viruses some of which resemble either the enteroviruses or the adenoviruses of man, although their precise significance in the aetiology of disease in simians has not yet been fully elucidated (Cheever, 1957; Sabin, 1957; Heberling and Cheever, 1960). Other virus infections may also occur and Lambert and Eustace (1950) reported the successful treatment of " atypical " pneumonia in a chimpanzee using chloromycetin.

The Dublin Monkey House

The general structure of the House, with two exceptions noted below, has not been changed since McGrath's report (1953), so that about 35 to 40 monkeys are housed in some 17 cages built around a large central hall; each of these opens into external cages which are used in warm weather. In February, 1949, aerosol disinfection using apparatus rented by Aerovap, Ireland Ltd. and employing first resorcinol, and later hexyl resorcinol, was instituted. This apparatus has been in constant use since that date. The mortality from all causes for each of the past ten years is shown in Table 1.

TABLE 1.

1953	1954	1955	1956	1957	1958	1959	1960	1961	1962
8	4	4	8	8	8	5	4	2	2

It may be noted that since the end of 1959 all the deaths have occurred in the winter months (November to February).

No case of tuberculosis occurred in the monkey house from the installation of the " Aerovaps " in 1949 until 1956 when one isolated case occurred. In 1957 there was a small outbreak confined to three animals —two chimpanzees and one orang-utan—in adjacent cages. No further cases of tuberculosis occurred in the house at that time but it was thought prudent to supplement the use of aerosols by B.C.G. immunisation. Accordingly all the animals in the House were tuberculin tested and, being found negative, all received B.C.G. In addition, the old wooden

flooring in the cages was replaced by asphalt. When a new orang-utan was obtained a glass fronted cage was provided for this very valuable animal. Otherwise no structural alterations were made. In 1958, a further case of tuberculosis occurred in a gibbon without spread to any other animals. This animal had been recently brought in from an island on the lake in the Gardens and—through inadvertence—had not been immunised. Otherwise all new arrivals since 1957 have received B.C.G. No case of tuberculosis has occurred in the Monkey House since 1958, so that since 1949 only five cases have been recorded.

This experience is in marked contrast with that of a colony of rhesus monkeys housed elsewhere in the Gardens. Over a period of several years this colony was almost wiped out annually by tuberculosis and had to be replaced. Since the institution of B.C.G. immunisation in the Monkey House new arrivals here have also been immunised and it has been possible to keep the colony in being.

The general health of the animals in the Monkey House has been excellent and respiratory disease has not been a problem.

The Dublin Zoological Gardens are visited annually by some 350,000-400,000 people, all of whom enter the monkey house, so that while it has a stable population the animals are daily exposed to infection. Although there is a guard rail about one yard from the front of the cages it is by no means unusual for visitors to go inside this, and many bring food from their homes which is fed to the monkeys in spite of recent attempts to stop this practice. The animals are therefore fully exposed to cross-infection from visitors and Dublin, like all other cities, has periodical epidemics of respiratory and other infections.

The most important of these for the monkeys is still probably tuberculosis. In common with many other countries the incidence in Ireland has declined in recent years but, as elsewhere, the fall has been more spectacular in mortality than in morbidity. The mortality from all forms of tuberculosis has fallen from 124/100,000 in 1947, through 73/100,000 in 1951 to 17/100,000 in 1960. Nevertheless, it has been estimated that in 1951 the number of cases in Dublin represented a figure equivalent to 0.65 per cent. of the population—which is very high (Deeny, 1954). In 1952, 5,577 new cases of respiratory tuberculosis were notified in the Republic. This fell to 3,358 in 1957 and had declined further to 2,395 in 1961. Gratifying as these figures are they suggest, in the present context, that the animals in the Monkey House have been exposed to tuberculosis throughout the period of this review.

