

RES MEDICA

Journal of the Royal Medical Society



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EDITORIAL

There are only two qualities in the world: efficiency and inefficiency — or so Shaw's literary hyperbole would have us believe. Perhaps romanticists still wistfully yearn for the days of the Artist-doctor, purveyor of the gifts and skills of healing, days when the theory of "God's will" could be invoked to explain away failures. Now we have the "change agents", the technologists, the computer men: protagonists of the efficiency creed. They herald the coming of automatic systems and computer control; the apotheosis of the Machine.

Most doctors welcome change that for them means less of the drudgery of medicine and for patients faster, earlier and more accurate diagnosis. All realize, perhaps, that automation and computerization can do these things. Their limited application so far (as compared to potential uses) has by and large confirmed this. What sort of information do we have, however, on the social and structural changes that widespread mechanisation will cause within the hospital service. Only a few, and on the whole inadequate, attempts to answer this question have been made in industry but they can maybe provide some clues to help avoid dangers and disadvantages.

Many people in medicine have a working knowledge of computer science. These are mainly in research whilst others are concerned with the automation of medical techniques — autoanalysis, automatic E.C.G. reading, etc. The systems analysts, programmers and computer operators must inevitably come from industry. Firms are already paying very high salaries to ensure that they get enough computer staff, bearing in mind that the National Computer Centre expects 5000 computers to be in use in 1970, doubling to 10,000 in 1975. If enough computer people are to be attracted to medicine, they must be offered high salaries. Job interest is also important for it is shown

in industry that these specialists take advantage of the ease of mobility between different fields to widen their experience.

If industrial line-managers can roughly be compared with hospital administrators, as responsible for the day to day running of the hospital services, experience has shown that two situations may arise: the administrators may resist any change likely to endanger their work satisfaction or position, by making their experience and administrative knowledge redundant, or they may fail to exert proper control over the period of change. This last case would not be so great a danger if computer technologists were aware of the social turmoil that their innovations can bring within a structured system such as the hospital service.

Few in industry have shown such awareness.

Those who see only in terms of the efficient handling of information could not be expected to understand the doctor's reluctance to alter his complete work pattern of history-taking, writing-up of physical examination, laboratory test requests etc. Results of biochemical screening at Queen Elizabeth Hospital, Birmingham, that "in up to 8% of patients abnormal results for tests that would not usually have been requested led to different or additional diagnoses," may, for example, point to the end of selective testing. Changes necessary for electronic data processing will affect people's roles, satisfaction, and employment — consultants, housemen, nurses, clerical staff — in ways as yet unknown.

The case for a new type of medical scientist, the medical computer technologist, trained in both computer science and the special problems of medicine would seem to be strong. Who is to train them is less obvious. Let us hope, however, that the pitfall will be avoided, as it has not always been in the past, of attempting to train every medical student to be fully proficient in this relatively new science.

ASSESSMENT OF THE PSYCHOLOGICAL STATE

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INTRODUCTION

A psychiatric examination consists of four parts:

1. The psychiatric history
2. Examination of the Mental State
3. Evaluation of the personality
4. The diagnostic formulation

The clinical method for history-taking is the interview. The clinician sets out to obtain a comprehensive history in his *first* interview with the patient. A series of interviews may be necessary before he acquires all the information he needs to understand both how the psychiatric illness came about and why it took the course it did. In his first interview the goal of the clinician is to get at least a preliminary overall *history*; in doing so, he will also detect the prominent signs of illness comprising the *mental state*; moreover, he will have the information enabling him to reach a tentative assessment of the patient's *personality*; and he will be able to arrive at a working *diagnosis*. A diagnosis is an hypothesis about the illness; and about the main aetiological factors operating. It is derived by the clinician from an informed synthesis of the facts elicited. Because diagnosis antecedes therapy, and the clinician will wish to begin the initial treatment after his first interview, he aims to reach his preliminary diagnosis where possible. A first interview takes an ex-

perienced practitioner half-an-hour. Subsequent interviews may be briefer, and can be arranged as required to get further information and to extend the psychiatric examination as necessary.

A theoretical knowledge of interviewing procedure is essential, but is not sufficient. Psychiatric interviewing is a practical skill which can be learnt only through actual experience with real patients. Furthermore, regular supervision is needed if technical errors are to be identified and progressively corrected. An invaluable aid is provided by the use of video-tape; the trainee interviewer has his psychiatric examination of the patient televised, and when re-played subsequently he and his instructor have the actual clinical data before them for review.

Another important training method is obtained from watching experienced interviewers at work.

When conducting a psychiatric examination the clinician inevitably makes use of his own personality: he relies on his own capacity for communication. He seeks to gain an objective view of the extent to which he succeeds in expressing himself as he intends. His instructor and such aids as tape recording and television show him if he is accurate in his impression about the way he affects people.

To conduct a psychiatric examination two chairs are needed, placed more or less at right

angles. The clinician and his patient are then free to look at one another when they wish, without imposing any requirement for fixed stares, as would be suggested if the two chairs were facing. (A directorial station behind the office desk is of course altogether inappropriate.) The room should be quiet and interruptions minimal.

THE CLINICIAN'S APPROACH

A question-and-answer technique which may serve, for example, in a general medical examination is not desired. The psychiatric history should flow smoothly from one topic to a related one, in a sequence meaningful to the patient. The clinician acts as a catalyst. His primary function is to assist the patient to generate a clinically useful account of personal experience. The clinician writes steadily, to obtain an accurate, factual and full record of the interaction. Any questions he asks are noted as well, so that the verbal stimuli offered to the patient are also recorded. A good history is neither nebulous nor abstract. When the patient mentions somebody, that person should be named. e.g. "I was going with a man friend at that time". The clinician asks, "What was his first name?" This is then recorded; if this person again enters the patient's account, in the present or a later examination, he can be rapidly identified and related to the earlier information.

The competent clinician does not take the patient firmly in a dull routine through each step in the sequence of historical areas. He leaves the patient relatively free to reflect, to overcome hesitations, to go back and amplify, and to alter earlier statements as confidence is established. The clinician gently guides the patient, advises him when inconsequential detail threatens to crowd out important events and indicates quite frankly when he thinks the patient is following a blind alley. The clinician's task is to gain possession of the necessary facts in each of the crucial areas.

This apparent discussiveness is easier to permit the more experienced the clinician becomes. It is appropriate for him to indicate quite plainly to evasive patients that he must have the necessary information. He does not need to encourage the patient with phrases of approval or expressions of sympathy. It goes without saying that he never conveys moral censure or disapproval, although unwittingly clinicians sometimes do. He has no call to become autobiographical himself, and tell the

patient about his own trying experiences, child rearing practices, or opinions and attitudes.

In the course of the examination the matters about which people are sensitive can be dealt with sensibly and directly as technical data. Behaviours usually regarded as wrong or unusual can be broached without equivocation, no suggestion of moral evaluation entering. e.g. "Have you tried to end your life?" Such an enquiry may be welcomed by a depressed patient as a much needed opportunity to disclose painful impulses towards suicide; in the process, speaking about the suicidal intention may effectively serve to deter the patient from making a suicide attempt. Sexual experience is discussed in terms which the patient is sure to understand, checking where necessary the patient's term for a part of the body or a sexual activity. The contemporary patient will almost certainly know what "masturbation" means, but not inevitably; often the clinician will perceive that more explicit explanations or simpler words are needed to obtain the information he seeks.

