Letters to the Editor

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NOTES ON POINTS IN SOME OF THIS WEEK'S LETTERS APPEAR ON P. 479.

CORRESPONDENTS ARE INVITED TO ATTACH SIMILAR SUMMARIES TO THEIR COMMUNICATIONS.

Precursors of Coprosterol and the Bile Acids in the Animal Organism

THE transformation of cholesterol into coprosterol in its passage through the body involves a reduction of the $C_5 : C_6$ double bond, and a transition from the *allo*cholanic- to the cholanic-ring system. Although it is established that the bacterial flora of the intestine is concerned in the reduction process, the mechanism by which the stereochemical change is brought about is unknown. A clue was afforded by a study of the properties of cholestene-3 : 4-diol, a primary oxidation product which is formed under various conditions of mild oxidation from cholesterol, and is also a constituent of the resinous product called 'oxycholesterol'[1]. Being an α-glycol, this substance easily rearranges by loss of water into the corresponding ketone, that is, cholestenone. Since cholestenone (= coprostenone) yields coprostanone on reduction, which in turn is reducible to coprosterol (= coprostanol) and *epi*-coprosterol[2,3], we formed the working hypothesis that the reactive primary oxidation product, cholestene-diol, may play a role in cholesterol metabolism, giving rise to the formation of cholestenone as an intermediary product. On this assumption, cholestenone and coprostanone, and not cholesterol itself, are the immediate precursors of coprosterol which is formed from them in the intestine by bacterial reduction. Further, an explanation is afforded for the origin of the *epi*-hydroxycholane system in lithocholic acid (and the other bile acids ?)[4], which may be derived from *epi*-coprosterol by oxidative cleavage of the side chain with loss of acetone.

On subjecting this hypothesis to experimental test by means of feeding experiments on animals, we found that the addition of cholestenone to various diets poor in cholesterol gave rise to a large increase in the excretion of faecal coprosterol. This increase did not, however, account for the whole of the ingested cholestenone, and since only a small amount was excreted unchanged, it is possible that the remainder may have been converted into bile acids. This question, as well as the action of intestinal bacteria on cholestenone, is being further investigated.

It may be pointed out that a similar mechanism may underlie the metabolic processes leading from cholesterol to certain sexual hormones (progesterone, androsterone) which contain either a keto group or an epimerised hydroxyl at C_3.

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Sept. 5.

[1] Rosenheim and Starling, *Chem. and Ind.*, **52**, 1056; 1933.
[2] Grasshof, *Z. physiol. Chem.*, **225**, 197; 1934.
[3] Ruzicka, Brüngger, Eichenberger and Meyer, *Helv. Chim. Acta*, **17**, 1407; 1934.
[4] Ruzicka and Goldberg, *Helv. Chim. Acta*, **18**, 668; 1935.

Statistical Tests

IN a letter to NATURE of August 24, Prof. Karl Pearson states: "From my point of view, the tests are used to ascertain whether a reasonable *graduation* curve has been achieved, not to assert whether one or another hypothesis is true or false."

This assertion must come as a surprise to many who are familiar with Prof. Pearson's writings. It should not, however, be permitted to divert attention from the points raised in Mr. Buchanan-Wollaston's letter of August 3, for whatever may have been Prof. Pearson's original intention in introducing the term 'goodness of fit', and in publishing a table of the distribution of χ^2 (the theoretical form of which had been previously determined by Helmert in 1875), it is certain that the interest of statistical tests for scientific workers depends entirely from their use in rejecting hypotheses which are thereby judged to be incompatible with the observations.

It is certain, too, from many passages which could be cited from Prof. Pearson's own writings, that he has himself used the χ^2 test, not only in connexion with the graduation of frequency curves, but also as a means of testing the truth of theories or hypotheses. As one example, I may mention an appendix of five pages entitled "On the Test of Goodness of Fit of Observation to Theory in Mendelian Experiments" (*Biometrica*, **9**, pp. 309–314). In this paper he insists very clearly, and quite in accordance with modern usage, taking the extreme case $P = 0$, that either the theory or the observations must be rejected.

Mr. Buchanan-Wollaston's point that the χ^2 test, like the other tests of significance, is cogent for the rejection of hypotheses, but, in the opposite case, by no means cogent for their acceptance, deserves to be widely appreciated. For the logical fallacy of believing that a hypothesis has been proved to be true, merely because it is not contradicted by the available facts, has no more right to insinuate itself in statistical than in other kinds of scientific reasoning. Yet it does so only too frequently. Indeed, the "error of accepting an hypothesis when it is false" has been specially named by some writers "errors of the second kind". It would, therefore, add greatly to the clarity with which the tests of significance are regarded if it were generally understood that tests of significance, when used accurately, are capable of rejecting or invalidating hypotheses, in so far as these are contradicted by the data; but that they are never capable of establishing them as certainly true. In fact that "errors of the second kind" are committed only by those who misunderstand the nature and application of tests of significance.

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