The Principles of Humane Experimental Technique

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CHAPTER 3

THE ECOLOGY OF EXPERIMENTAL ANIMALS

We may infer that our domestic animals were originally chosen... because they were useful...
The rat and mouse... have been transported by man to many parts of the world...

The L.A.B. Data: A Further Analysis[1]

The Material

Through the great courtesy of Lane-Petter, I have had access to the complete data on which their paper was based, under conditions of strict confidence which I have naturally respected. The information I have abstracted is published here with Lane-Petter's consent, and includes no references to any individual laboratory of a nature which might identify it. I should like to express my cordial thanks to Lane-Petter, for a unique opportunity, of which I hope I have taken full advantage. The results of my analysis are presented in this and the next section and in the remainder of the tables, to which reference may be made from now on.

My analysis differs slightly from that of Lane-Petter and his associates. First, unlike them, I have included fishes (all teleosts). Second, I have almost certainly used slightly different material. Thus, I have tried to discard animals used for breeding stock. These are irrelevant for my purpose, but were important for the bureau authors, who probably included them. Conversely, I was able to include the returns of some laboratories which did not give sufficient information about provenance, and were probably excluded by the Bureau authors on this ground. I have ended up with 10 more laboratories altogether, of which only seven were exclusive fish-users. Like the bureau authors, I naturally had to exclude a number of laboratories which gave no numerical information at all.

In view of these facts, and our different orientations interacting with material which was not always perfectly unambiguous, there are some discrepancies between their tabulations and mine. In the circumstances, they are gratifying slight, and the two analyses accord closely in most respects. Table 4 compares the numbers of animals of each species used according to the two analyses. I seem to have produced rather more rabbits from the common hat, and my conjuring skill is further attested by the transformation of 108 canaries into 72 ducks. There are a few other discrepancies that can readily be explained by the factors mentioned. No really serious differences are present; the figures are often equal or remarkably close, and the ranking of the species is, with one or two trivial exceptions, identical in both lists.

My grouping of species is, on the whole, similar to that of the bureau workers. Like them, I have lumped a number of species under the common head of "monkeys". The returns specified rhesus monkeys, W. African monkeys, Indian green longtail and pigtailed monkeys, but the great majority were unlabeled. "Hamsters" include golden and Chinese, and in general different strains (e.g. hooded and albino rats) are lumped together. I have distinguished more mammal species, and in one table I have separated reptile orders and urodele genera. All the reptiles and urodeles mentioned were, however, used for dissection or for in vitro work, and they have been lumped in most tables. I have lumped Salmonid fishes and, in all but one table, the other four teleosts returned. It is probable, as Lane-Petter et al pointed out, that a number (not substantial) of lower vertebrates were omitted from the returns. Probably also many animals used for dissection were not given; this is very likely for cats and frogs. From our present point of view, it was only necessary to eliminate these, so this omission is of no consequence.

The Classification of Laboratories

My classification of laboratories was somewhat different from that of the bureau workers, though following the same lines. I profited by their discovery that three characteristic types could be distinguished, and tried with some success to reduce the overlap and make the division more clear-cut. This success is reflected in the tables.

I used altogether five groups. Group I was made up by laboratories almost exclusively given up to medical or veterinary diagnosis. It was further divided into HP (Hospital Pathology) laboratories (those attached to non-teaching hospitals) and PH (Public Health) laboratories. Group III contains those laboratories concerned almost exclusively with the production and testing of therapeutic substances and with pharmacological research. (In the tables, this group is sometimes referred to as Ph C--that is, Pharmacological Commercial. In fact a few of them are not profit-making.) Group II might be described as The Rest. I have divided it (with apologies to Mitford) into "U" and "Non-U", or U and N laboratories. The former are all attached to universities or technical colleges. The latter are independent research institutes, mostly supported more or less directly by public organizations, though a few are commercial. On the whole, N are larger than U laboratories, PH are larger than the very small HP laboratories; Group III laboratories are the largest of all. Group II is concerned with research and teaching, but also with the other purposes, U rather more with diagnosis (probably on account of the teaching hospitals), N with pharmacology. We shall see that these differences can be numerically specified.