While the patient is not constrained to give a formal, chronological and precisely sequential account, the clinician examining the psychiatric patient has a technical task to carry out, a schedule of operations to be performed. This he aims to carry out as methodically as he would examine any other clinical sector, the neurological system, for example. If he has not examined the fundus he will be aware of this omission, and if he neglects to test the plantar responses the trained clinician likewise knows that his examination is incomplete. Similarly with the psychiatric assessment. If the clinician has not found out about the patient's father, his understanding of the patient's personality is the poorer; if the patient's job record has been neglected, the history is also incomplete. The psychiatric examination is a technical skill, within the competence of all clinicians, and is not in any way a nebulous or impressionistic procedure. One can know about a person's mind with more or less certainty according to one's ability to carry out the relevant clinical procedures.

THE PSYCHIATRIC HISTORY

1. *The Description of the Patient*: The patient's name, age, occupation, marital status, sometimes his religious affiliation and — finally — the method of his referral are facts the clinician will want to record. Eliciting such relatively neutral information may be a

useful way of starting the history-taking; the patient is able as he replies to settle in his chair as comfortably as possible, and to assess the situation he finds himself in. The patient also needs an opportunity to size up the clinician as the examination begins.

2. *The Reasons for the Consultation*: The clinician then ascertains why the patient has come, and what the patient requires of him. The patient's reason for the interview may on occasion be straightforward and at times bizarre. The mythical patient who requests a certificate of sanity wants the clinician to study his mind and then pronounce on its stability. The police may send a patient and be equally explicit — e.g. as occurs when a psychiatrist is asked to examine a woman who has harmed her children physically and has then attempted to kill herself. It may be a relative who brings the patient, as occurs when a mother tells the clinician she has been worried recently about her small son, and describes mannerisms which alarm her. The presenting reason for the referral of course may be merely the introductory gambit, to be extended when the clinician has gained the patient's confidence: a man complaining initially of indigestion may later confess that he has actually come on account of impotence.

3. *The Present Illness*: Having established why the patient has requested to be seen, the clinician then obtains a detailed account of the patient's symptoms. Each complaint is to be recorded scrupulously, in terms close to the patient's own. If the patient mentions a pain in the heart, that is to be recorded as his symptom; it should not be translated into clinicalese, such as "praecordial pain". If the clinician rephrases the patient's actual self-description into clinical jargon he sacrifices veracity and impairs his own grasp of the patient's experience of illness. An adequate description of the illness has been reached when the clinician has traced chronologically each manifestation of the disorder.

4. *The Family History* consists of a verbal sketch by the patient of both his parents and of all his brothers and sisters. "You mentioned your father — what sort of person is he?" The question causes some patients to pause in perplexity, until after hesitation they describe the father as one of the best, or portray him as strict but perfectly fair, or as a mean man

who terrorized the family when drunk at weekends. The clinician can usually gather whether the father was perceived positively, in a neutral light, or negatively. The importance of this information is that it conveys the role a parent took in a patient's personality formation: a parent is incorporated during growing-up, and constitutes an inner psychological representation forming an aspect of the patient's self.

The mother often is characterized with less trouble. Patients fairly readily say whether she was kind and gentle, or two-faced, or a virago who started her persecution before the patient's birth by striving to abort herself. Again, in describing his mother the patient is disclosing a significant relationship which contributed to his character structure.

His position in the sibship may be important. If he was an only child, alone with his mother until five years of age when his father was demobilized from the army, then to have a baby sister arrive on the scene, the patient may proceed to describe a rivalry which agitated his childhood and coloured his subsequent adult social relationships with envy and competitiveness. The size of the sibship is obviously relevant. The clinician's perception of the parental family is filled out when the patient is asked to comment on the general atmosphere which existed in the home.

5. *The personal history* can follow naturally from the account of the parental family. The clinician finds out if the patient thought he was a wanted child, avoiding the pitfalls of asking about breast-feeding and toilet-training when the patient is both in the dark about these early circumstances and also mystified regarding their relevance to his present distress. The clinician will naturally want to know whether the patient acquired control of his sphincters at the usual age, whether he bit his nails, and stopped using temper tantrums as a means of attempted mastery of the household — but these crucial facts are seldom elicited by blunt questions. To grasp in addition whether the patient separated from his mother without difficulty and managed to start his school attendance without anxiety, whether he had an early conduct disorder like stealing, or an early neurotic illness such as a childhood obsessional state, calls for an ability on the part of the clinician to empathize with the patient, and to achieve this so accurately that the patient realizes the level of perceptiveness obtaining.

One then discovers from the patient about the onset of puberty, the development of his sexual awareness and information, and the form of his erotic imagery. He conveys whether he had a chum, a first close friendship. His progress at school is studied. The course of his adolescence discloses whether he was able to separate off gradually as an independent individual from his parents, and whether this social growth — if it occurred appropriately — was relatively untroubled, or took the form of a disruptive rebellion. Identity-formation proceeds rapidly from the middle teens, and if arrested the youngster does not arrive at an understanding of his personal potentiality, nor a decision about the work he is fit for, nor a definition of the values he wants to advance. He may be greatly troubled about sexual aspects of this stage of maturation, with prolonged and recurrent fears about homosexuality or masculine inferiority. The girl may reject aspects of femininity. In the later teens the capacity for close relation with another person begins to develop if personal maturation is sufficiently orderly, the individual finding greater purpose when in intimate association with somebody else.

The clinician then inquires about courtship, marriage and the patient's own children. He completes the account of the personal history by following the jobs the patient has had during the course of his working life.

6. *Previous Illnesses* are then studied. Physical illnesses are described more readily by the patient. One is not so closely associated with one's body as with one's psychological state, therefore past somatic disorders and hospitalization can be rapidly surveyed. (They are often not accurately remembered). Physical disorders, quite apart from their somatic expression, can of course have emotional con-

sequences, especially if they occurred early in life or left a handicap which interfered with the patient's social participation.

Previous psychological disorders are sometimes more difficult to track down. They are often revealed if careful questioning is directed to the major stressful epochs in the biography; the start of schooling, puberty, later adolescence, courtship, marriage, and the onset of middle life when youthful perspectives have outrun their applicability. The past psychiatric disorders and the way they were managed are recorded in order of occurrence.

7. The previous personality is especially important when the patient has a serious illness, a psychosis. The onset of psychosis may constitute a break with the patient's former self. Suddenly, out of the blue, the delusion took form; the cheerful, busy man altered to become anxiously preoccupied and troubled by convictions that he suffered from cancer.

The previous personality is important not only to define the time of onset of illness. It is also important because from his understanding of it the clinician can identify especial strengths — perhaps obscured by the symptoms of illness — which the patient will be able to call on when recuperating: values and habits of mind, degree of initiative, friendships and other social relationships, membership of groups, clubs and organizations, and special interests.

As the patient speaks the clinician writes. His transcript of the interview may not be orderly, but were he to cast his material in systematic form he would have obtained data in each of the important sectors of the patient's biography.

The second part of this article will appear in the next issue of Res Medica.

Trial by Fire

The Chiefs being met, a hurdle or a kind of wooden gridiron is fixed about an ell from the ground, sufficiently large and strong to receive the body of a man. The candidate places himself on this couch, lying on his back, putting into his mouth a hollow cane which is to serve him in breathing; then they cover him entirely and closely with plantain leaves, observing to pierce those that are over his head so that his cane may pass through them. A fire is then kindled under him, so managed that the flame shall not reach the grate but may give enough heat to broil their ignorant victim. If he endure the whole patiently and unmoved, he is saluted as one of their Caliques.

