

# BRITISH MEDICAL JOURNAL

LONDON SATURDAY 25 NOVEMBER 1967

## Pointers

**Advancement of Learning:** Lord Platt voices some salutary home truths about clinical research and warns against trying to prove everything by contrived experiments (p. 439). Leader this page.

**Relieving Infertility:** Clomiphene therapy is more efficacious in patients with amenorrhoea of short duration who have normal-sized ovaries (p. 444). Similar findings reported in large series from Israel (p. 446). Leader at page 434.

**Porphyria in Sweden:** Variegata type in three families totally unrelated to families with sufferers from acute porphyria intermittens (p. 449).

**Peanuts and Bleeding:** Controlled study does not bear out clinical impression that haemophiliacs have fewer bleeding episodes on diet which includes peanut extracts (p. 453).

**Gastric Acid Secretion:** Pentagastrin may supersede histamine in testing for complete vagotomy as results are comparable and side-effects minimal (p. 456).

**Effects of Cold Storage:** Red cells and intra-erythrocytic enzymes appear to survive five years at minus 196° C. satisfactorily (p. 458).

**Haemorrhagic Enterocolitis:** Association with heart failure, rather than with disease of splanchnic vessels, is postulated, and condition may be precipitated in certain climatic conditions by proliferation of normally harmless organisms in the bowel (p. 460).

**Case Reports:** Prevention of traumatic Bell's palsy (p. 464). Sarcoid myopathy improved with corticosteroids (p. 465). Transfusion malaria (p. 466).

**Postgastrectomy Syndrome:** Concluding the review of complications (p. 467).

**Clinicopathological Conference:** Cushing's syndrome with misleading urinary steroids (p. 472).

**Employing the Computer:** Inpatient statistics more accurately derived by taking the person rather than the hospital discharge as the unit (p. 476).

**Television Medicine:** Role of television in medical education discussed at B.M.A. lecture (p. 479).

**Hospital Administration:** Functions of hospital boards and their composition questioned in first letter (p. 482).

**Christmas Cards:** Christmas cards purchasable from B.M.A. House: profits to medical charities (p. 490).

**Public Health Medical Officers:** Firm offer received in response to salary claim (*Supplement*, p. 58).

## Cui Bono?

William Harvey was by contemporary accounts a brilliant scientist but an indifferent medical practitioner. The antithesis is not altogether unexpected, because the cool, objective approach to ideas and hypotheses—the scientific method—is not always compatible with the emotional involvement of caring for sick people. Until recently a doctor could choose between laboratory and clinical practice, but with increasing technological advance and emphasis on man as the most suitable experimental model in which to study the effects of disease the division between scientist and practitioner has become blurred. The medical profession is thus faced with a new dilemma—the need to preserve human dignity while ensuring that medical advance is not retarded. Its manifestations have not gone unnoticed. Hospitals have been attacked for alleged indignities to patients used for teaching purposes, and research institutions have been accused in a celebrated *exposé* of carrying out questionable experiments on human patients. Doctors would be less than human if they did not attempt to minimize these criticisms as rare exceptions to the general rule of high ethical standards. But when a former professor of medicine and member of the medical establishment voices similar doubts about the path along which academic medicine is travelling our attitudes towards the role of scientific research and teaching must be re-examined.

Lord Platt, in his Harveian oration, which we print at p. 439, accepts that the application of the scientific method has brought much benefit to the investigation of bodily function and of disease. But he points out that academic clinical departments have hardly been responsible for any of the revolutionary advances in therapy in the last 40 years. The sort of clinical research which they teach may indeed be detrimental to the advancement of treatment and prevention of disease. In general they are concerned increasingly with the chronic and rare diseases for which treatment is not yet available, and the research physician becomes a physiologist with a passion for measurement. Given ever more sophisticated apparatus it is necessary to find something to measure, and research becomes more and more dictated by the tools available, with the result that time, energy, and money are too often squandered on "the trivial, the irrelevant, and the obvious."

The need for thought, observation, ideas, and hypotheses—the hard work of science—recedes, and the clinical scientist is relieved of the even harder task of practising medicine. Moreover, we are apt to forget that clinical research is applied research, and in carrying out experiments on human beings we should first pause to ask whether the research is likely to be wholly beneficial or actively detrimental. *Cui bono?* Do academic clinical departments absorb too many of our brightest young graduates who would be better employed in solving the pressing problems that confront humanity? Is the yield in ideas and results sufficient to justify

their existence, or do they merely provide, as Professor Martin Roth has put it, "occupational therapy for university staff"?

The pursuit of research has, of course, its own merit in creating an atmosphere of intellectual inquiry, and the able physician will be constantly stimulated by the problems posed by the individual patient. But his research must be relevant and it must be directed with the needs of the patient in mind. The beneficial collaboration between physician and surgeon in the accurate investigation and treatment of cardiac disease is a case in point, and advances in other fields are to be expected with the increasing partnership between doctors and technologists. But Platt's chief plea is to break the bonds imposed by measurement (which implies that man is merely a machine) and to repair what he believes to be the greatest failure of clinical science—the almost complete neglect of psychological factors in disease.

