The number of patients with breast cancer, these are impressive figures. If the subcommittee can achieve its aims and institute a new generation of large collaborative trials continuing assessment will have become an accepted part of the treatment of breast cancer. Controlled therapeutic trials will not discover a cure; but they are an essential part of the assessment of new methods of treatment, and they spare women the potential morbidity of unsuitable and untried methods of treatment.


Cardiac surgery in infancy

Some congenital heart lesions may be found in about eight per 1000 live births.1-3 Of these, nearly one-third are ventricular septal defects. Seven other lesions—atrial septal defect, patent ductus arteriosus, coartation of aorta, aortic and pulmonary stenosis, Fallot’s tetralogy, and transposition of the great arteries—among them account for a further 50%. Many of these lesions, such as small atrial and ventricular septal defects, carry an excellent prognosis. Others, such as transposition, are fatal. Most deaths from congenital heart disease occur within the first year of life, most of them within the first month. Transposition, ventricular septal defect, coartation, and the varieties of left heart hypoplasia are responsible for half the deaths. These facts of infant life explain how many children can develop normally despite having congenital heart disease, but others, usually with more complex and less common lesions, will not survive without surgical treatment, which must be undertaken early if it is to be successful.

The surgical treatment of congenital heart disease may be palliative or “corrective.” The technical problems of operating on infants led to the development of a number of lifesaving and relatively simple palliative procedures, such as the Blalock shunt (in which the subclavian artery is anastomosed to the pulmonary artery, thereby increasing the blood supply to the lungs and improving systemic arterial oxygenation); banding of the pulmonary artery to diminish pulmonary blood flow in infants with large left-to-right shunts; and atrial septostomy to increase systemic and pulmonary venous mixing in transposition. “Corrective” procedures may either be simple and truly corrective, such as the ligation of a patent ductus arteriosus, or may be corrective in the sense that they restore the circulation towards normal without correcting the anatomical fault, as in the Mustard operation for transposition, in which an atrial baffle is constructed to redirect the venous blood into the appropriate ventricle and arterial system.

How good are the results of surgery in infancy? A recent paper4 from the Hospital for Sick Children, Great Ormond Street, London, has looked at the survivors of cardiac surgery on 599 infants between 1955 and 1976. The outcome was determined by the risk of the operative procedure and its efficacy. Primary closure of ventricular septal defect gave both a low initial mortality and a high late survival rate. Relief of pulmonary stenosis and aortic coartation and correction of total anomalous pulmonary venous drainage all carried a high initial mortality but gave a high late survival rate. Mustard’s operation and shunts for Fallot’s tetralogy resulted in a low initial mortality but low late survival rate. Pulmonary artery banding for ventricular septal defect or transposition, shunts for pulmonary atresia with ventricular septal defect, and atrial septostomy for transposition all resulted in low initial and low late survival rates.

This study reflects the increasing emphasis and success of cardiac surgery in infancy (320 open heart operations were performed in Britain in children aged under 1 year in 1978), and provides evidence against which future developments can be compared. One conclusion drawn from the study is that two-stage procedures—palliation in infancy followed by correction later—give unsatisfactory results: the low overall survival from pulmonary artery banding should mean that this procedure has limited application in the future.

A trend towards primary correction of congenital heart disease is also described in a study from San Francisco of 509 infants operated on between 1975 and 1979.5 Conventional palliative procedures were necessary for only about 5% of infants with more complex lesions, and some 84% underwent corrective procedures. Though there are exceptions to this trend—for example, small babies with Fallot’s tetralogy and hypoplastic pulmonary arteries—infants requiring surgery for congenital heart disease should be offered corrective procedures whenever possible.

Hunting rare adverse drug reactions

Adverse reactions that occur in an incidence of about 1 in 100 are likely to be detected in the premarketing tests of a new drug. Nevertheless, less common adverse reactions and those that occur in patients not included in premarketing studies—pregnant women, for instance—often cannot be detected before marketing. The public, doctors, the drug industry, and the media all remember painfully the problems encountered with thalidomide and pradcol, and there is strong pressure for adverse reactions to be detected as quickly and efficiently as possible. Hence various drug companies have tried systems of “monitored release,” where doctors are encouraged by the company to report adverse reactions of new drugs, but these have not been successful and sometimes have come dangerously close to being disguised promotion.