—from a Dissertation read before the Society in 1785.

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CARDIOGENIC SHOCK

Andrew G. Leitch, B.Sc.

Based on the essay that won the Chest and Heart Association, Scottish Branch, Competition, 1968

DEFINITION AND PATHOGENESIS

INCIDENCE

Cardiogenic shock is shock occurring after myocardial infarction. It has been variously described as occurring in 6%, 8%, 10%, 12% and 20% of patients with myocardial infarction. Shock accompanies the onset of pain in few cases and most cases occur in the first twenty-four hours after infarction although they may occur several days after.

CLINICAL CRITERIA

The criteria for diagnosis of shock may vary with different authors (hence the anomalous 20% above) but, in general, it is agreed that shock is suggested clinically by the following features: cold, clammy extremities, pallor and cyanosis, rapid, thready pulse, anuria or oliguria, anxiety, restlessness or apathy, and prolonged hypotension. The only objective assessment is of blood pressure and this alone does not define shock. Considerable variation may therefore be expected in diagnosis.

In view of the difficulties in defining the criteria for diagnosis of shock, the individual criteria and the interpretations placed upon them warrant further discussion.

The pallor, coldness, clamminess and oliguria are taken to indicate an increase in activity of the sympathetic nervous system leading to sweating and a reduction in blood flow to the skin and the kidney respectively. Similarly, signs of anxiety, restlessness or apathy are taken to indicate a reduction in cerebral blood flow or cerebral hypoxia. Anxiety or restlessness might be expected in patients who are

in pain and apprehensive of their mortal future. Adequate methods for the measurement of arm and cerebral blood flow exist but the measurements do not yet appear to have been made in cardiogenic shock. The tachycardia also reflects the increased activity of the sympatho-adrenal system, the increased rate being due probably to an increase in sympathetic activity to the heart and to the high level of blood catecholamines in shock. The increase in urinary noradrenaline and adrenaline which has been demonstrated after myocardial infarction appears to be related to the clinical severity of the condition. The thready pulse may be taken as an indication of the reduction in stroke volume.

Cyanosis represents an increase in the amount of reduced haemoglobin visible in the sub-papillary venous plexuses and is influenced by the haemoglobin content of the blood. So-called central cyanosis is said to represent an arterial oxygen saturation of less than 90-95% but trained clinical observers are unanimous in their observation only when the oxygen saturation of blood is as low as 75%. The misleading effects of fluorescent lighting are important. Such cyanosis may be due to inadequate pulmonary oxygenation, increased deoxygenation of arterial blood or veno-arterial shunts. All three may be important in cardiogenic shock.

Hypotension is difficult to define in view of the wide range of normal blood pressures in the general population. Indirect measurement of brachial systolic blood pressure with a sphygmomanometer compares favourably with direct intra-arterial recording (at least at normal levels of blood pressure) within certain limitations, e.g., cuff width and length. Whether

the agreement is of the same order in hypotension is not recorded. A systolic blood pressure of less than 100 mm. Hg. or less than 90 mm. Hg. has been taken as indicating shock while others feel that a systolic blood pressure of less than 80 mm. Hg. is a necessary criterion of shock. Others again adhere to 80 mm. Hg. with an "allowance" of 90 or 100 mm. Hg. for previously hypertensive patients. Mutual agreement about the value of blood pressure taken to indicate shock is desirable if therapeutic trials are to be comparable. Hypotension in shock can be taken to indicate that the heart is unable to maintain blood pressure by an adequate output in a situation where the total peripheral resistance is normal or raised. It must be distinguished from the initial hypotension often seen in myocardial infarction which is relieved by analgesics or sedatives and is attributed to pain. Vaso-vagal attacks and excessive doses of morphine, pethidine or sedatives may also be misleading causes of hypotension.

HAEMODYNAMIC CRITERIA

The clinical definition of shock is not entirely satisfactory and since the early classical studies of Coumand attempts have been made to find a haemodynamic expression of shock. Right heart catheterisation is essential in haemodynamic studies if one is to measure cardiac output, central venous pressure and pulmonary artery pressure. It is used for withdrawing samples of "mixed" venous blood for direct Fick or injecting dye for dye diffusion estimations of cardiac output. Cardiac output is traditionally expressed as cardiac index (L/min./m²) in an attempt to eliminate variations in cardiac output related to body size. The total peripheral resistance can be calculated from the relation

$$\text{Cardiac Index} = \frac{\text{Mean Aortic Pr.} - \text{Central Venous Pr.}}{\text{Total Peripheral Resistance}}$$

In animals the haemodynamic consequences of shock have also been studied after coronary embolisation with spores or microspheres, coronary ligation or occlusion.

The outstanding feature of haemodynamic studies has been the uniform demonstration of a fall in cardiac index in cardiogenic shock. It is important to remember that this is an acute fall in cardiac index. In general, the lower the cardiac index, the more severely ill the patient is, although specific instances have

recently been described where a very low cardiac index has been present in patients without shock. Hypotension itself is not sufficient to define shock since sympathectomised patients may have adequate tissue perfusion with a slow pulse and a low blood pressure. The effect of fever on the total peripheral resistance may cause a similar phenomenon. Although reduction of cardiac index may be present in non-shocked patients, severe reduction of stroke volume seems to be more "specific" to cardiogenic shock and coupled with the demonstration of an increased cardiopulmonary blood volume indicates failure of the left ventricle as a pump.

Total peripheral resistance in shock has been described as being increased, normal or decreased. Gunnar divides his cases into two groups: one with an increased peripheral resistance which is considered to represent the normal reflex response to a fall in cardiac index and one with a decreased peripheral resistance which is believed to be the result of some vascular reflex from the damaged heart. Patients with a low total peripheral resistance responded to noradrenaline by increasing peripheral resistance which is taken to indicate that the vasoconstrictor mechanism is still functional although reflex vasoconstriction is inhibited by a reflex from the damaged heart. However, in cats the vascular tree can be responsive to noradrenaline in the "shock state" long after it has ceased to respond to sympathetic nerve stimulation.

REFLEX SHOCK?

The heart has many receptors. Stimulation of some of them may lead to hypotension as, for example, in the left ventricular Bezold-Jarisch reflex with veratrine. This may be the mechanism of the bradycardia and hypotension seen in "shocked" dogs which is abolished by vagotomy. Possible receptors for such a reflex have been described. Agress has described another possible reflex in dogs mediated by the dorsal sympathetic roots, but his attempts to identify and block such a reflex in man have not been continued and were presumably unsuccessful. The higher frequency of shock in patients with branch rather than main stem occlusions in the coronary arteries has been given as a possible indication of reflex mechanisms in human cardiogenic shock. However, the significance of a reflex from the injured myocardium remains un-

determined. Dogs with denervated hearts may still be shocked after infarction. Presumably people with transplanted hearts will still be liable to develop shock after myocardial infarction. This and the slow onset of shock do not favour a reflex mechanism.

An acute fall in cardiac index is the basic lesion in cardiogenic shock. Shock is not associated with any particular size or site of infarction. In one study shocked patients had a higher incidence of previous infarction than non-shocked patients whereas the post-mortem hearts examined by Cronin indicated that shock cases had a lower incidence of previous infarction. Cronin suggests that a previous infarct might protect the heart through the development of significant inter-coronary anastomoses. The impairment of cardiac function has been briefly described by MacKenzie et al. In their study measurements of myocardial performance indicated "gross impairment" in cardiogenic shock.

