

# Acquired Tuberculosis in the Primate in Laboratories and Zoölogical Collections\*

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TUBERCULOSIS has been a recognized major problem wherever primates have been kept for as many years as the organism *Mycobacterium tuberculosis* has been recognized in domestic animals and man.<sup>1, 2</sup> The gross and histologic picture of primate tuberculous pathology in its various forms has been well described<sup>1, 2, 3</sup> and compared with lesions in man both in this country and abroad. This order of mammals has not had the opportunity to build up a genetic resistance, inasmuch as the monkey does not usually encounter the disease in his native habitat.<sup>4</sup> The majority feel that there is small likelihood of active tuberculosis existing in the primate in his native forest. Before a monkey could become an open case and disseminate virulent organisms, his natural enemies would have destroyed him. There is always the possibility of making contact with organisms in and adjacent to native villages while feeding on refuse. The high incidence of tuberculosis in man in and near the habitats of primates suggests a source of infection by contact after capture. Tuberculosis

mortality statistics from the League of Nations report for 1932 shows 307 deaths per 100,000 in Singapore and 613 in Manila; 294 in Panama, and 554 in Guayaquil as compared to 69 in New York and 55 for the United States as a whole. The number of primates born in captivity, which might eventually build a more resistant strain, is extremely small. Because of this lack of selective mortality, susceptibles continue to be placed in human communities where they make direct contact with frequent large doses of virulent *My. tuberculosis*, an organism to which they and succeeding generations have or will have little or no resistance.<sup>5</sup>

According to dealer reports, the traffic in primates is increasing. Laboratories are using greater numbers for the investigation of virus diseases; for physiological, psychological, bacteriological, anatomical studies, and experimental surgery. New zoölogical gardens, the construction of which was made possible by the Works Progress Administration, are making their appearance, some operated by city governments and others by zoölogical societies. Parks and laboratories have both made a very definite advance in the improvement of primate hygiene. The dealer on the other hand has not made

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any marked change in his method of importing or holding primates for sale. If the animal is to be kept as a permanent exhibit and is expected to live through or exceed a normal life span, special precautions should be taken to prevent contact with large or frequent doses of *My. tuberculosis*. Usually the preventive program is weak. Shipping crate sanitation is notoriously bad. The type of construction, overcrowding, and neglect in transit is inexcusable. Paddy rice is not a satisfactory diet for a 30 day journey, and certainly not acceptable when thrown into a crate contaminated with tuberculous stools or dead specimens. Indian, Philippine, and like crews are an excellent source of virulent tubercle bacilli. Expectoration into the monkey shipping crate is almost a routine with them and the incidence of tuberculosis in this group is high. Monkeys may or may not be transferred or redistributed in new crates after receipt by the dealer. Usually the original crate continues to the monkey's destination—the laboratory, zoological garden, or circus. The method of shipping is as old as the business itself.

A tuberculosis-free collection must be protected from contact with new importations which may disseminate virulent organisms shortly after their arrival. Some form of diagnostic test should be used for the detection of tuberculosis and must be routinely used to eliminate those primates which may develop the disease during their period of exhibit. To understand fully the problem and to accumulate definite statistics, we prepared a questionnaire with portions acceptable to the varied groups which take part in primate traffic. It was sent to those institutions which we felt had the broadest experience. The average findings in the returned questionnaires indicate that the Bengal monkey, *Macaca mulatta*, decidedly exceeds all others in

number of importations, and is the most popular laboratory animal.

The poor response to our questionnaire, and incomplete reports, indicate that little is being done to curb the rising incidence of infection.

The incidence of primate tuberculosis including all forms is about 10 per cent annually. Of all primates that die 80 per cent are attributed to tuberculosis. One laboratory states that they can demonstrate tuberculous lesions, often latent, in every monkey destroyed over a period of years—325 specimens. The primate incidence of 10,000 per 100,000 mortality is exceedingly high as compared with the national rate of 55 per 100,000 in human beings in the United States. However, in the report by Whitney & McCaffrey,<sup>6</sup> using Purified Protein Derivative in group testing in the United States, they find 47.0 per cent reactors in the all-age group, and 60.1 per cent reactors in the over 20 years group. The American Indian had the highest incidence, 72.4 per cent, the Negro second highest, 43.3 per cent.

Possibly man's allergic response is an indication of his immunity. The primate has some tissue reaction following acute infection but not enough to excite a typical allergic response of sufficient degree to be able satisfactorily and routinely to produce a tuberculous reaction. The Mantoux, Von Pirquet, Calmette, and intrapalpebral tests all give unsatisfactory results. The high susceptibility and poor or completely lacking allergic reaction in the primate suggests a relationship between immunity and allergy. Occasionally a typical reaction is seen which probably is a demonstration of temporary individual resistance. As the disease progresses dermal reaction to tuberculin diminishes. The reaction of most primates to tuberculin is similar to the reaction of man in the terminal stages of acute miliary tuberculosis.

