which indicates that if the polygenic hypothesis did not exist it would have to be invented. Winter[6], for instance, selected from commercial varieties of corn, two diverging lines for high and low protein and two lines for high and low oil content. After years of selection experiments, the difference between the high and low lines for oil content was more than 20 times the original standard deviation. Discussing these results, Student[7] concluded that they could not be explained "on the basis of a few easily detected genes". He estimated the number at 100–300. Noting that there was no evidence that the selection had reached its limits, he concluded "that the number of genes affecting oil (or protein) content . . . may run up to thousands".

Fisher[4] was critical of Student's[7] estimate but felt that, in conjunction with other evidence, the results ". . . force one to the conclusion that all commercial varieties may be segregating in hundreds, and quite possibly, in thousands of factors influencing the normal development of a plant".

There seems to be no alternative hypothesis to account for these facts. Student[7,8] did suggest an hypothesis to explain Winter's[6] experiment, namely, that "species tend to accumulate a sufficient store of genes of no particular value until they meet with a change in environment when the store provides material for selection far beyond the normal range". This in no way diminishes the importance of the polygenic hypothesis; on the contrary, it strengthens it.

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1 Thompson, J. N., *Nature*, **258**, 665–668 (1975).
2 Fisher, R. A., *Trans R. Soc. Edinb.*, **52**, 399–433 (1918).
3 Fisher, R. A., *Nature*, **150**, 154 (1942).
4 Fisher, R. A., *Nature*, **131**, 400–401 (1933).
5 Falconer, D. S., *Introduction to Quantitative Genetics* (Oliver and Boyd, Edinburgh, 1960).
6 Winter, F. L., *J. agric. Res.*, **39**, 451–476 (1929).
7 'Student', *Eugen. Rev.*, **24**, 293–296 (1933).
8 'Student', *Ann. Eugen.*, **6**, 77–82 (1934).

THOMPSON REPLIES—Although I appreciate the position taken by Vetta[1] in defending the common hypothesis that quantitative variation is produced by the segregation of a large number of genes, much work has been done in the 30 or 40 years since Fisher, Winter, and 'Student' first considered the problem (see refs in Vetta[1]). Among the most significant recent contributions to this problem have been those by Thoday and his colleagues[2–5], particularly Spickett[6–8], and those by Scharloo[9] and Rendel[10]. It is well past time to reconsider our understanding of quantitative genetic traits, incorporating this information[11]. This is not to say that the older facts are necessarily wrong, but rather that our perspective of the problem should be reconsidered.

Genes affecting continuously distributed phenotypes have small effects relative to uncontrolled environmental variation, and allelic substitutions at individual loci are essentially equivalent. This often makes precise genetic analysis difficult. It is clear from biometrical literature that models based on assumptions of many genes having similar phenotypic effects can explain quantitative variation quite elegantly. But are these assumptions generally valid? What experimental evidence is there to support the assumptions (that is, experimental evidence which is independent of the statistical tests, themselves)? Are there equally satisfactory models based on other reasonable assumptions about the number or magnitude of polygene effects?

An alternative assumption, to which Vetta objects, concerns polygene number. Evidence comes from both theoretical and experimental sources and is summarised briefly in my original article[11]. One important observation is that theoretical distributions essentially indistinguishable from normal phenotypic distributions can be produced by segregation at a few loci, or even at a single locus. Several such examples are discussed in detail by Thoday and Thompson[12]. The conclusion is that there is no justification for automatically assuming that an apparently normal phenotypic distribution is caused by the segregation of a large number of genes. Experimental evidence confirms this[11].

Some, but by no means all, characters continue to respond to artificial selection for "20 to 30 generations". Vetta is quite correct, therefore, in pointing out that there are some traits for which it is likely that a comparatively large number of factors contributes to the variance. Indeed, I did not deny that this may often be true (ref. 11, p. 666). I suggested, however, that these are examples of highly complex characters (that is, they are the result of the interaction of a large number of contributing developmental processes) and that polygenic influences on each of these contributing processes would tend to be cumulative. Quantitative variation in body weight, for example, may be produced by polygenes affecting the rate of bone growth or the adult bone size, the efficiency of nutrient uptake from the intestine, endocrine function, the rate of cell division, cell number and size, the size of muscles, and numerous other contributing processes which, if looked at carefully, could each be considered quantitative characters in their own right. It is the analysis of these contributing processes which will give us the most rewarding insight into polygene number and function.

The point of contest should, therefore, not be whether there are "few" or "many" (at best, very unspecific terms), but whether the number of polygenes affecting any character is exceptionally large (the "hundreds" and "thousands" sometimes quoted). I believe that the balance of evidence provides no compelling reason to think that the number of polygenes affecting any particular trait is exceptionally large, and indeed, it is probably quite a lot smaller than generally thought.

The usual impression of multigenic effects is probably attributable, in many instances, to an unsophisticated approach to phenotypes and the processes of development. What is needed is an experimental approach to quantitative genetic variation which concentrates, not on the sheer number of factors[1], but on their functions and influences on development? The work by Spickett[7,8], Milkman[13] and others shows that this is potentially more informative, for often the number of genes involved is not particularly large, and in appropriate conditions they can be isolated and manipulated readily[2].

As long as continuously distributed phenotypes are regarded as necessarily the product of segregation at a large number of loci, straightforward chromosome substitution and other direct manipulations of the genome may not be given sufficient attention as possible alternatives to the more time-consuming and less precise techniques generally available to applied geneticists.

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1 Vetta, A., *Nature*, **261**, 525–526 (1976).
2 Thoday, J. M., *Nature*, **191**, 368–370 (1961).
3 Gibson, J. B., and Thoday, J. M., *Heredity*, **17**, 1–26 (1962).
4 Wolstenholme, D. R., and Thoday, J. M., *Heredity*, **18**, 413–431 (1963).
5 Thoday, J. M., Gibson, J. B., and Spickett, S. G., *Genet. Res.*, **5**, 1–19 (1964).
6 Spickett, S. G., and Thoday, J. M., *Genet. Res.*, **7**, 96–121 (1966).
7 Spickett, S. G., *Nature*, **199**, 870–873 (1963).
8 Spickett, S. G., Shire, J. G. M., and Stewart, J., *Mem. Soc. Endocrinol.*, **15**, 271–288.
9 Scharloo, W., *Genetics*, **65**, 681–691 (1970).
10 Rendel, J. M., *Canalisation and Gene Control* (Logos, London, 1967).
11 Thompson, J. N., Jr, *Nature*, **258**, 665–668 (1975).
12 Thoday, J. M., and Thompson, J. N., Jr, *Genetica* (in the press).
13 Milkman, R. D., *Adv. Genet.*, **14**, 55–114 (1970).