It is, of course, important to notice the status of this sort of fact. It is no surprise that laboratories intuitively selected for certain properties turn out to have them on analysis. But it is perfectly proper to tabulate data in such a way that real, clear-cut groupings appear. The bureau workers began this task, and I have--for our special purposes--carried it a stage further. However, HP laboratories at least were chosen on a definite criterion (attachment to non-teaching hospitals) independent of the almost exclusive concern with diagnosis that they turn out to have. It is not uninteresting that in 1952 so little work of other kinds was done in them; this may not be so in the future. The detailed pattern of the tables is often instructive.

The numbers of laboratories in my subdivisions and those of Lane-Petter et al are as follows:

Table A: Distribution of Laboratories

Division	**W.M.S.R.**	**Lane-Petter *et al***
Group I		
HP	118	0
PH	51	0
Total	169	182
Group II		
U	110	0
N	64	0
Total	174	147
Group III (Ph C)	22	26
TOTAL	365	355

The table shows my 10 extra laboratories (of the exclusively fish laboratories, six were N and one was U). As it also shows, I have striven to make Groups I and III more uniform by diverting borderline cases to Group II. (In particular, I have shifted several large veterinary laboratories concerned with both research and diagnosis from Group III to N.)

The Classification of Purposes

My classification of purposes requires more discussion. I have separated eight general divisions, of which four are numerically important (they are italicized in the following list):

1. Production of Antisera
2. Source of Blood
3. Non-sentient Minimum
4. Teaching
5. Pregnancy Diagnosis (P.D.), etc.
6. Diagnosis
7. Bioassay, etc.
8. Research

These eight divisions may now be discussed. In the first, I have placed the production of antisera for research, diagnostic, or unspecified purposes. (Much larger numbers of animals yielding directly therapeutic antisera are probably included under the categories of the seventh division, q.v. below.) I have divided it into animals used for antipathogenic or antitoxic sera on one hand, and on the other those injected with materials (e.g. erythrocytes) which can produce no ill-effects in themselves. I have added a third sub-category of unspecified2 antisera: it may include either of the previous categories, which must, therefore, be regarded as minimum returns.

A second small division consists of animals used as sources for whole blood, plasma, blood cells, and so forth. This again may be for many different purposes. It is separated on account of the relatively trivial discomfort it involves, when properly executed--no more, we may presume, than that which we ourselves suffer as blood donors. Animals may be used repeatedly for this purpose, and be available elsewhere in the tables; this is not numerically important. Some of these animals may have been bled out after being killed.

A third category contains two types of essentially humane usage: non-recovery experiments under anesthesia, and procedures not applied to the living animals at all. The second of these subdivisions confounds dissection and the use of isolated organs and tissues in vitro, either immediately or after culturing. From our present point of view, it was worth segregating these numerically quite substantial usages. The numbers given here are absolute minima. It is very probable that many more such procedures were returned under such headings as "teaching", "biochemical studies", and "bioassay". I have only included certainties in this third category.

The fourth purpose distinguished is that of teaching, including both demonstration and classwork. The latter must normally belong to the third category, but where not separately specified I have left it in the fourth.

We come now to the numerically important headings. The first is that of Pregnancy Diagnosis (P.D.). Here I have included not only human pregnancy diagnosis proper, but FSH3 estimation (from human material) and the diagnosis of pregnancy in mares. Each subdivision is separately listed.

The sixth category is that of diagnosis. When specified in the returns, I have separated the organisms suspected in the material inoculated into the animals4. This material was nearly always pathological specimens from man or domestic animals. In the case of TB5 and Brucella, however, many of the animals were inoculated with milk, especially in PH laboratories. Many animals are used as sources of blood for complement fixation tests or the procedurally identical Wasserman Reaction. These should logically have been included under the "source of blood" category. But in the returns on the guinea pig (the main source of complement), this purpose was often confounded with other diagnostic procedures, and may form a substantial part of the compartment in the tables devoted to "unspecified diagnosis". I have, therefore, included it under the general diagnosis heading. After listing each specified purpose, I have totalled all these, and finally given a figure for unspecified diagnosis. This figure may contain other specific purposes which happened never to be individually returned, but also most probably includes many of the purposes already specifically listed in the general category of diagnosis. The figures for specific diagnostic usages are therefore minimum returns. This applies also to the remaining two general headings. In each of these three major divisions, individually specified purposes made up a substantial majority of all returns. The individual items may therefore be taken to reflect fairly the proportional distribution of animals between specific usages in each major category. This is certainly true at least of the numerically important items. Thus, in the diagnosis category, even if none of the unspecified cases were inoculations of TB (which is very unlikely), TB work would still enormously preponderate in the category as a whole over all other diagnostic procedures. On the whole, a considerable amount of information about specific usages was provided in the returns.