In a group of 25 rhesus tested by me, we found 2 reactors in Mantoux and intrapalpebral tests. On the basis of experience with shipments from the same dealer, and postmortem findings, we should have had 50 per cent reactors.

Possibly a satisfactory test will be devised, which should have the following qualifications:

1. Ease of administration and interpretation (not requiring special technicians)
2. Requiring the use of a readily available tuberculin of standard manufacture
3. Requiring a minimum of animal restraint
4. Giving regular and satisfactory reactions
5. The test should be applicable to all primates so that it could become standard.

Complement-fixation has been suggested, but the routine collection of a satisfactory serum sample from all primates would be extremely hazardous. The Mantoux test is difficult to apply because of extremely thin vascular skin. We have found the belly the best field to be shaved. Here skin can be picked up between thumb and finger and with care an intradermal injection can be made using a 28 gauge needle. The point of injection can be outlined with mercurochrome. The reaction, should it occur, can be definitely measured. The Von Pirquet test can be applied at the same site, using two types of tuberculin and plain broth. The scarified areas here also may be marked with mercurochrome and numbered. The intrapalpebral test is easily given, using the 1 c.c. tuberculin syringe and 28 gauge needle. The monkey is held on his back, arms behind him, legs extended. The lower eyelid is picked up with the needle point bevel up, the needle inserted and tuberculin injected to leave a lentil-sized raised area. The Calmette ophthalmic test is of course the most simple to give, and some report satisfactory results.<sup>7</sup> We have not had

routinely satisfactory reactions with any of the described tests. We have used bovine type K.O.T. (synthetic media), 0.25 gm. per c.c.; human type tuberculin K.O.T., and also the dilution "C," 0.1 mg. per 0.1 c.c.; human tubercle bacillus protein MA-100, 0.01 mg. of protein per 1.0 c.c.; and Purified Protein Derivative (P.P.D.), using the human first strength dose of 0.1 c.c. containing 0.00002 mg. P.P.D.; and 0.1 c.c. containing 0.005 mg. P.P.D. second strength; and also double strength using 0.01 mg.<sup>6</sup> Even the concentrated tuberculins failed to produce a reaction in known tuberculous monkeys. The subcutaneous test depending on a systemic thermal response, applied to primates by Penrose, White, Brown, and Pearson of the Philadelphia Zoological Society,<sup>8</sup> is successfully used in the hands of Fox and Ratcliffe of the<sup>9</sup> same institution. The objection to it lies primarily in the long continued restraint necessary to establish the peak 3 P.M. rectal temperature and subsequent temperature reactions following the subcutaneous administration of tuberculin. The weight curve represents an important diagnostic criterion in all acute forms but it loses its value in the young growing monkey. Roentgenographs have real value but involve too great expense for routine tests. Some laboratories rely almost entirely on the relationship of weight curve to chest picture for a diagnosis. Probably 80 per cent of *My. tuberculosis* infection in primates is acquired between the time of capture and eventual delivery. A program of control which would aim first at importations should be instituted with federal control. Such a measure, however, would be entirely impractical until a satisfactory diagnostic test is devised. Sputum, if it can be secured, and stool concentrations are interesting sources of tubercle bacilli but routine dependence on these is not practical. Some primatologists

feel that they can identify the tuberculous animal by its appearance. In the course of its investigations a tropical laboratory destroyed 539 monkeys at large in the forest and never demonstrated a tuberculous lesion; however, the species investigated has a high incidence in its own captive group.

The order Primates should be an ideal source of study of tuberculosis from the epidemiologist's point of view. Contacts can usually be traced. It does not usually develop active immunity and presumably it comes from a tuberculosis-free community. The disease is usually epidemic during shipment and early handling and only becomes endemic where control measures are in force. The Philadelphia Zoological Society has proved that it is possible to maintain a tuberculosis-free collection where the disease had peak 20 years ago. It is understood that to establish tuberculosis in the primate as in man, large or repeat doses of virulent organisms are necessary to bring about an active infection, but when the disease becomes established in the primate its prospect of developing a passive congestion with resulting fibrosis and calcification is quite remote. If it had no resistance at all we might expect 100 per cent mortality, for certainly every primate in captivity has ample opportunity to contact small doses of *My. tuberculosis*. Old World monkeys are most susceptible; however, acute epidemics are possible in New World species. A tropical research institution experienced a tuberculous epidemic in its Spider monkey (*Ateles ater*) colony. All were destroyed and the colony reestablished. The contact here was a known open case in the human attendant. There is apparently a zoological family and genus variation to resistance; however, the degree of susceptibility and sub-

sequent active infection is dependent on the extent and degree of contact.

