

The Principles of Humane Experimental Technique

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CHAPTER 7

REFINEMENT

... endless forms most beautiful and most wonderful have been, and are being evolved.

Neutral and Stressful Studies

Replacement can be considered under a number of general headings, and admits readily of a general approach. Reduction is a compact subject, centering on the problem of variance control. Refinement, the third great path of advance, presents more formidable difficulties to the would-be taxonomist of techniques. It is indeed so protean in its aspects, that it would almost seem to require a separate solution in every single investigation, and refinement might be regarded as an art or an ability to improvise. It is true that the greatest experimenters have been artists in this sense, and that is one reason why we read with such aesthetic pleasure the accounts of their experiments. Nevertheless, the subject of refinement does admit of some generalizations. In this chapter, we shall try to make them.

Suppose, for a particular purpose, we cannot use replacing techniques. Suppose it is agreed that we shall be using every device of theory and practice to reduce to a minimum the number of animals we have to employ. It is at this point that refinement starts, and its object is simply to reduce to an absolute minimum the amount of distress imposed on those animals that are still used.

We can begin with a broad division, in terms of objective, into two distinct kinds of investigation. In one category fall studies which have as their main or subsidiary object the acquisition of knowledge about the mechanisms of pain and distress, and/or their autonomic and endocrine sequelae. We shall call these *stressful* investigations. Into the second category fall all other studies, which do not have such objectives. These we shall call *neutral* investigations (Russell, 1957b).

In neutral studies, the imposition of any degree of distress, however slight, is likely *a priori* to disturb the efficiency of the investigation. This conclusion need not be

labored, in view of the contents of Chapters 1 and 6. True, as Chance has cautiously observed, there is still no adequate evidence for the view that physiological variance is a simple function of distress; and the conditions for minimal variance may quite conceivably differ in different responses. Nevertheless, the *inadvertent* imposition of any degree of distress must always introduce a source of confusion, which will find its ultimate expression in terms of cost, error, and wasted effort. In neutral investigations, then, refinement is a major factor for success, and can be simply described as the elimination of contingent inhumanity. It merges into good husbandry, where, as we have seen, the general argument acquires still more cogency.

In stressful investigations, there seems at first sight an irreconcilable conflict between the claims of humanity and efficiency. For how can we eliminate, or even reduce, the distress imposed, without prejudicing the end in view? This is indeed difficult terrain, where we must proceed with greater subtlety. But the ground becomes a little clearer if we discriminate the various particular objects of stressful studies--special kinds of distress, pain in itself, physiological stress responses, and so forth. For instance, much is already known about the pathways or channels by which central nervous distress is translated into the physiological stress responses (see especially several papers in the CIBA Colloquium, 1952). There is ground for hope that, perhaps when a little more is known, the responses themselves may be evoked, as required, by intervention at a more peripheral or coordinative level (Russell, 1954) than that of the sites of integration of distress itself. In other words, we may soon be able to get *stress without distress*, by intervening further round the circuit. At the other peripheral extreme, the study of peripheral pain mechanisms is methodologically quite independent of their central effects. Finally, even some aspects of central integration may be amendable to humane study: Delgado (1955) cites a number of studies in which characteristic faciovocal responses could be elicited by electrical stimulation of tracts and nuclei in the brainstem in *decerebrate or anesthetized mammals*. Such analytical studies make up in discrimination for what they lack in fidelity. The tremendous advances in neurophysiology which we owe to the Sherrington school could never have been made without such discriminative analysis.

There may seem to be a stubborn residuum of inevitably inhumane study--that of the main forms of distress itself. Now one of the most important of these is what we call *fear*. In a later part of this chapter, we shall outline some methods whereby fear itself can be studied with perfect humanity and at an appreciable gain in efficiency. Paradoxical as this may appear, we hope to demonstrate it in a quite practical way. This may afford hope that even the toughest of problems in stressful investigation are ultimately amenable to refinement. *A fortiori*, we should expect no insuperable obstacles to the refinement of neutral studies.

In all types of investigation, refinement can take two different forms, which we shall consider in turn. The first of these is the case of generally superimposed procedures.