The seventh major division I have called "Bioassay, etc.". As with diagnosis, a number of specific purposes are listed as minimum returns, and the total specified and total unspecified figures are given. For the sort of reasons discussed in connection with complement fixation, I was obliged to include both pure and applied pharmacological research (not distinguished) as a specific subdivision of "Bioassay, etc.", and not of the next (Research) category--thus isolating it from all other types of research. It is lumped with a few cases of toxicological research (including research on the metabolism of lethal poisons such as fluoracetate). Here and there within the list of specific items are relatively unspecified purposes, such as hormone assay, which may include any of the hormones previously listed, and probably others. A similar procedure is adopted with chemotherapy and vaccine titration.

The final division is allotted to research, pure or applied. With the information given in the returns, it was impossible to classify research in terms of procedure, and I had to resort to subject-matter as the criterion. I have begun with a long list of subjects which are probably largely studied as pure research, as follows:

Hematology; adrenal, thyroid, carbohydrate (mainly pancreas), and reproductive endocrinology; endocrinology unspecified (which may include any of these and also studies on the interrelation of several endocrine systems and on their nervous control); nutrition; biochemistry or metabolic studies (probably overlapping a little with nutrition); growth (study of growth factors other than nutritional, and of aging); hibernation study; population study (study of growth and fertility of whole populations); renal, gastrointestinal, respiratory, circulation, and behavior research; physiology unspecified (which may include any of the last-mentioned, or the next-mentioned); neurology and neurophysiology; ophthalmology; anatomy (probably often not employing experimental procedures at all); embryology (which may include some experimental procedures applied to parents of embryos); dental; surgical (i.e. studies on surgical procedures as such); radiobiological (i.e. study of the effects of radiation--work with isotopes would be listed under metabolic studies); and immunological.

I have then summed these--their only numerical important member is nutrition research. Next, I have listed separately genetical research (which includes no experiments in the Home Office sense), cancer research, and a heterogeneous and large group of experiments which I have described as bacteriological/pathological/parasitological. (Lane-Petter, 1953b, used a similar category for qualitative purposes.) Within this last, I have distinguished specified virus research and an unspecified residue, of which the most important components are probably studies of pathogenic bacteria and protozoa. These are totaled, and a total given for all specified purposes, followed by three degrees of nonspecificity, which I thought worth separating: Medical Research, Veterinary Research, and wholly Unspecified Research. The veterinary figure is almost certainly always an understatement.

Of all these divisions and subdivisions, apart from the ambiguity of unspecified purposes within categories, many are probably quite clear-cut and distinct. There must be considerable overlap between the bacteriological/pathological/parasitological division and the diagnosis and bioassay groups. Chemotherapeutic research, for instance, is probably divided about equally between the B/P/P category of the eighth division, and the "chemotherapy unspecified" of the seventh (which includes both research and routine). Nevertheless, I was able to isolate a considerable number of purposes which seem to be quite "pure" (in the biological, if not in the sterner chemical sense!).

Tables

Like the bureau workers, I now had three dimensions available: species, purposes, and laboratory type. I was thus in the dilemma of the famous inhabitant of Flatland when confronted with three-dimensional revelations. Perspective tables are possible but too cumbersome when many items are separated. I have, however, assembled a number of tables which exhibit the main relations to be observed.

Table 5 shows, in descending order, the numbers of animals of each species used. (This and all subsequent tables are based on my own analysis--cf. Table 4.) The number of species are rather small for determining the nature of the distribution, but I have grouped the species logarithmically in batches to illustrate it.

Tables 6, 7, 8, and 9 show the distribution of purposes among laboratory types for each of the four (numerically) important mammals--respectively, the mouse, rat, guinea pig, and rabbit.

Tables 10, 11, 12, and 13 show the distribution of purposes among all species. Of these, Table 10 and 11 are devoted to the eight most numerous mammals; the totals for each species are given in Table 11. Table 12 covers the remaining mammals, and Table 13 the other vertebrates. These last two tables are shorter, since the species concerned sprawl over far fewer purposes altogether.