Unfortunately, all primates do not have a postmortem examination. The group that do are usually those valuable specimens in zoological gardens or the experimental monkeys in the laboratory that require an accurate postmortem report to complete the experiment. Some laboratories make a detailed report but seldom include a case history. A number fortunately do conduct a satisfactory examination and give pointed information, usually of a comparative nature, which should lend further impetus to the epidemiological investigation of human tuberculosis.

Deaths in young monkeys are usually found to be the acute miliary form and generalized, with outstanding pulmonary lesions. The older primate may have more extensive lesions with pulmonary caseation and cavitation, and caseous lesions in spleen, lymph nodes, and liver. We do not often see meningitis or bone involvement and serositis. Pott's disease is occasionally seen and recently we demonstrated a tuberculous serositis in a *Hamadryas* baboon (*Papio hamadryas*). Another of the same species had an acute tuberculous meningitis. A performing chimpanzee, 5 years old, had a tuberculous meningitis with cerebellar infiltration. Tuberculous pneumonias are common, especially in the anthropoid apes. It is decidedly uncommon to have fibrosis with calcification. Scrofula is occasionally seen. In all probability the older primate has developed some resistance and consequently the organism produces larger and more extensive lesions than in the young. Routinely, sections should be cut from suspected tissue, especially lung. Much gross atypical tissue proves to be tuberculous. Most laboratories routinely make a gross observation and attempt to demonstrate acid fast organisms.

Where guinea pigs have been injected and tissue concentrates cultured, the human type of bacillus has usually been found.

To assure a good source of tuberculosis-free primates for zoölogical gardens and laboratories, we recommend that the local dealer be advised of the necessity of improving the primate hygiene immediately after capture. The monkey must avoid contact with human open cases and be held in smaller groups than is the custom (maximum: 10 in a cage). Where possible the shipping crates and holding cages should have some form of open mesh floor to prevent contact with tuberculous stools. A satisfactory disinfectant should be used routinely. All sick and suspected open cases of tuberculosis are to be isolated or destroyed. The use of a diagnostic test is not recommended at this stage, inasmuch as the most reliable subcutaneous test, with thermal reactions, could not be conducted practically.

The experienced animal dealer and keeper recognizes a sick monkey—if not tuberculosis—and it is our belief that those monkeys which are disseminating organisms will demonstrate either respiratory symptoms, draining scrofula, or diarrhea. These monkeys should be destroyed or isolated. It is most difficult on shipboard to remove one or more dead or sick specimens from a small crate, 2 by 3 feet, with 30 to 50 young *M. mulatta* active and alert awaiting an opportunity to leap out. Monkeys enjoy and need their mutual warmth but they will have a greater survival rate if they are given more room. The shock of capture, crating, holding, and eventual shipping to a new life zone can most satisfactorily be cared for by giving best possible food with the necessary vitamin supplements. The time consumed in transport should not be considered as part of quarantine because it is not a

tuberculous quarantine at all, but a period of likely exposure. When the shipment arrives at the port of destination a further physical stress is experienced in the transfer from ship to dealer's quarters or to train for final destination.

Holding quarters in metropolitan areas are poor. There is a general lack of sanitation. The lack of satisfactory disinfection is often due to improper claims by the manufacturer or his representative. The efficiency of their product is usually determined by its ability to replace an obnoxious odor with a pleasant one. The standard 4 per cent solution of liquor cresolis comp. U.S.P. used hot makes an efficient cleanser and disinfectant. Coal tar derivatives are well tolerated by primates. Often an odorless disinfectant is desired and according to the U. S. Department of Agriculture, *Circular Letter 1750*, B.T.B. (Sodium orthophenolphenate) used in a hot aqueous solution, 2 per cent by weight, is quite satisfactory for the specific destruction of *My. tuberculosis*. If unpainted stainless steel or galvanized metal is used in cage construction, lye 1:200 is quite satisfactory. Concrete makes cheap permanent construction but is too damp, cold and uncomfortable for monkeys. Paraffin-saturated wood, rubber compositions, cork block, or especially compounded materials are used with success. The most satisfactory floor from a sanitary standpoint is the electric weld 12-14 gauge wire with  $\frac{3}{4}$ " squares for small monkeys,  $1\frac{1}{4}$ "- $1\frac{1}{2}$ " for larger animals. In permanent buildings structural glass or smooth finished plaster walls and ceiling are recommended. Sheet metal is best for the temporary or portable cage. It is also important to avoid contact between the primate and the visitor in the zoo. The most effective method is to erect a full glass partition between them. This method prevents the pas-

sage of various upper respiratory infections to the monkey from man, in addition to preventing the carriage of pathogens on food from visitor to exhibit.