LUNG FUNCTION

MacKenzie's fuller and more important studies in the same paper demonstrated that in shocked patients the PaO_2 was very low (mean 47 mm. Hg.) compared with non-shocked patients (mean 67 mm. Hg.) and that whereas PaO_2 rose to expected levels (mean 391 mm. Hg.) on administration of 87% oxygen to non-shocked patients, in shocked patients with oxygen the PaO_2 still remained remarkably low (mean 119 mm. Hg.). This has since been described by others. A markedly increased alveolar-arterial oxygen tension gradient was also described and has been confirmed by others in cardiogenic shock and in acute myocardial infarction without shock. A significantly increased gradient is present even six to twelve months after infarction. The hypoxaemia is not due to inadequate ventilation since the PaCO_2 is normal or even decreased in these cases. The hypoxaemia is due partly to an increased physiological dead space; partly to venous admixture and also in some patients to the presence of a true shunt. The disturbed ventilation-perfusion ratios are probably due, in part, to the fall in cardiac index observed in shock leading to perfusion changes, and, in part, to the increased pulmonary venous pressure accompanying pump failure leading to pulmonary congestion. The rise in left ventricular end-diastolic pressure which is implied in the genesis of pulmonary

congestion and oedema in cardiogenic shock has recently been demonstrated. Detailed investigation of the ventilation-perfusion ratio changes in different parts of the lung should be possible with the techniques which have been described, but investigations of this nature have yet to be carried out in cardiogenic shock. They should demonstrate more clearly the nature of the ventilation perfusion imbalance.

The presence of pulmonary congestion in cardiogenic shock probably depends partly on the enthusiasm with which it is sought and partly on the severity of the cases described. For example, Cronin found crepitations absent in most of his 140 cases while Nielson describes frank pulmonary oedema necessitating treatment with digitalis in 30% of his 34 cases. McNicol basing his diagnosis of congestion on the presence of crepitations or rhonchi in the absence of a history of bronchitis found pulmonary congestion in 13 out of 15 shocked patients. Radiological criteria are also valuable. McNicol has demonstrated unequivocally the importance of congestion in the genesis of hypoxaemia after acute myocardial infarction. Two of his shock cases had no clinical evidence of congestion and it is suggested that in these cases the hypoxaemia is due solely to a gross disturbance of perfusion. Indeed, an increased physiological dead space was very evident in these patients. It is in such cases particularly that a regional analysis of ventilation-perfusion ratios would prove interesting.

The true shunt which has been described is thought unlikely to be due to arterio-venous anastomoses "since it disappeared on recovery in two cases". The possibility of arterio-venous anastomoses as a factor in shunt at high altitude has been described in association with an elevated pulmonary arterial pressure but no such relationship between presence of shunt and pulmonary arterial pressure exists after myocardial infarction. It has been suggested that the shunt may be due to "collapse, oedema or blockage of alveoli in some areas of the lung where there is continued circulation." This is more likely.

ACID-BASE BALANCE

The hypoxaemia of cardiogenic shock is associated with a significant acidosis due principally to a rise in the concentration of blood lactate. Kirby and McNicol note that the acidosis found in acute myocardial infarction

is most severe in patients with hypotension (<90 mm. Hg.) plus left ventricular failure (? shocked). The demonstrated rise in lactate/pyruvate ratio is indicative of tissue hypoxia and reflects an increase in the oxidation of NADH_2 by the conversion of pyruvate to lactate in the cycle of anaerobic glycolysis. Anaerobic glycolysis is more active in hypoxia because less molecular oxygen is available for the operation of the cytochrome system and aerobic glycolysis.

The increased mortality found with severe acidosis is probably causally related and represents an association between two accompaniments of tissue hypoxia. In man correction of the acidosis leads to an increase in blood pressure in non-shocked patients but this may have been related to the procedure and to the volume infused. The effect of correction in shocked patients is not documented. Other reports associate acidosis with arrhythmias in man, decreased myocardial contractility in dogs, and vasopressor antagonism in dogs. In dogs the combination of acidosis and hypoxaemia is particularly lethal: the survival rate is increased by correction of both.

CORONARY AND OTHER REGIONAL BLOOD FLOWS

The following functional points are also worthy of note. The hypotension of shock will lead to a significant reduction in coronary blood flow since in the human case of infarction (but not the dog and hence partly the dubious relevancy of experimental cardiogenic shock in dogs) the coronary vessels will almost certainly be atherosclerotic, arteriosclerotic or even calcified. This will limit or even eliminate any faculty for vasodilatation in response to hormonal, nervous, metabolic or any other demands. In this situation the coronary flow becomes to a greater or lesser extent dependent on aortic diastolic pressure since most coronary flow occurs during diastole. The existence of coronary autoregulation is still debated but where demonstrated it probably ceases, like cerebral autoregulation, at pressures of 50-80 mm. Hg. The effect of degenerative arterial disease on coronary autoregulation is not known and it should be possible to study this in a suitable animal preparation with and without the complications of myocardial infarction since its effect can only be guessed in man. Arterial disease is found in a wide range of animals including snakes, lizards, tortoises and vultures. Disease can also be pro-

duced by altering the diet of rabbits, rats and pigs and this disease closely resembles that found in man. The effect of coronary artery disease on autoregulation of coronary blood flow would be most easily studied in the pig. (For similar reasons the pig would seem to be a more suitable animal than the dog for investigating the efficacy of different forms of therapy in cardiogenic shock). For the moment it is agreed empirically that a pressure of 50-80 mm. Hg. is usually adequate to maintain coronary and cerebral blood flow. Regional flow studies might be interesting here also. In view of the need for a minimum blood pressure difficulties arise in therapy (see later) since attempts to increase the aortic pressure by vasoconstriction to maintain coronary flow will increase the afterload of an already embarrassed heart.

The sympathetic vasoconstriction in shock leads to a reduction in renal blood flow, glomerular filtration rate and urine secretion. If this oliguria (or anuria) is maintained microscopic changes may be visible in the kidney structure. Similarly impairment of liver function has been demonstrated in acute myocardial infarction which is probably related to hepatic vasoconstriction. This may be a factor in the lactic acidemia.

MICROCIRCULATION

The changes observed in the peripheral circulation in shock have been investigated by many workers. Microscopic examination of the microcirculation in shocked animal preparations has shown great species variation in the behaviour of the microcirculation during shock and it is difficult from the observations which have been made to indicate any consistent microcirculatory defect in shock. However, disturbances of vasomotion and of the flow patterns in exchange vessels have been observed. The role of arterio-venous shunts in the microcirculation remains uncertain.

Coupled with disturbances of flow, pressure and exchange relationships in the microcirculation may be disturbances of the coagulation mechanism which have been observed in shocked patients by the proponents of a hypothetical mechanism for disseminated intravascular coagulation or sludging. This will lead to further disturbance of the exchange and nutritive functions of the microcirculation. If present in cardiogenic shock sludging should be visible in the bulbar conjunctiva.

