

# THE BENEFITS OF GIVING EXPERIMENTAL ANIMALS THE BEST POSSIBLE ENVIRONMENT

---

by Michael R.A. Chance\* and William M.S. Russell\*\*

\*) 12 INNAGE ROAD, NORTHFIELD, BIRMINGHAM, B31 2DX,  
UNITED KINGDOM

\*\*\*) 12 DOWNSHIRE SQUARE, READING, BERKS, RG1 6MH, UNITED  
KINGDOM

When drugs are tested on animals, there are both economic and humane grounds for using as few animals as possible. The more the experimental animals vary in their response to the test-drug, the more animals we have to use to get a statistically representative sample. From this it follows that, if we can make the animals more uniform in their response fewer of them are needed in the experiment.

It used to be thought that if the animals are kept in a uniform environment, however uncomfortable or socially disturbing, they will show more uniform responses. In the 1950s, Chance discovered that “the size of the variance is related to the exact nature of the conditions,” and that the better the conditions for the animals’ well-being—in housing, treatment and social situation—the lower the variance. He was led to this discovery by an awareness that, just as in human psychosomatic medicine, environmental conditions affecting the behavior of animals will automatically also affect their physiology. Here are some examples:

In 1956, Chance reported the results of a study investigating the test response of immature female rats to the sex hormone serum gonadotrophin. The variation in ovary weight (the test response) was *greater* if the cages were small and cramped, if there was frequent disturbance by changing cages and cage-mates, and if the rats were caged either singly or in groups larger than two (with the floor area per rat roughly constant). These results led him to reexamine his own 1946-47 studies of the toxicity of certain drugs for mice, and Chen’s 1943 studies of the potency for mice of certain other drugs. In both cases, Chance (1957a) found notable effects of environmental conditions on the variance of the animals’ test-responses, though both Chen and he himself had failed to notice this at the time when they conducted the studies. In 1962, Chance’s colleague John Mackintosh reported a study of the responses of male mice to a barbiturate anaesthetic, and he showed that the variance of the response was greater if the animals were caged either singly or in groups of eight than if they were caged in pairs.

Some of these findings can be understood in terms of known aspects of rodent behavior—for instance, a preference for *familiar* surroundings, and a failure to form *stable* social hierarchies when caged in too large numbers (Chance & Mead 1955; Chance 1957b, 1964; Grant & Chance 1958; Silverman 1978; Cooper & Hendrie 1994).

Evidently, then, if animals are being kept in a physical and/or social environment that is less than optimal for their well-being, they will vary more in their test-responses, and so more of them will have to be used in the tests. But this is not all. Uncomfortable, species-inappropriate and distressing situations also have psychosomatic physiological effects which must disturb *any* experimental results, and will thus make tests *unreliable* when repeated or performed in different laboratories. Surveying the literature as early as 1957, Chance was able to find striking examples of this:

- \*The incidence of cancer in mice is related to the numbers of animals in a cage.
- \*Blood cell levels in mice are altered by disturbing sounds.
- \*Crowding increases the susceptibility of rats to tuberculosis.

An overwhelming mass of such evidence is available (Clough 1982; Fox 1986; Claassen 1994).

The lesson to be learned from all this is unmistakable: *If we use ethological sophistication to provide laboratory animals with the very best physical and social environmental conditions for their well-being, we need to use fewer of them in research experiments or routine tests, and our results will be accurate and reliable.*

## References

**Chance MRA** 1946. Aggregation as a factor influencing the toxicity of sympathomimetic amines in mice. *Journal of Pharmacology* 87, 214-222.

**Chance MRA** 1947. Factors influencing the toxicity of sympathomimetic amines to solitary mice. *Journal of Pharmacology* 89, 289-296.

**Chance MRA and Mead AP** 1955. Competition between feeding and investigation in the rat. *Behaviour* 8, 174-182.

**Chance MRA** 1956. Environmental factors influencing gonadotrophin assay in the rat. *Nature* 177, 228-229.

**Chance MRA** 1957a. The contribution of environment to uniformity. *Laboratory Animals Bureau Collected Papers* 6, 59-73.

**Chance MRA** 1957b. Mammalian behaviour studies in medical research. *The Lancet* Oct. 5, 687-690.

**Chance MRA** 1964. Population size and variation in small populations. *Proceedings of the Royal Society of Medicine (UK)* 57, 174.

**Chen KK, Anderson RC, Steldt FA and Mills CA** 1943. Environmental temperature and drug action in mice. *Journal of Pharmacology and Experimental Therapeutics* 79, 127-132.

**Claassen V** 1994. *Neglected Factors in Pharmacology and Neuroscience Research*. Elsevier: Amsterdam.

**Clough G** 1982. Environmental effects on animals used in biomedical research. *Biological*

*Reviews* 57, 487-523.

**Cooper SJ and Hendrie CA (eds.)** 1994. *Ethology and Psychopharmacology*. Wiley: New York.

**Fox MW** 1986. *Laboratory Animal Husbandry: Ethology, Welfare and Experimental Variables*. State University of New York: Albany.

**Grant EC and Chance MRA** 1958. Rank order in caged rats. *Animal Behaviour* 6, 183-194.

**Mackintosh JH** 1962. Effect of strain and group size on the response of mice to "second" anaesthesia. *Nature* 194, 1304.

**Silverman P** 1978. *Animal Behaviour in the Laboratory*. Pica Press: New York.