The Principles of Humane Experimental Technique

W.M.S. Russell and R.L. Burch

CHAPTER 4

THE SOURCES, INCIDENCE, AND REMOVAL OF INHUMANITY

The three chief principles stated...

The Diagnosis of Disease

A cursory glance of the tables (Tables 6,10, and 18) shows that the overwhelming majority of diagnostic experiments on animals are inoculations of milk or human specimens for TB. Probably most "unspecified diagnosis" returns were also of this type. It is therefore worth examining this test.

"Several animals should be inoculated since some are likely to die of peritonitis caused by other organisms before the Mycobacterium tuberculosis has had time to produce its characteristic lesions" (Todd et al, 1953). We have already noted this source of contingent inhumanity with its rarity. The next question of interest is that of incidence. How many positive responses are obtained, i.e. how often is the pathogen present in the inoculate?

The pathologist of a large urban hospital has very kindly provided some figures bearing on this point, which are reproduced below:

Table C: Positive Responses in TB Inoculations

YearNumber of pigs inoculated for TB	**Number positive**	
1952	66	13
1953	80	25
1954	94	30

1955	127	27
TOTAL	367	96

Contrary to the fatalistic advice of the textbook just cited (and apparently without detriment), one animal was used per test. The inoculates included human pleural fluid, urine, endometrial tissues, pus, and cultures of acid-fast organisms. Sputum was rarely used, "since we consider in vitro culture just as sensitive as animal inoculation in this case".

The hospital in question was atypical in containing about 10% TB beds. This must have inflated the numbers of positives above the average for pathology departments in general. We may be safe in assuming that more than three-quarters of all inoculations of human material for TB are likely to have been negative. Bovine tuberculosis had already declined considerably by 1952: 23,716 cases were dealt with in 1936, only 2,831 animals slaughtered in 1952 (Ritchie, 1954). So we may reasonably suppose that the positive total ratio was even lower for milk inoculations. Both conclusions are inferential but plausible, and in personal contacts we have heard nothing to conflict with them. If they are true, we may conservatively estimate that about 60,000 virtually innocuous experiments were included in the 1952 returns (cf. Table 18).

Hoyland (1957) has recently reported some interesting records of a large Public Health laboratory at Wakefield, where as usual 95% of tests are inoculations for TB. Between 1949 and 1956, the number of experiments (about 2,000) per annum has remained fairly constant, but the number of pigs used annually has dropped from over 5,000 to less than 2,000. This is ascribed to the effects of the L.A.B. Accreditation Scheme for laboratory animal breeders (Lane-Petter, 1953b; Lane-Petter et al, 1955). Fewer pigs were now used, concluded Hoyland, because those obtained from the accredited breeders are more uniform and because far fewer die contingently (cf. also Lane-Petter, 1956). Here is a triumph of husbandry. This laboratory is probably typical, for the proportional number of pigs in use is in fact declining, and we have seen that pigs are almost exclusively diagnostic animals.

Can we speak of great direct severity in the case of the positives? In spite of the recommendation of the textbook cited earlier, it seems to be practice in Britain to kill pigs as early as possible, and by the time of death the symptoms do not usually exceed slight swellings of lymph glands. It is, however, probable that not all animals are killed before more serious symptoms develop, leading to emaciation. It is, therefore, of interest to see whether and how the number of positives, or of inoculations, may be decreasing.1

The rise in the figures for total inoculations in Table C, coupled with an apparent absence of increase in the number of positives, is curious but inconclusive on account of the small numbers and the atypical nature of the hospital. TB has been steadily declining in this country since 1950 (notifications and mortality--Charles, 1955; see also B.C.G. Vaccination, 1957). But this is not the only factor, and we may not have to wait for the disappearance of the disease to diminish or abolish the inoculation of guinea pigs.

