Congenital Malformations. A Report of a Study of Series of Consecutive Births in 24 Centres. Prepared on behalf of their colleagues in the 40 co-operating hospitals by Alan C. Stevenson, Harold A. Johnston, M. I. Patricia Stewart, and Douglas R. Golding. (Pp. 127; tables. 12s.; \$2.25.; Fr.s. 7. Free to the subscribers of the Bulletin of the World Health Organization) Geneva: W.H.O. 1966.

The report under review represents a remarkable international exercise carried out under the aegis of the World Health Organization. It is a prospective study of malformations occurring in 24 centres in 16 countries, including ones in each of the continents, and includes the data on the occurrence and types of malformations as they were found in stillborn and liveborn infants. In total, 421,781 pregnancies were investigated (416,695 single births, 5,022 sets of twins, 63 sets of triplets, and 1 set of quadruplets). The frequencies of specific types of malformations or of grouped malformations are discussed, with particular reference to geographical variations, and associations with parental consanguinity. The data are presented in detail in tables (on special request to the authors the basic tables for each centre are made available).

The study took its origin from discussions in 1958, in which the W.H.O. took part, on global needs for medical research. It was then suggested that a prospective study of congenital malformations was perhaps a good example of the type of undertaking which would be difficult to carry out except under the auspices of some international authority, and that a straightforward study of this kind might be useful in a field with wide gaps in factual data. Moreover, useful experience in the methodology, or logistics, of international studies could not help but accrue.

Eventually a recommendation that a simple prospective study of the malformations occurring in a consecutive series of hospital births in a number of countries should be initiated was made and accepted. Dr. A. C. Stevenson was asked to undertake the organization of this study from the Population Genetics Research Unit of the M.R.C. in Oxford. The methods of organization and conduct of the study are described, including a summary of the administrative difficulties encountered in dealing with so many centres in different parts of the world. It included interference by customs authorities and clearly showed that even the W.H.O. cannot be regarded as completely international.

The study as presented is a summary of a summary. As the authors point out, the large amount of information they have made available has precisely the values

anticipated when the project was initiated. For all the births considered, particular emphasis was given to geographical variation and to associations due to parental consanguinity. Such consanguinity was usually associated with an increased stillbirth rate, a higher frequency of early infant death, and an increased instance of neural tube defects. Data from all the centres indicated that neural tube defects determined more stillbirths and early death than in other types of abnormality. These defects also had an unexpected positive correlation with dizygous twinning; but the frequency in monozygotic twins of concordance, when considered together with the wide span of social classes and the geographical variation within countries, suggests that environmental influences play a major aetiological role.

The data include, of course, the full range of abnormalities identifiable at the time of birth in the whole series. Many abnormalities receive special attention, e.g. congenital heart defects (with or without Down's syndrome), perinatal mortality associated with tracheo-oesophageal abnormality, exomphalos, diaphragmatic hernia, and certain urogenital defects. There is also some special attention to harelip and cleft palate, alone or in combination. There are, of course, gaps, sometimes very wide ones, in presentation. In particular, the embryologist and the geneticist may regret the absence of more references to their work. When it is realized, however, how much work has gone into the report, and what an immensely impressive set of data have been provided, anyone with an interest at any level in congenital malformation must be extremely grateful to Dr. Stevenson and to his immediate colleagues and remoter collaborators.

J. D. BOYD

The Sex Chromatin. Edited by K. L. Moore. (Pp. xx + 474; 101 figures. 112s.) Philadelphia and London: W. B. Saunders. 1966.

Sex chromatin studies have for a number of years played an important part in the practice and theory of cytogenetics. The present volume is the first book devoted entirely to this subject. It contains a collection of 26 contributions by 22 authors, under the editorship of K. L. Moore, now professor of Anatomy at the University of Manitoba, who was one of the pioneers of sex chromatin studies. Moore himself has written six of the chapters as well as the Introduction.

The chapters with most obvious relevance to medical genetics are the following: 'The Development of Clinical Sex Chromatin Tests' by Moore; 'Sexual Dimorphism

in Nuclei of Polymorphonuclear Leukocytes in Various Animals' by Davidson; 'Sex Chromatin in Smears from the Reproductive and Urinary Tracts' by Carpenter; 'Sex Chromatin Surveys in Newborn Babies' by MacLean, describing an application of sex chromatin studies which has been outstandingly successful; 'Sex Chromatin and Antenatal Sex Diagnosis' by Riis and Fuchs, two Danish investigators who give an objective account of their experiences with amniocenteses for possible termination of pregnancies in women who are heterozygous carriers of sex-linked abnormalities; 'Sex Chromatin, Klinefelter's Syndrome and Mental Deficiency' by Ferguson-Smith; 'Sex Chromatin in Gonadal Dysgenesis' by Moore; 'Sex Chromatin, Sex Chromosomes and Sex-linked Characters' by Polani; 'The Sex Chromatin and Hermaphroditism' by Lennox; 'Sex Chromatin in Tumours' by Tavares; 'The Sex Chromatin in Psychosexual Differentiation' by Money; 'Sex Chromatin and Developmental Abnormalities' by Benirschke; and 'Sex Chromatin and Medicolegal Problems' by Moore.

