primitive thrombocytes with mammalian platelets, which aroused much speculation about the function of mammalian platelets. It became obvious that knowledge of the human haemostatic mechanism is decades ahead of comparable knowledge of mammalian haemostasis, and similarly in fibrinolysis there has been much more progress with the human system than with mammalian systems. Factors VII and X seem to be absent in animals lower than mammals, but there may be modified forms of these substances which cannot be detected by the crude methods available at the moment. It was also interesting to observe that evolutionary changes in species affect the non-functional rather than the functional part of the fibrinogen molecule.

Dr Christine Hawkey (Zoological Society of London), however, emphasized the problems encountered in comparative studies. She observed that although systematic investigation has been good in arthropods, many of the animals studied represent the available ends of evolutionary lines. She stressed our ignorance of congenital clotting defects in animals, with the exception of a few in domesticated animals. She asked many questions and made suggestions for further study; for example, what is the effect of ADP and other activators of platelets on invertebrate cells? This symposium should have stimulated a search for the answers to such questions.

MONGOLISM

Investigators Criticized

from a Correspondent

AN unusually critical review of the published literature in a branch of research was made on November 25 by Dr Alexander G. Bearn at a symposium on mongolism (Down's syndrome) held at the New York Academy of Sciences. The most distressing feature of this common inborn error of metabolism, which occurs in about one in 600 live babies, is pronounced mental retardation. The fundamental abnormality in the syndrome (first described by Langdon Down in 1866) is a defect, usually trisomy, of chromosome 21. This defect was reported by Lejeune in 1959. Recently there has been controversy over the possibility that mongolism results from fertilization of the ovum at a late stage of the ovulation cycle, possibly connected with low frequency of coitus (*Nature*, **217**, 516; **218**, 300; **219**, 1280 (all 1968); **221**, 173 and 642; 1969).

Both before and since 1959, biochemical abnormalities characteristic of Down's syndrome (also called Down's disease and Down's anomaly) have been sought. Reviewing the literature on such abnormalities, Dr Bearn (Cornell Medical School) commented that enthusiasm, or the will to succeed, were the only laudable features of some reported studies that "displayed the appurtenances of scientific inquiry without satisfying the requirements of scientific method". False conclusions had been reached in almost every case. Subsequent work (which would otherwise have not been necessary) had shown that, for example, there is no characteristic elevation of serum cholesterol or β -lipoproteins in mongoloids, their carbohydrate metabolism is not deranged in any typical way, and the observed changes in serum γ -globulins are characteristic more of the institution in which the patients are treated than of the disease itself.

Bearn's purpose in reviewing the errors in published work was two-fold: to point out that progress is hindered if unjustified conclusions are published, and to define in detail what features of experimental design and interpretation are essential for future work. They include (as with most investigations) the use of appropriate controls, the application of appropriate statistical methods and the avoidance of equating correlation with cause and effect.

The most obvious weakness in studies of mongolism has been the inadequate selection of controls. Most studies are carried out in children, in whom biochemical changes occur rapidly from year to year, and yet pair-matching with controls for age and sex has only recently been adopted. Mongoloid children tend to be overweight, and yet matching or allowing for degree of obesity has rarely been considered. In some studies, institutionalized children have even been compared with non-institutionalized, normal children. The length of time in the institution can also be important. The only proper controls are therefore mentally retarded non-mongoloid patients, matched for age, sex and degree of obesity, who have been in the same institution for about the same length of time. These requirements are demanding, but if they are not met the study reported must be regarded as suspect if not invalid.

Adequate and appropriate statistical treatment of the results is also essential, especially because mongoloids, with their extra genes, are expected (and found) to show greater variability than normals in most biochemical measurements. Poor use of statistics, including the application of chi-square tests to percentages, has often been used to establish unreal differences as "statistically significant".

Even when a biochemical difference between mongoloid patients and appropriate controls has been satisfactorily proved, this has too often been hastily ascribed to the genetic defect when a more obvious explanation was possible. For example, the well-documented higher concentration of serum immunoglobulins in mongols might more rationally have been attributed not to mongolism but to the frequent occurrence of non-specific infections (mongols, especially those in institutions, are particularly prone to infection). This suspicion has recently been neatly confirmed by a group (Griffiths, Sylvester and Baylis, *J. Clin. Pathol.*, **22**, 76; 1969) working at hospitals at Caterham and Epsom, England.

Bearn criticized most of the faulty work not by citing later contradictory evidence but by applying the principles of scientific method to the original articles. His contribution to the symposium therefore amounted to an indictment not only of the authors but of editor, reviewers and departmental reviewing committees for allowing the inaccurate and misleading reports to be published.

PROTEINS

Multi-purpose Enzyme

from our Molecular Biology Correspondent

THE process by which the monomeric constituents of DNA are produced from their ribose analogues is now recognized to constitute a biochemical control mechanism of the greatest importance and interest. The