Mellander using his technique for the indirect study of the microcirculation in cat skeletal muscle has noticed in shock a progressive decline in the precapillary resistance response to sympathetic nerve stimulation while the capacitance response remains. However, unphysiological doses of noradrenaline will retrieve the resistance response when sympathetic nerve stimulation fails. If shock is prolonged the capacitance response to sympathetic nerve stimulation is abolished and intravascular pooling may occur. At the same time disturbances of the relationship between pre- and post-capillary resistances and hence the Starling mechanism will lead to haemoconcentration. Mellander interpreted the refractoriness to sympathetic nerve stimulation as being due to the presence of tissue hypoxia and accumulated "metabolites". The nature of such metabolites remains uncertain but acidosis is probably a factor.

Cat skeletal muscle in haemorrhagic shock is not the human peripheral circulation in cardiogenic shock but comparisons are useful and apparently valid since recent publications allow the following tentative interpretation of peripheral circulatory failure in cardiogenic shock: after infarction cardiac function is severely impaired and although increased sympatho-adrenal activity may be adequate at first to maintain blood pressure it is later inadequate. If the vasoconstriction is severe or prolonged enough it leads to tissue hypoxia and acidosis. Hypoxaemia will exaggerate this phenomenon and total peripheral resistance may fall. Progressively the resistance vessels become refractory to sympathetic nervous stimuli while maintaining some sensitivity to noradrenaline. Ultimately this response also disappears along with the capacitance response. This may lead to acidosis, loss of capillary integrity, haemoconcentration, stagnation, disruption of lysosomes, coagulation of blood and tissue destruction with consequent loss of organ function and death. Prominent among the ultrastructural changes in shock is mitochondrial damage.

The role of the sympatho-adrenal system in this sequence of events is prominent enough to make one wonder what the effect of coronary embolisation or ligation might be in dogs or other animals which had either been sympathectomised or made tolerant of catecholamines. Would the same percentage of sympathectomised or catecholamine-tolerant dogs develop shock as compared with normal animals? If so, would the mortality be altered?

Would chemical sympathectomy show the same effect? If the effect was beneficial might it be applicable to human cases as a form of "preventive" treatment for cardiogenic shock? Do people who have been sympathectomised develop cardiogenic shock as often as the rest of the population? If so, do they also have an 80% mortality?

The sequence of events in shock is never seen in its undisturbed entirety since therapy is usually instituted early in the march of events and may modify the picture considerably. However, it obviously fails to alter the picture enough since the mortality remains at 80%. More optimistic figures for mortality are misleading and probably reflect the inclusion in the diagnosis of shock of patients with the brief initial hypotension often seen after myocardial infarction.

THERAPY

The following agents have been, should be or will be, used in the treatment of cardiogenic shock.

INITIAL THERAPY

The supine position in the absence of pulmonary oedema, morphine or pethidine in moderation (hypotensives and respiratory depressants) to relieve pain, bicarbonate for acidosis and standard therapy for arrhythmias may all be required initially.

OXYGEN

In cardiogenic shock, the tissue P_{O_2} is probably much lower than it should be, and PaO_2 is certainly low. $PaCO_2$ being essentially normal, the administration of 100% oxygen is preferred since the PaO_2 of some patients may be refractory to oxygen therapy.

Hyperbaric oxygen protects against death from arrhythmias in "cardiogenic shock" in dogs and pigs but Cameron has only noticed a "non-statistical suggestion of a reduction in arrhythmias" with such therapy in man.

VASOCONSTRICTORS

Pure vasoconstrictors such as angiotensin have no place in therapy since they increase blood pressure by increasing peripheral resistance at the expense of increasing cardiac overload and decreasing cardiac index.

$\alpha\beta$ drugs such as noradrenaline and metaraminol have been used in classical therapy for years. They:—

1. act in small doses to increase myocardial contractility and cardiac index, and in larger doses to vasoconstrict all regional circulations except the coronary and hence to increase cardiac work and decrease cardiac index.
2. may cause shock.
3. may lead to reversal of the Starling mechanism (which causes net movement of fluid into the circulation in shock) and thus cause haemoconcentration.
4. do not alter the mortality in shocked dogs from the control value in untreated dogs.
5. have not affected the mortality from cardiogenic shock in man which remains at 80%.

The value of these drugs is limited solely to the inotropic effect observed with small doses which is probably useful in a few cases.

α -BLOCKING DRUGS

α -blocking drugs such as phenoxybenzamine or chlorpromazine can be used to provide a low pressure/high flow system which is probably more useful in preventing tissue hypoxia than the high pressure/low flow system achieved with noradrenaline. The logic of α -blocking is that vasoconstriction will be reduced, resistance will fall, capacitance will rise and the reduction in pressure will mean less pressure work for, and a lower oxygen consumption by, the heart. The fall in resistance will lead to increased cardiac emptying and the increased capacitance may be useful in the treatment of pulmonary oedema.

Infusion of fluid—plasma, L.M.W.D., blood—is often combined successfully with this therapy but central venous pressure must be monitored to warn of impending pulmonary oedema. The following facts are known:—

1. Work on "shocked dogs" shows that phenoxybenzamine plus intravenous fluid leads to a very significant increased survival from cardiogenic shock as compared with control or noradrenaline treated animals.
2. In general, survival is improved when the pressure work of the heart is decreased and the volume work is increased—however, the use of intravenous fluids alone, as recommended by Nixon, is not a desirable procedure since the damaged heart

is unlikely, in most cases, to operate on the ascending portion of its starting curve in response to distension.

3. α -blocking drugs have been useful in the treatment of low output surgical shock.

LOW MOLECULAR WEIGHT DEXTRAN (L.M.W.D.)

L.M.W.D. decreases blood viscosity, increases circulating blood volume, activates fibrinolysis and is valuable in the treatment of disseminated intravascular coagulation or sludging. In shocked dogs it improves prospects of survival.

HYPOTHERMIA

Reduction of body temperature to 33°C reduces oxygen consumption to $\frac{2}{3}$ normal and therefore decreases the demand for oxygen in the tissues. The technique has been used successfully in septic but not in cardiogenic shock. It may be that the enhanced myocardial efficiency is not enough to compensate for the increased risk of arrhythmias.

DIGITALIS

Digitalis should be used in cardiogenic shock where the improved myocardial efficiency which results probably outweighs the increased risk of arrhythmias.

STEROIDS

Massive doses of glucocorticoids (30 mg./kg. prednisolone, 150 mg./kg. hydrocortisone) are in vogue for the treatment of low output surgical shock in man and experimental cardiogenic shock in dogs. Such large doses cause vasodilatation and may help to maintain the integrity of cell membranes and sub-cellular particles such as lysosomes. The use of such large doses in cardiogenic shock is not recorded; smaller doses are ineffective.

ASSISTED CIRCULATION

Most cases of cardiogenic shock are going to die in spite of the administration of oxygen, drugs, etc. Such cases could be helped by some form of assisted circulation. The following are the most likely to be developed.

1. *Counterpulsation*—blood is withdrawn from the femoral artery during systole and pumped back during diastole. The technique is successful in dogs and the minor

surgery required has allowed it to be tried in refractory cases of cardiogenic shock in man. Surgery can be avoided if the vascular tree of the lower limbs is used as the pump and subjected to appropriately phased pressure variations.