Table 14 shows the numerical distribution of species to laboratory types--the number of each species used in each type of laboratory. Table 15 is complementary, and shows the number of laboratories of each type which use each species.6 This table may be compared with Table 2, from Lane-Petter et al. The bureau workers made use, in that table alone, of all laboratories giving quantitative or qualitative returns. In my table, I have used only laboratories giving quantitative information which I have used in the rest of my tabulations. I did this in order to derive from Tables 14 and 15 another one, Table 16, which records the mean number of animals used in each type of laboratory for the eight commonest species.

Finally, in Table 17, I have distributed the major purpose divisions to laboratory types. This has been done in three stages of combination:

a. with all five laboratory types separated, and all eight purpose divisions (of which the last if further subdivided into Cancer Research plus B/P/P Research and the remainder);

b. showing only the three major divisions but still with the five laboratory types (pregnancy diagnosis has been added to general diagnosis);

c. with divisions as in (b) and laboratory types reduced to the three main groups.

Validity of the Tables

Before turning to the results, I must add one qualification if the tables are to be interpreted fairly. Many returns were quite unambiguous--so many of such and such a species for such a purpose, more or less specific. Others took the form of a figure followed by more than one purpose. Where I encountered this, I made use of certain arbitrary but not unreasonable conventions.7 The use of these conventions in no way affects the total number of each species used, or their distribution to types of laboratory. It does, however, affect their distribution to particular purposes, and also the numerical distribution of purposes to laboratory types.

For several reasons, I am confident that the need for and use of these conventions have not seriously impaired the analysis. First, in 19 of the 34 species used (sometimes genera or families, etc.), no such ambiguity occurred at all, and I was not obliged to resort to the conventions. This group luckily included almost all the numerically very small species. In a further 12 species, the directly recorded greatly exceeded the conventionally estimated figures (mouse, rat, rabbit, chicken, cat, dog, pigeon, cow, goat, hamster, frog, Xenopus). In only three species did the conventionally estimated exceed the directly recorded figures: ferret, pig, and guinea pig. The conventional estimate for the ferrets almost entirely concerns their distribution between the production of canine distemper prophylactic and unspecified pharmacological purposes. Of the 24 pigs used altogether, 20 had to be conventionally distributed between circulation and nutrition research. Now that both cases have been explicitly mentioned, they can hardly cause any misinterpretation.

The guinea pig, a numerically important animal, calls for more thought. There was a simple test to apply, and I applied it. (Similar problems arise in sociology, and are similarly tackled--e.g. Anderson and Schnaper, 1952.) In the case of HP and PH laboratories, I totalled the directly recorded and also the combined (direct plus conventional) numbers for TB inoculations and for the total usage of these types of laboratories. If the ratios coincide, we need not suppose the conventions to be distorting the results as a whole, at least so far as numerically important purposes are concerned. The results of this trial follow below:

Table B: Test of the Conventions

Guinea Pig
Group I

Ratio of number of animals used for inoculation of milk or pathological specimens for TB to total number of animals used for all purposes:

HP		
Directly recorded numbers only	9454/13301	71.1%
Directly recorded + conventionally estimated numbers	25992/37267	69.6%
PH		
Directly recorded numbers only	24610/35292	69.7%
Directly recorded + conventionally estimated numbers	49028/69299	70.7%

The agreement is astonishing close. (Incidentally, so is that between the two types of Group I laboratory; we shall see that these types have much in common.) So far as numerically large purposes are concerned, the conventions seem to approximate very closely the intentions of those who filled in the returns.

This is substantially a final judgement on the results as a whole. Nobody supposes (cf. Lane-Petter et al) that all the returns themselves were impeccably accurate; some of them bear clear traces of rounding. Nor does this matter seriously. The compartments with small numbers may not always be reliable--and in any case, the incidence of minor usages must change considerably from year to year. Many of the larger figures may be approximations. But of the general reliability of these larger figures we need have little doubt, and the same may be said of the faithfulness of the tables as a whole in reflecting the pattern of experiment in Britain in the year 1952.

1This and the following section are by W.M.S.R. alone.
2I.E. unspecified by those completing the questionnaire returns.
3Follicle-Stimulating Hormone.
4Such experiments normally consist in the inoculation of suspected tissues or fluids and the recording of symptoms or death and recovery of pathogenic organisms from the inoculated animals.
5Tubercle bacillus.
6The bottom row does not show the totals of the columns, which would be meaningless, but the total number of laboratories in each type.
7For instance, "mainly" = "chiefly" = 3/4 to nearest integer; "almost exclusively" = 49/50; etc.