and uncontrived pain. The dolorimetrist cannot distinguish between stimulation and injury; all he does is register degrees.

Splitting the pain experience into "specific" components has not had a convincing demonstration. It is, moreover, doubtful whether on biological grounds the separation of perception, or sensation, from response is desirable. It probably was unhelpful of Hardy, Wolff, and Goodell to pit subjective perception as a constant against objective reaction as a variable: to warm up the old epistemological issue between feeling and observation, not to solve but to confuse it even more. Attacked on theoretical grounds, the dolorimetrists concede only that resynthesis may be "difficult," but maintain in favor of their theory that "the practical importance to the physician in controlling the various aspects of the pain experience is unquestioned." Nevertheless, one cannot help asking the practitioner what he has learned from the dolorimeter toward a more enlightened use or understanding of analgesics, narcotics, sedatives, and placebos.

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## Estimation of Gene Frequencies from MNS Data

THE increasing use of blood group data in anthropology is shown by many recent publications (*1–4*). Next to the Rh system of genes, the MNS system is probably the most useful. In order to make use of all the information contained in each set of data, it is desirable to estimate the gene frequencies by an efficient method. A simple method of doing this for MNS data does not seem to have been published.

Maximum likelihood estimates of the gene frequencies are easily obtained as follows. Start with "consistent" estimates of the frequencies of the genes $M$ and $N$. For a first shot the estimates $m_s = \sqrt{M}$ and $n_s = \sqrt{N}$ may be used, but formulas due to Mourant, which are shortly to be published (*4*), are better.

The total $m$ frequency, which includes the frequency $m_s$ (the frequency of the gene $Ms$) and $m_S$ (the frequency of the gene $MS$) can be found by the usual gene-counting method as $m = M + MS + MN/2 + MNS/2$. Similarly $n = N + NS + MN/2 + MNS/2$. Consequently our estimates of the frequencies of MS and NS are $m_S = m - m_s$ and $n_S = n - n_s$.

Using these frequencies, calculate the expected frequencies of the six phenotypes:

$$\begin{aligned} M &= m_s^2 \\ MS &= m_S^2 + 2m_s m_S \\ MN &= 2m_s n_s \\ MNS &= 2(m_s n_S + m_S n_s + m_S n_S) \\ N &= n_s^2 \\ NS &= n_S^2 + 2n_s n_S. \end{aligned}$$

Then calculate the two measures of the degree to which the provisional gene frequencies depart from the maximum likelihood values, from the equations:

$$\partial L/\partial m_s = (2M + MN)/m_s - 2MSm_s/(m_S^2 + 2m_s m_S) - MNSn_s/(m_s n_S + m_S n_s + m_S n_S)$$
$$\partial L/\partial n_s = (2N + MN)/n_s - 2NSn_s/(n_S^2 + 2n_s n_S) - MNSm_s/(m_s n_S + m_S n_s + m_S n_S),$$

where $m_s$, $m_S$, $n_s$, and $n_S$ are the provisional gene frequencies, and M, MS, etc., are the observed numbers of individuals in the respective classes.

Then calculate three quantities

$$I_m = 4G[1 + (M)/(MS) + (N)/(MN) + (N)/(MNS)]$$
$$I_n = 4G[1 + (N)/(NS) + (M)/(MN) + (M)/(MNS)]$$
$$I_{mn} = 2G[1 + (MN)/(MNS)]$$

where (M), (MS), etc., represent the expected values as calculated above and $G$ is the total number of individuals tested.

$$\begin{aligned} \text{Let } V_m &= I_n/(I_m I_n - I_{mn}^2) \\ V_n &= I_m/(I_m I_n - I_{mn}^2) \\ W_{mn} &= -I_{mn}/(I_m I_n - I_{mn}^2). \end{aligned}$$
$$\begin{aligned} \text{Then } \delta m_s &= \partial L/\partial m_s (V_m) + \partial L/\partial n_s (W_{mn}) \\ \delta n_s &= \partial L/\partial m_s (W_{mn}) + \partial L/\partial n_s (V_n) \end{aligned}$$

and the adjusted estimates of the gene frequencies are

$$m'_s = m_s + \delta m_s \quad \text{and} \quad m'_S = m - m'_s$$
$$n'_s = n_s + \delta n_s \qquad n'_S = n - n'_s.$$

If the corrections $\delta m_s$ and $\delta n_s$ are large, the process can be repeated with the improved estimates, although in general this is not necessary, as one application of the process yields efficient estimates (*5, 6*).

A similar method can be applied to the case of nine phenotypes resulting when an anti-s serum is also used. Calculations for this and other cases, as well as formulas for the variances of the estimates obtained, will be presented elsewhere.

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*Erratum.* In the abstract of the paper, "The Direct Observation of Hapten-Antibody Equilibria" presented before the National Academy of Sciences, which was published in the Nov. 13th issue of SCIENCE, p. 570, there is an error due to a miscalculation. A value of 5.5 kcal is given for the free energy of formation (per mole) of a hapten-antibody bond. This value should be 7.6 kcal.

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