From earliest times man has built up elaborate defences against the analysis of his subconscious mind, and this is apparent in the medical schools of today. Patients are interrogated and examined in open outpatients and wards in the presence of numerous students, or are presented as "cases" at grand rounds. Clinical research is directed almost entirely towards organic disease, and until recently the mentally ill, together with psychiatrists, were conveniently segregated in separate institutions. And there are the additional defences that psychological medicine cannot be taught objectively and that the time is not ripe for serious

research. Yet no one denies the importance of such factors as heredity, emotional development, social, environmental and cultural influences, chemical changes, and organic cerebral disease in the causation of psychological illness. Each of these can be studied by modern techniques, and even the psychiatric interview is amenable to analysis by computer. Measurement and controlled experiment may not be possible, but "the unbiased collection and verification of observations"—the central feature of the scientific method—can still be satisfied. Human behaviour is surely a subject worthy of the clinical scientist.

Platt does not expect everyone to accept his views on the shortcomings of academic medicine nor his attempt at a solution. Nevertheless, he is really only reiterating what has been said before in other contexts—that in our effort to teach medicine as a scientific discipline we are in danger of losing those very qualities of understanding, compassion, and a carefully practised technique which are the essence of the good doctor. Science is in danger of becoming the master rather than a servant to be dismissed on the many occasions when the patient is better without its services. Man is presented to medical students today as a corpse or as a machine, and it is natural that their approach to illness should be largely mechanistic. A change in emphasis towards the scientific study of psychological factors in health and disease might well be the bridge to close the gap between the differing qualities of mind that often seem to separate the clinical scientist from the practising physician.

## Clomiphene for Ovulation

The two articles on the artificial induction of ovulation in the *B.M.J.* this week come at a time when treatment with clomiphene citrate is passing from the research to the clinical stage. Preparations of human pituitary gonadotrophin are at present available for very few patients and under restricted circumstances. They are more dangerous than clomiphene, and their safe use necessitates elaborate facilities for hormone assay. Few would dispute that in the foreseeable future treatment with gonadotrophin preparations should be restricted to a few highly specialized units. Clomiphene, on the other hand, is available on prescription, and its untoward side-effects are slight.<sup>1</sup> Thus it is appropriate to consider the indications for prescribing the drug.

The first reports on treatment with clomiphene appeared nearly seven years ago,<sup>2</sup> and there is now general agreement on the indications for its use, its dosage, its side-effects, and the changes in ovarian hormone production which follow.<sup>3-5</sup> The means by which its effects are brought about are not clear, so that some caution in prescribing it is wise. It is suitable only for the treatment of infertility associated with anovulation. In disorders of menstruation such as amenorrhoea it seldom brings any prolonged amelioration of the disorder.

In a woman having periods of amenorrhoea for more than three months it may be presumed that ovulation is sufficiently rare to be regarded as absent for clinical purposes. Among the questions that need to be determined before treatment for infertility is begun are whether she has a pituitary capable of producing gonadotrophins, ovaries capable of ovulating, and a uterus able to sustain a pregnancy. Clinical common

sense can do much to clarify the diagnosis before elaborate laboratory investigations need to be undertaken. A considerable proportion of patients with primary amenorrhoea have genetic defects such as Turner's syndrome or testicular feminization, or anatomical defects such as congenital absence of the uterus. None of them can be expected to respond to clomiphene. Primary amenorrhoea should therefore be investigated thoroughly before clomiphene therapy is undertaken. Secondary amenorrhoea poses more difficult questions. Some women have signs of low production of ovarian hormone, such as underdeveloped breasts, scanty pubic hair, and a flat vulva. Often this is due to deficient secretion of gonadotrophin by the pituitary. Treatment in this group is apt to be unsuccessful, as Dr. E. Rabau and colleagues show in their paper on page 446 this week. But enough of such women have a pituitary capable of response to make treatment worth trying, particularly if the results of laboratory tests are favourable. If the secondary sex characters are fully developed the outlook is more hopeful, particularly if ovarian enlargement can be detected or some virilization is evident.<sup>6</sup>

Infertility associated with secondary amenorrhoea can often be successfully treated with clomiphene. In carefully selected patients the success rate approaches 50%, but this can be achieved only after exacting preliminary laboratory investigation. Probably the most useful single test in selecting those amenorrhoeic patients who are suitable for clomiphene is an

<sup>1</sup> Lamb, E. J., and Guderian, A. M., *Obstet. and Gynec.*, 1966, 28, 505.

<sup>2</sup> Greenblatt, R. B., Barfield, W. E., Jungck, E. C., and Ray, A. W., *J. Amer. med. Ass.*, 1961, 178, 101.

<sup>3</sup> Bell, E. T., Loraine, J. A., Harkness, R. A., and Foss, G. L., *J. Obstet. Gynaec. Brit. Cwlth.*, 1966, 73, 766.

<sup>4</sup> Whitelaw, M. J., *Fertil. and Steril.*, 1966, 17, 584.

<sup>5</sup> *Brit. med. J.*, 1966, 1, 1436.

<sup>6</sup> Kistner, R. W., *Obstet. gynec. Surv.*, 1965, 20, 873.