In the last few months three new schemes have been mooted. The Government’s scheme, Retrospective Assessment of Drug Safety (RADS), has been abandoned for economic reasons. The Royal College of General Practitioners’ scheme, where drug companies commission a study of a new drug, has been...
criticised because it may change prescribing habits. The latest one to appear is the Prescription Event Monitoring scheme, which has been devised and will be run by the Drug Surveillance Research Unit, an independent, non-governmental, non-regulatory body that is part of the faculty of medicine in Southampton. Its director is Dr W H N Inman, who when he worked with the Committee on Safety of Medicines helped to devise the yellow-card system.

Prescription Event Monitoring, for which money is already available, will work in three phases and will start as soon as possible. In the first phase copies of prescriptions for the new drug being studied and a control drug will be obtained from the Prescription Pricing Authority (PPA), which deals with some 300 million prescriptions a year. In the second phase several months later simple questionnaires will be sent to doctors who have prescribed the drugs and they will be asked to record any new events (that is, any new diagnosis, unexpected deterioration, accident, or new symptoms) that have happened to the patient since starting to take the drugs. No fee will be paid, and as no medical opinion will be wanted it is possible that a non-medical person could fill in the form. In the third phase all events associated with the drug being studied and with the control drug will be analysed; events that are linked with the drug will be investigated further.

The unit will decide for itself which drugs to study, and at first will be testing the scheme as much as the drugs chosen. These will be single-agent drugs that are prescribed medium to long term in sufficient quantities for about 10 000 patients to be collected in one year. Prescription habits will not be altered; collaboration will be voluntary; confidentiality is guaranteed (Dr Inman points out proudly that in 16 years of the yellow-card system with 30 000 doctors submitting 90 000 reports there was not one breach of confidentiality); and the scheme should not be expensive. Adverse reactions that occur with an incidence of about one in a 1000 should be detected, but, as Dr Inman emphasises, the yellow-card system must continue: using any different system to detect very rare adverse reactions would be prohibitively expensive.

Dr Inman thinks that this scheme would have been able to detect early the adverse reactions of practolol, but it must be remembered that the scheme’s advantages are as yet theoretical. Indeed, no serious adverse reactions have yet been detected by any of these schemes, and it will be an interesting day when that happens.

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**Regular Review**

**Psoriasis and its treatment**

**R H CHAMPION**

To the unthinking, psoriasis might seem to be a harmless enough condition of little but cosmetic importance and requiring only simple reassurance and advice that it is a fluctuating disease which cannot be cured and must therefore be lived with. All that is partly true; but the distressing symptoms and the huge numbers of patients regularly attending for treatment (costing $250 million per year in the United States) testify that such a negative attitude is misplaced. Large research interests and budgets ensure a continuous stream of publications, yearly providing more and more information but still no definitive answers. Two international conferences on psoriasis have been held at Stanford with another due later this year.

The cosmetic problem is indeed of great importance—and has been from time immemorial. Despite the emphasis in much undergraduate teaching that lack of itching is a simple way to distinguish psoriasis from eczema, psoriasis does frequently itch and causes other symptoms. Severe psoriasis may be a socially crippling, even life-threatening disorder.

This article will not attempt to review the well-known and varied clinical features of the disease but will discuss some of the new work on the complex aetiology and in particular the now numerous treatments for more severe cases.

**Aetiology**—Central to an understanding of psoriasis and its treatment is the too rapid turnover of cells in the epidermis, particularly in the lesions but to some extent also in the clinically normal skin of psoriatics. The approximation that epidermal turnover is normally about 25 days, reduced to two to five days in psoriasis, has had to be modified by the uncertainties about how much the increased turnover is due to frequent mitosis in the dividing basal cells and how much to recruitment of epidermal cells that would normally be resting rather than dividing.

But what is the cause of this rapid turnover? A genetic factor, with HLA associations, is undisputed. The underlying chemical changes have been eagerly sought and very many candidates have been found. So many of them, however, are the result of the rapid epidermal turnover and not its cause. Changes in cyclic adenosine monophosphate and cyclic guanosine monophosphate have claimed attention for many years; more recently there has been interest in polyamines such as putrescine and spermidine. Migration of polymorphs into the skin is a cardinal feature of psoriasis, and changes in chemotaxis are demonstrable, both due to substances in the epidermis which attract polymorphs and to changes in the leucocytes themselves, notably in basophils. This is one of several findings which takes psoriasis away from being a purely cutaneous disorder into the realms of a systemic disease. Immunological changes may also be shown, but again which of these underlie the pathogenesis and which are secondary remains uncertain. Of both theoretical and practical interest is the ability of such drugs