2. **Implantable Prosthesis** — the in-series, air-powered, prosthetic auxiliary ventricles of Soroff and Kantrowitz function well but require modification in view of the high frequency of clotting and embolism from the prosthesis.
3. **Artificial Intracorporeal Hearts** — Twenty-six have been reported since 1958 and as yet no animal has survived more than thirty hours with a functioning artificial heart. However, W.H.O. gaily prophesies cardiac factories for the future.
4. **Cardiac Transplantation** — Homograft transplantation is complicated by the difficulties of tissue typing, graft vs. host reaction, catecholamine hypersensitivity, homograft rejection phenomena and its detection and control with immuno-suppressive therapy, but is possible. Whether the development of a successful artificial heart will precede the breakthrough in the problems of cardiac trans-

plantation remains to be seen. Meanwhile, there is adequate time to consider the implications of either.

SUMMARY

An attempt has been made to present an up-to-date account of the pathogenesis and therapy of cardiogenic shock and to pursue as far as possible, the relationship between them.

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1 J.Amer.med.Ass., 1967, 202, 8

2 Lancet, 1967, *ii*, 681.

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TISSUE TRANSPLANTATION

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HISTORICAL BACKGROUND

The transplantation of tissues from one site to another has been the subject of surgical endeavour for many centuries. Simple flap procedures for the repair of defects in the skin of the nose, mouth and ears were known to the Greeks and Romans of the first century A.D., and a form of rhinoplasty was carried out by Indian surgeons, using local flaps, more than two thousand years ago. A more sophisticated technique of rhinoplasty, involving the transfer of a pedicled skin flap from the arm, was used by Tagliacozzi in the fourteenth century. Powerful opposition to such interference in the works of the Almighty came from the Ecclesiastical authorities, and not only was Tagliacozzi discredited, but further progress in this field was firmly suppressed until the eighteenth century.

In 1785, in Edinburgh, a series of experiments of some interest were carried out by a certain Mr. Fife and other members of the Royal Medical Society, and their work is recorded in the Society's Experimental Committee Records for that year.¹ They were interested in the possibility of blood transfusion, and used as their experimental subjects pairs of calves, one of each pair being bled via the carotid artery into a jugular vein of the other. In one instance they used as a conduit a pair of ivory cannulae connected by a piece of intestine which they had previously removed from a cat, and on other occasions they used simple metallic tubes.

The results of their work are carefully documented and, since they preceded Pasteur's

discoveries by seventy-five years, and those of Landsteiner on blood groups by one hundred and fifteen years, the experimenters may be excused for marvelling that the recipient animals almost invariably took a violent rigor and expired shortly after the transfusion, and for concluding that blood transfusion was not a practical procedure.

In the ensuing years numerous advances were made which marked the development of transplantation surgery as we know it today. Throughout this period technical ability has usually been more advanced than understanding of the fundamental biological problems involved. Thus the nineteenth century saw developments in the field of bone transplantation, notably by Ollier of Lyons, who made observations on the fate of bone fragments transplanted both subcutaneously and into skeletal defects, and noted the importance of an intact periosteum to the fate of such grafts; and by McEwen of Glasgow who performed the first successful allograft (v. infra) of bone to reconstitute the humeral shaft of a child with osteomyelitis in 1878. Early attempts to transplant cornea, tendon, nerve, and cartilage were also made during the nineteenth century, but the transplantation of whole organs on a vascular pedicle had to await the development of satisfactory techniques of anastomosis of blood vessels, an exercise that was not accomplished with reliability until the early part of the twentieth century.

Although Humphrey Davey described the narcotic properties of nitrous oxide in 1798, and suggested its possible use in surgery, almost half a century was to elapse before

anaesthesia was applied, first in dentistry by Wells and Morton in the States, and later in surgery and midwifery by Liston and Simpson in Britain. These discoveries transformed surgery from the art of the lightning craftsman into a more leisurely exercise which would allow the more time-consuming and exacting work required for transplantation.

Any tissue that is severed from its blood supply in order to be placed in a new situation passes through a period of susceptibility to infection, a complication that was the fear of nineteenth century surgeons. The discovery of microbes in the 1860's led first to the eradication of infection by antiseptics and later to the notion that it was better to avoid it by the aseptic method that is a corner stone of modern surgical technique. The importance of these events to transplantation surgery cannot be over emphasised, but without the more recent discoveries of sulphonamides and antibiotic substances in the 1930's and later, the advances that were to follow the elucidation of the immunological rejection of transplants from one individual to another could not have taken place.

In the first two decades of the twentieth century there was much debate concerning the failure of allografts of tumour and normal tissues to survive. There is not space here to discuss all the theories that were advanced, but among them was the notion that the host developed an active immunity to the graft. Several clinical instances were reported of the behaviour of skin allografts used in burns and in extensive trauma during this period, but understanding that a failed allograft was fundamentally different from a failed autograft was slow to develop. In 1943 Gibson and Medewar¹ reported the accelerated rejection of a second set of allografts from the same donor to the same recipient in a case of burns, and this led on to Medewar's systematic study of allografts published in 1944 and 1945.^{5,6} He established that in rabbits, such grafts were invariably rejected with a mean survival time of 10.4 days, and that if a second graft was made from the same donor to the same recipient twelve or more days after the first, rejection was accomplished more rapidly, with a mean survival time of 6.0 days. He also found that whereas first set grafts developed vascular connections and became infiltrated with mononuclear cells prior to rejection, second set grafts of skin failed to become vascularised at all; they rapidly became necrotic, and such mononuclear cells as were seen

were heavily amassed in the recipient tissue which was the graft bed.

IMMUNOLOGICAL THEORY

These observations have been amply confirmed, and present day theory on transplant immunity may be summarised as follows: after the introduction of a graft into a recipient animal, material from the graft is carried into the host, either in the form of soluble antigens which pass into the bloodstream, or else by way of host mononuclear cells which, on encountering the tissues of the graft, pick up antigenic material and carry it via the bloodstream, or via lymphatic channels, into the recipient's lymphoid tissues. Some of these mononuclear cells are members of the long-lived group of lymphocytes in the peripheral circulating pool, cells which are concerned in recognising foreign antigens. This may be referred to as the afferent mechanism.

Afferent antigenic material gains contact with the lymphatic tissues of the host via the bloodstream, but in particular with the regional lymph nodes which receive lymph directly from the graft. Lymphocytes in the paracortical areas of the lymph nodes respond to the antigenic stimulus brought to them by macrophages returning from the graft by transforming into a new, and now highly specialised group of cells, which are able to produce specific antibody to the antigens concerned. This change is in some way imprinted on the genetic mechanisms of the nucleus, so that the progeny of such transformed cells will possess this specific potentiality. These events may be called the central response.

These specialised cells may behave in two ways. Some, remaining in situ, produce specific antibody which passes into the circulation. Others, migrating from their lymph node origins, enter the blood stream and are able to penetrate the graft where, by mechanisms unknown, they exert a harmful effect on the graft. Such is the effector mechanism of transplantation immunity. It should be emphasised that a very great deal remains to be clarified about these immune responses, in particular with regard to the role and interrelationships of the cells involved; the foregoing is no more than a brief outline of prevalent theory. For more detailed information, the interested reader is referred to the series of articles by E. J. Holborow in *The Lancet* 1967 Nos. 7494-7503.

At this stage the current nomenclature of

transplantation surgery must be introduced. A graft transplanted from one site to another in the same individual is an autograft. If the recipient is a monozygous twin of the donor, or a member of the same highly inbred strain in the case of animal work, then the term isograft is used. A transplant to a different member of the same species, e.g. Jack to Jill, is an allograft, and when the donor belongs to a different species to the recipient, e.g. baboon to man, rat to mouse, the term xenograft is used. The last two of these terms were formerly referred to as homografts and heterografts respectively.