In 1953, The Chief Medical Officer (Charles, 1953), reporting on the public health in 1952, the year of the first survey, stated:

"The only way of making certain that an acid-fast bacillus is a genuine tubercle bacillus is to inject it into a susceptible animal, such as the guinea pig, and prove that is virulent. This confirmation of the cultural test should be carried out whenever there is any doubt in the clinician's mind as to whether the patient on whose sputum a positive laboratory result has been received is suffering from tuberculosis, and always on organisms isolated from the genito-urinary tract, cerebro-spinal fluid or pleural fluid."
It is doubtful whether this is still true today. Even in 1952 progress in reducing inoculations was evident. Three laboratories (one of them associated with a hospital having many TB beds) reported a considerable decline in requests for inoculations, and ascribed it to improved in vitro culturing methods. One of them used 71 pigs in the first and 16 in the fourth quarter of 1952. Culturing methods have been improving steadily (cf. Melvin, 1951; Yamane, 1957).

The progress of in vitro methods is considerably more important, from the humane point of view, in the other specific tests of the Diagnosis division. Though numerically far fewer (Table 18), they are very much more severe (for the effects of diphtheria and leptospirosis on the animals, cf. Todd et al, 1953). The spectacular decline of diphtheria may soon eliminate the use of pigs by default of suspected material. The following extract from the Public Health Report for 1954 (Charles, 1955) portrays the virtual elimination of this once widespread disease, as a result of the immunization campaign which got into its stride by about 1943:

Table D: The Decline of Diphtheria

Animal Average	Corrected Notification	Deaths
1916-25	51,573	4,214
1933-42	55,125	2,783

1943-47	18,810	749
1948	3,575	156
1959	962	49
1952	376	32
1954	173	9

The bare figures record one of the greatest of all medical triumphs: it has brought its rewards for the experimental animal, too. It is very likely that the figure for diphtheria tests in our tables is an overestimate. A proportion of it was derived by conventional estimate from figures given for "TB, diphtheria virulence", or similar returns. One laboratory reported as follows: "Although this is a 'Fever' Hospital, the isolation of Diphtheria organisms has dropped virtually to nil--5 in 2 1/2 years, 3 of these during the first six months. In the 'Diphtheria Age' this laboratory was isolating appr. 100 strains per month."

This, along with a reported infrequency of requests for TB inoculations, was given as the reason why this laboratory was terminating the breeding of pigs. The decline in inoculations is assisted by a rather subtle factor: clinicians now rarely expect the vanishing disease, and are less prone to want confirmation of doubtful conclusions than it its heyday.

Diphtheria seems to be an instance--of great general interest--in which the use of animals in one context has virtually abolished their use in another. But as long as any animals are used for this purpose, we may hope to see in vitro methods promoted (King and Frobisher, 1949). Now that the pathologist is less pressed on this front, he should be readier for innovation. And this raises a further point. If culture methods and declining bacterial disease reduce the use of animals in diagnosis, will the guinea pig drop to a low place on the list of animals in use?2 (Its susceptibility to TB has been chiefly responsible for its large-scale use--cf. Table 8--and it is a curious twist that has made this very specialized subject the type in popular speech of the experimental animal.) Or will it, and its chief user, the Group I laboratory, turn over to research? We have heard the opinion that pathologists are moving in this direction, and TB is still the subject of extensive research (cf. Hobson, 1956). Perhaps the 1957 survey (when fully reported) will show the beginning of such a trend.

Several other pathogens occupy specific places in the tables (especially Tables 10 and 18). The Clostridium organisms accounted for a minimum of 450 (mice and guinea pigs). The numerical triviality is offset by the almost unique severity of the symptoms, which must be among the most distressing produced by any experiment. In vitro developments here would be welcome indeed. It is worth noting that Clostridium botulinum toxin has specific effects on peripheral autonomic neural tissue, which can be examined in isolated organs (Ambache, 1951a, b), and that a toxin of Clostridium welchii (the organism of gas gangrene) has a known biochemical activity, and produces selective lesions in tissue cultures (Shaffer, 1956).

In general, the small size, extreme homogeneity, noncommercial nature, and practical preoccupations of Group I laboratories (where most diagnosis is done--Table 17) make for relatively rapid progress in the widespread application of new knowledge; here advances in humane technique can make themselves rapidly felt on a large scale especially if they bring immediate and obvious rewards in terms of efficiency. Most of the remainder of this book will be concerned with the other major types of work and types of laboratory, where the situation is very much more complex.

1Since the following paragraphs were written, Lane-Petter's interim report for 1956 has appeared.
2This trend, as we have seen, is in fact already to be observed.