The chapters of more general or theoretical interest are: 'The Discovery of the Sex Chromatin' and 'Sex Chromatin Patterns in Various Animals' by Moore; 'Morphological Characteristics of the Sex Chromatin' by Klinger; 'Staining Affinities and Cytochemical Properties of the Sex Chromatin' by Culling; 'Single-X Derivation of Sex Chromatin' by Ohno; 'Correlations between Sex Chromatin Patterns and Sex Chromosome Complexes in Man' by Barr; 'Behavior of the Sex Chromatin during Altered States of Cell Metabolism' by Bertram; 'The Sex Chromatin in Cultured Cells' by Miles; 'The Sex Chromatin of Freemartins and Other Animal Intersexes' by Moore; 'Sex Chromatin in Embryonic and Fetal Tissues' by Austin; 'Sex Chromatin in Transplanted Tissues' by Basu; 'Sex Chromatin and the Sex Ratio in Man' by Stevenson; and 'Sex Chromatin and Gene Action in the X-Chromosome of Mammals' by Mary Lyon.

Regarding terminology, the Editor on p. 3 disapproves of the term 'Barr body' 'partly because Dr. Barr has discouraged its use, but mainly because the term is neither informative nor descriptive'. 'Barr body', however, has two advantages compared with 'sex chromatin', in certain contexts: (1) it excludes drumsticks, so that the subheading by Davidson 'The Relationship of the Drumsticks to the Sex Chromatin in Tissue Cells' might have become more simply 'The Relationship of Drumsticks to Barr Bodies'; (2) the term 'Barr body' is a countable, whereas 'sex chromatin' is not. The very considerable advances which have been made in our knowledge of the nature and origin of Barr bodies have largely come as a result of relating the maximum numbers of Barr bodies present in cells with the numbers of X chromosomes in the karyotype, as shown in the contributions by Barr and by Klinger. The term 'Barr body' is clearly adapted for the quantitative approach, whereas such subterfuges as 'sex chromatin masses' or 'sex chromatin bodies' discourage it. The fact that the quantitative approach still needs fostering in this subject is perhaps indicated by a subscript on p. 98— 'A typical neutrophil in a blood

film from a *male*. A drumstick is not visible.' This gives no indication to the uninitiated that, on an average, 97% of neutrophils in females also fail to show a drumstick. Again, on p. 334 there appears a statement 'There is evidence to show that about 5 per cent of XO zygotes are spontaneously aborted', which should read: 'There is evidence that about 5 per cent of spontaneously aborted zygotes have an XO sex chromosome constitution'.

The varying outlooks of the different authors may be illustrated by the following two quotations: 'Thus, the sexual dimorphism of somatic interphase nuclei first found in 1949 and the realization 10 years later that each sex chromatin body represents a single heterochromatic X is now seen to be a mechanism for dosage compensation in placental mammals' (Ohno, p. 120). 'According to the inactive-X hypothesis, the single heteropyknotic X-chromosome which forms the sex chromatin of female mammals is genetically inactivated. This inactivation is postulated to occur early in embryonic development . . . etc.' (Lyon, p. 383). In spite of the undoubted success of sex chromatin studies, most investigators will agree that the more theoretical aspects are still largely in the realm of hypotheses. For the time being, this book provides useful summaries of the achievements which have been made as well as of some of the problems which remain for the future.

URSULA MITTWOCH

Biochemical Genetics. Compiled and edited by Hubert J. van Peenen. (Pp. xviii + 332; illustrated. \$12.75). Springfield: Charles C. Thomas. 1966.

This multi-author monograph is not intended to be a textbook for the student reading molecular biology, but rather a way of bringing up to date the scientist or physician whose studies were completed before the present knowledge explosion. As such it fills a gap in genetics and biochemistry, and is an important addition to the literature of molecular biology. The authors have achieved a remarkable combination of depth of treatment with easy readability and have included very recent work while maintaining a balanced presentation.

In each chapter (except the last) the basic processes of life are considered rather than a particular species or group; the similarity in these respects of man, insects, plants, fungi, bacteria, and viruses is exemplified. The structure and function of the different nucleic acids, DNA, mRNA, tRNA, and ribosomes, are considered with admirable clarity and completeness. The chapters on protein synthesis and its control are outstanding among reviews of this subject. It is particularly gratifying that the quantitative aspects of gene action and its control, and of the activity of enzymes, are discussed so fully. The section on inborn errors of metabolism is the weakest; there are several serious errors in the table on pp. 195–196, and the treatment of thalassaemia is rather superficial by present-day standards. A final chapter on human cytogenetics is very clearly written and informative, but seems a little out of place in a book on molecular biology. The index is inadequate; it is