Clinical transplantation involves largely the use of autografts and allografts. In the case of paired organs, i.e. the kidney, transplants between monozygous twins are feasible, and some cases of transplantation across species barriers have been reported. The absence of an immunological problem in the case of autografts led to their widespread adoption many decades ago and the details of their application can be read in standard works on plastic and orthopaedic surgery.

METHODS OF IMMUNOSUPPRESSION

The fundamental problem to be overcome in the case of allografts is simply stated; the ability of the host's immunological mechanisms to destroy the graft must be suppressed without at the same time suppressing his immunity to other foreign material, e.g. bacteria, viruses and fungi. The reader will be quick to point out that these difficulties have not prevented the successful transplantation of corneas obtained from cadavers. The reason for this is that since cornea is an acellular and avascular structure, it is not subject to the cell mediated immune response mounted by the recipient. Any process leading to vascularisation of the graft results in its rapid rejection.

Even a cursory study of the complex nature of the immune mechanism will suggest that it may be possible to interrupt it at several points by agents which interfere with cellular multiplication or function. In fact numerous methods of immunosuppression have been developed, and some have found application in human transplantation.

Irradiation

Whole body irradiation using about 150 rads was used about a decade ago in the early

days of renal transplantation. Irradiation interferes with the molecular structure of deoxyribonucleic acid, and thus with cell division, cells being most susceptible to this injury during early mitosis. The tissues most affected by this treatment, therefore, are those which divide most rapidly, namely, the cells of the bone marrow, lymphoreticular system, skin, and mucous membranes. In practice, the use of a non-specific agent of this nature may result in a dangerous and prolonged pancytopenia. This, and the difficulties of choosing the correct dose to suit each case led to its early discontinuation as a clinical immunosuppressant. Nonetheless local irradiation of the graft, by destroying cells infiltrating the organ, and in the regional lymph nodes, is thought by some to be of value in the treatment of rejection crises.

Antimetabolites

It is possible to interfere with nucleic acid synthesis in other ways, however. The antimetabolite 6-mercaptopurine, by its similarity to certain naturally occurring purine compounds, can modify purine metabolism, thus interfering with the production of nucleoprotein and therefore with cell division. It also should be expected to affect all dividing cells, but in comparison with irradiation it has the advantage of manoeuvrability, the effect of a change in dose being more rapidly seen than in the case of irradiation. Despite this advantage, 6-mercaptopurine itself does not prove to be a very suitable agent for human use, because of the high incidence of toxic side effects. Investigation of a large number of related compounds led to the development in 1959 of azathioprine, a derivative of 6-mercaptopurine with broadly similar effects but with much better patient tolerance. This agent holds a position of great importance in human transplantation, and has been largely responsible for the improvement in renal transplant survival in the past decade.

Corticosteroids

The ability of corticosteroids to suppress inflammatory responses, including the immune response to transplants has long been known. Their mode of action is not clear, and although in some species, e.g. rabbits, guinea pigs and mice, cortisone prolongs the survival of skin grafts, in others, e.g. dogs, monkeys and

humans, it is ineffective when given alone. As an adjunctive treatment to azathioprine, prednisone has come to play an important part in clinical immunosuppression. Large doses of prednisone, e.g. 2-4 mg. per kilogram, are effective in reversing acute rejection phenomena, and in fact, in the case of renal transplants, many patients become dependent on a dose of 0.25-0.5 mg. per kilogram.

Actinomycin

Actinomycin C is a mixture of a group of antibiotic substances derived from *Streptomyces chrysomallus* which has a cytotoxic effect. This appears to take the form of an interference in the control which deoxyribonucleic acid exerts over messenger ribonucleic acid. It is most useful in the treatment of rejection crisis, when it is given as a short course of one or two intravenous injections in conjunction with increased doses of prednisone and maximal doses of azathioprine.

Antilymphocytic globulin

The above agents, by their nature, have an effect on all the cells and tissues of the body, and therefore produce various unwanted side effects. The antimetabolite and cytotoxic drugs may be responsible for agranulocytosis, thrombocytopaenia, ulceration of the alimentary mucosa, and loss of hair. Prolonged treatment with steroids produces the typical Cushingoid facies, with triac, moon face, osteoporosis, and increased incidence of hypertension and peptic ulceration. It has long been hoped that a more specific agent might be produced which would inhibit the mechanisms primarily responsible for transplant immunity without at the same time interfering with resistance to bacterial infection, or damaging other important groups of cells, e.g. the epithelial cells of the alimentary tract. To some extent, these hopes are fulfilled by antilymphocytic serum, which has recently been the subject of intense study in many laboratories throughout the world, and has been used in a number of cases of renal transplantation. The concept of an antilymphocytic serum is not new, and such a serum was prepared as early as 1937 by Chew and Lawrence, who demonstrated its ability to suppress the peripheral blood lymphocyte count *in vivo*. Similar suppression was obtained by Woodruff, Woodruff and Forman in 1950⁵ when it was noted

that the lymphopenia was relatively short-lived; because of this, it was at that time thought that antilymphocytic serum would be unlikely to have a significant influence on allograft survival.

Slight prolongation of skin graft survival was shown in 1961 by Waksman, Arbouys and Arnason,⁷ but later observations in Edinburgh by Woodruff and Anderson, in 1963 and 1964,⁹ demonstrated that skin graft survival in rats could be significantly prolonged by the administration of a serum raised in horses against rat lymphocytes. It was then shown that prolonged lymphopenia was not a necessary prerequisite for graft survival. In the past four years, extensive research into the production and properties of these sera has been carried out, and highly significant contributions have been made in our own medical school.

Antilymphocytic serum is made by injecting a preparation of the lymphocytes of the species in which grafting is to be carried out into another species. Usually the serum is raised in a large animal for transplant experiments in a smaller animal, for example, horse anti-dog serum, rabbit anti-mouse serum, and so on. It is possible to prepare cell suspensions rich in lymphocytes from spleen, thymus, lymph nodes, thoracic duct lymph, or peripheral blood. After a course of active immunisation by these cells, the animal is bled and the serum so obtained is heated to 56°C to destroy complement.

At this stage dangerous anti-erythrocyte activity is present, irrespective of the origin of the inoculated lymphocyte suspensions; the serum also contains large amounts of unwanted protein which must be removed. Purification may be carried out by several techniques, but our method has been to carry out sodium sulphate precipitation and batch chromatography on diethylaminoethyl cellulose, restoring the salt concentration to physiological levels by dialysis prior to storage at -20°C. The final preparation consists of immunoglobulin G, or IgG for short. It is absorbed against red cell stroma and platelets in order to reduce its activity against these elements in treated animals.

Animal experiments have shown that antilymphocytic globulin (ALG) possesses powerful immunological properties. For instance, it has been shown to suppress the production of humoral antibodies to primary immunisation by numerous antigens; it can inhibit cutaneous phenomena which are due to the cellular re-

sponse of delayed hypersensitivity, for example, the tuberculin reaction; it can prolong the survival of allografts of skin, kidney and other tissues, and it can modify the course of certain auto-immune diseases, for example allergic encephalomyelitis in mice.