We can approximate the number of primates sold annually from the estimated and actual sales figures of the Eastern dealers; *Macacus* sp. 25,000 (*rhesus* and sp.); anthropoids 250; all others 10,000. The incidence of tuberculosis is likewise a relative figure, probably exceeding 50 per cent, including latent forms, and 5 per cent open cases. There are major inaccuracies in our submitted figures. We know that the majority of *M. mulatta* originate from the same dealers, and we do not believe it possible to have 95 per cent tuberculosis infection with approximately 30 per cent acute phthisis in one group and a negative report from another—all monkeys originating from the same dealer. The incidence of tuberculosis is apparently directly proportional to the accessibility of a competent pathologist. We do not propose to state that all primates die as a result of *My. tuberculosis* infection. Trauma with or without septicemia, common cold, and bacillary dysentery cause many deaths.

Let us critically review the experience of typical buyers. A zoölogical society received 200 *M. mulatta* to populate a monkey island. Ten days after receipt they experienced 10 per cent mortality. During the course of the summer 125 monkeys died. All deaths were attributed to acute tuberculosis on pathological diagnosis by a competent pathologist. A physician who purchased 40 *M. mulatta* for experimental surgery had a 50 per cent loss attributed to tuberculosis before his experiment was complete. A city laboratory lost 30 per cent of a group during the course of titrating poliomyelitis pooled sera. A state institution found 98 per cent tuberculous

lesions in all *M. mulatta* that died or were destroyed, with a major incidence of active infection. The dealer is, usually, not knowingly, a party to the sale of animals with infectious disease. He is sincere in his belief that he is selling a normal specimen.

The zoölogical garden's aim is longevity. Consequently because of a long quarantine, attempted early tuberculosis diagnosis, a definite sanitary program, and best possible nutrition, it usually has a lower incidence of infection than the experimental laboratory.

#### SUMMARY

Primate tuberculosis and its pathological forms have been a major problem as long as *My. tuberculosis* has been recognized. It has become both an economic and public health problem. Its incidence has not decreased, because of lack of genetic resistance and poor hygiene. The 10,000 per 100,000 mortality rate is 200 times that of man. The human type of organism is usually demonstrated. There is family and genus resistance variability but no measured resistance within a species. Antemortem recognition of the disease in the order of popular application consists in

1. Physical examination
2. Weight curve
3. Subcutaneous tuberculin test with thermal reaction. Mantoux and related tests are not routinely successful. (The primate has an indifferent allergic response to tuberculin.)
4. Roentgenography (usually in combination with weight curve)

Postmortem diagnosis consists routinely in demonstrating an acid fast organism (usually primary Ziehl-Neelson stained smear, occasionally animal inoculation or culture with subsequent smear) from typical lesions (histopathological if gross lesion is atypical). Better shipping hygiene with improved final housing and avoidance of contact with open cases

in primate or man, are most important if the incidence of acquired primate tuberculosis is to be lowered.

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3. *Proceedings and Report of Zoölogical Gardens*. New York Zoölogical Society; Zoölogical Society of London; Philadelphia Zoölogical Society; etc.
4. Harry M. Wegeforth, M.D., President of the Board of Directors of the Zoölogical Society of San Diego, Calif.:  
 "In my travels in the Orient I found a high incidence of tuberculosis in the native popula-
- tion . . . Native monkeys adjacent to populous areas do make contact with tuberculous sputum. Herbert C. Clark, Director Gorgas Memorial Laboratory, Ancon, Canal Zone, has killed 539 monkeys in their native forest and has never demonstrated tuberculosis in the native troupe."
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## American Verbosity

THE responsibility for American verbosity, I feel sure, lies with the very efficient American stenographer, and the temptation to garrulosity provided by the skill of her fingers. In some offices it seems that letter-writing has become a major undertaking, like writing for publication, and not a means to an end. There is no one who appears to be quite so well satisfied with the result of a day's work as the American business man who has dictated so many letters that his secretary has to work overtime transcribing them. The first practical evidence I had of the existence of the depression in America came when I noticed that the letters I received were fewer and shorter. Obviously, it had been necessary to reduce the staff of stenographers. Business must be improving now, the letters are growing in fre-

quency and length and will soon be what they were in 1928.

It is my candid opinion, after reading these letters for about 20 years, that half the typewriters in America could be scrapped and half the stenographers married off, and the wheels of business would run just as fast and with a good deal less noise and waste effort. Businesses in other countries are conducted successfully with only a fraction of the amount of correspondence Americans appear to find necessary. Every man whose business it is to dictate letters should be compelled to read over, at the beginning of every business day, the copies of the letters he dictated one year before and see for himself how many of them were twice as long as necessary, and how many were not necessary at all.—Carl Crow—Harpers', June, 1937.