A question raised by McGrath (1953) was that of possible injurious effects on animals—or even on humans—of breathing hexyl resorcinol vapour over long periods of time. It may be said at once that no clinical evidence of any ill-effects has been observed over fourteen years observation. McGrath (1953) reported on the autopsy findings in two animals which had been exposed for three to three and one-half years without ill-effects. In 1956, two animals—one baboon and one macaque—which had been exposed to the aerosol for seven years had to be destroyed. Sections from these were sent to Dr. Vernon Udall of the Wellcome Research Laboratories who reported that he could find nothing in the

lungs of these animals that could be attributed to being exposed to hexyl resorcinol for a considerable time (Udall, 1962). The lungs of a chimpanzee which had been in the monkey house from 1950 until December, 1961—during all of which time the aerosol was in operation—showed no changes attributable to it (Farrelly, 1962).

Discussion

It has already been mentioned that laboratory studies with hexyl resorcinol suggest that this agent has definite bactericidal properties. MacKay (1952) found that, using *Chromobacterium prodigiosum* as a test organism, aerial concentrations of between 6 and 7 microgrammes/cu. ft. would reduce the bacterial content of the air from more than one million bacteria per cubic foot of air to less than ten in approximately 30 minutes. Darlow *et al.* (1958) found comparable killing rates using a variety of micro-organisms but, in addition, described a phenomenon which they called the " initial kill ". This occurred when spraying bacterial aerosols into an atmosphere already containing hexyl resorcinol. It was shown that in these circumstances the recovery rate of the organisms sprayed was, immediately after spraying, frequently far lower than could be accounted for by the killing rate calculated from subsequent samples. It appears, therefore, to be an additive effect and in certain circumstances enhances very considerably the elimination of viable bacteria. This effect was not found when hexyl resorcinol was sprayed into an already existing bacterial aerosol, but here, too, a killing effect comparable to that described by MacKay (1952) was found. It would seem reasonable to suggest that although no such experiments have been done in the Dublin Monkey House, these findings may have a bearing on the situation there, where hexyl resorcinol aerosols have been used constantly since 1949.

The use of B.C.G. may well have supplemented the value of the hexyl resorcinol in the control of tuberculosis although it may be stressed that the aerosol alone was used for a period of seven years during which no case of tuberculosis occurred. Furthermore, although those animals which were in the Monkey House in 1957 received B.C.G., as did all subsequent arrivals, no booster doses have been given at any time. Ruch (1959) is of the opinion that immunity is conferred for only a matter of months and that even then there is no absolute immunity to challenge, nor are all immunised animals protected against transmission from one to another. On the other hand, experience with the outdoor rhesus monkey colony suggests that B.C.G. is of value and it would seem that at least there is nothing to be lost by combining aerosols and immunisation.

Finally, it should be clear that the experience recorded here is in no sense a controlled experiment, and in evaluating the results described this fact should be kept in mind. Nevertheless, the findings seem to be of sufficient interest to warrant further experiments in the field. The only recent study was that of Holland (1961) who concluded that it had significantly reduced the numbers of air-borne bacteria in a hospital under the conditions of his experiment. The difficulties of mounting a completely controlled trial under field conditions are obviously very

substantial and may well be insuperable. It is hoped, however, that this report, covering fourteen years experience of hexyl resorcinol bactericidal aerosol, may stimulate others to an interest in this field.

Summary

1. The literature concerning respiratory infections and especially tuberculosis in monkeys, is reviewed.

2. Fourteen years experience using hexyl resorcinol aerosols (Aerovap, Ireland, Ltd.) in the Monkey House of the Dublin Zoological Gardens is recorded.

3. During this period, in contrast to experience elsewhere, only five cases of tuberculosis have occurred.

4. Other respiratory infections have not been a problem in spite of ample opportunities for visitors to the house to infect the animals.

5. No clinical or histological ill-effects of the constant breathing of hexyl resorcinol vapour over a period of years have been observed.

6. In the light of the satisfactory results obtained it is suggested that interest in air disinfection should be revived.

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