Evidence is now available, notably from Starzl in Denver,¹¹⁰ that ALG, used in conjunction with reduced doses of azathioprine and prednisone, gives results in human renal transplantation that are at least as good as, and probably better than, those obtained with these agents administered together in their usual dosage. Since both azathioprine and prednisone have potentially serious side effects, this observation is highly significant. However, this powerful new tool is not without its problems; its antiplatelet activity is sometimes troublesome, and the injection is often painful. Although it is able to suppress humoral and cellular immunity, it is itself a foreign protein, and in fact it has been shown to be if anything more antigenic than normal gamma globulin derived from the same source. The reason for this probably lies in the fact that it homes onto lymphocytes which, being altered in some way, are taken up by macrophages resulting in the absorbed ALG being concentrated in the very centre of the treated animal's immune defence mechanism.

The mode of action of antilymphocytic globulin is only partly understood. There is no doubt that the active molecules in an ALG preparation adhere to lymphocytes, but what they do in this situation is less certain. Three main theories have been advanced; that the lymphocytes are destroyed by ALG; that their cell membrane is so occupied by ALG molecules that it is unable to respond in the normal way to other antigens (blind-folding); and that lymphocytes are transformed into a type of cell which is immunologically inactive (sterile inactivation). Space will not allow a discussion of these and other theories, and the experimental evidence which supports or refutes them, for which the reader is referred to specific works on the subject.¹

TISSUE TYPING

These then are the ways at present available to overcome the homograft reaction. At best they are imperfect tools, and therefore the problems involved in avoiding or minimising rejection achieve the greater importance. The laws governing the transfusion of blood which

concern the ABO grouping system must not be transgressed. Rhesus antigens are of much less importance, as are the numerous antigens which have been identified on the red cell membrane. In recent years attention has been turned to antigenic determinants which are present in the leucocytes of peripheral blood. Pioneers in this field have been Terasaki in Los Angeles, Dausset, Van Rood and Cepellini in Europe, and Batchelor in London. They have collected sera from patients who have been sensitised to foreign leucocytes, for example from pregnant women, or from people who have received multiple blood transfusions. The antibody content of these sera has been characterised and it is possible by their use to define which antigens are present on a given patient's cells, and to correlate the degree of compatibility between recipient and donor with the clinical course of a transplant. Evaluation of leucocyte typing continues, but it would appear already that there is in many (but not all) cases a correlation between high donor-host compatibility and smooth clinical course, free from rejection episodes. That some cases of complete compatibility nevertheless develop a rejection crisis may be taken as evidence that there are other parameters of compatibility testing of which we are not as yet aware. Among them may be preformed humoral antibodies, particularly in the case of kidney recipients who may have been transfused with scores of bottles of blood during their period of rehabilitation on dialysis prior to transplantation. Although the importance of such antibodies has been doubted, it may be necessary to revise this view when sufficient information becomes available.

BACTERIOLOGICAL PROBLEMS

The management of patients on immuno-suppressive treatment presents certain problems, especially in the case of renal transplants where general resistance to infection is diminished and the rate of excretion of drugs uncertain. The effects of a change in dosage of azathioprine are not seen for a few days, and it is sometimes very difficult, demanding considerable experience, to negotiate the narrow way between too little suppression, with the dangers of rejection, and too much, with the equally unwelcome dangers of infection. It is because of this problem that it is preferred to manage these patients in a sterile area such as has been constructed at the Nuffield Trans-

plantation Unit in Edinburgh, where all possible precautions such as the design of the unit, an elaborate ventilation system, bacterial surveys and decontamination of nursing and medical staff, have been taken to minimise the colonisation of the patient by organisms other than his own.

ARTIFICIAL AIDS TO VISCERAL FUNCTION

A patient who is in the terminal stages of disease of one of his visceral organs, be it kidney, liver, lung or heart, such that his only hope is transplantation of a new organ, is usually in a desperate clinical state. Looking back at the early days of renal transplantation, there is no doubt that a great deal of the peri-operative mortality, and the early failures, were due to the fact that the recipients were often moribund, having been saved from death itself by one or two hair-raising haemodialyses. The developments in dialysis technology in the early 1960's, leading to the introduction by Scribner of long term intermittent dialysis for chronic renal failure, transformed the situation in two ways. Firstly, an alternative to transplantation became available in what has become known as repeated dialysis treatment or, by that habit of abbreviation to which medical men are so addicted, as "R.D.T." Secondly, repeated dialysis treatment allows a patient with terminal renal failure to be rehabilitated so that his physical condition is no longer a bar to the relatively major operation of transplantation with its attendant hazards relating to immunosuppression. Such complications as hypertension, oedema, ascites, congestive heart failure and infections can usually be eliminated or controlled during this period, leading to a greatly improved chance of surviving the operation.

For some patients, notably those with lower urinary tract anomalies or disease, transplantation is not successful, and management by R.D.T. is preferable. Opinions may differ as to whether and when a patient successfully launched onto repeated dialysis should have his transplant, but since dialysis treatment and transplants fail for entirely unrelated reasons, a combination of the two methods of treatment can significantly prolong the life expectancy of patients with terminal renal failure.

When one surveys the transformation that repeated dialysis treatment has brought to the scene of renal transplantation, one is bound

to ask how similar facilities, if available would affect hepatic and cardiac transplantation. Perhaps the greatest advances in these branches of transplantation surgery in the next decade will be the development of artificial aids capable of adequate patient rehabilitation.

THE WAY AHEAD

Looking to the future, there are several problems in transplantation surgery which require careful thought and well directed research. One of the most difficult of these is the procurement of organs. Of necessity, cardiac and liver transplants are obtained from cadaver donors, but so also are a large proportion of renal grafts. In the latter case sufficient time is available to ensure that by all necessary criteria, death has occurred. A more urgent time scale in the case of the liver, and, in the case of the heart, cessation of function in the organ to be transplanted being a previously essential criterion of demise, has led to serious suspicions of ambivalence on the part of the physicians responsible for the treatment of the donor, and of excessive zeal on the part of the would be transplanters. For our part we have gone to great lengths to avoid any influence whatever in the good treatment of any potential donor, and have preferred to allow an organ to pass by rather than become the object of such suspicions. It is quite clear that a period of several years will be necessary in which painstaking effort is applied to the forming of public opinion, and perhaps new legislation enacted to facilitate the procurement of organs while safeguarding the interests of the potential donor.

Having obtained an organ for transplantation, time is vital, and the complex logistic problems involved in mobilising the surgical team, the recipient, and such ancillary services as for example, blood transfusion, blood coagulation and clinical chemistry would be much simpler if the organ could be stored in a viable state for a number of hours or even days. Certain advances have been made along these lines in the case of the kidney, and, more recently, the liver, using hypothermic perfusion with electrolyte solutions, blood, low molecular weight dextran, mannitol, or combinations of these materials, in conjunction with hyperbaric oxygen and, when temperatures below freezing point have been employed, such anti-freezing agents as dimethyl sulphoxide. These crude methods have allowed experimental preservation of the kidney for up to 24 hours in

a viable state, but much greater reliability would be required before they could justify so great a delay in a case of human transplantation.

The immunological battle is the central and most difficult problem to be solved. Improved

methods of tissue matching, and more specific immunosuppression probably along the lines of antilymphocytic globulin, will no doubt be developed, but there remains the immunologist's dream that specific tolerance to an organ transplant may one day come within the bounds of clinical possibility.

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DIAGNOSTIC PROBLEM

SET BY A. STRONG, B.A.(Oxon), M.B., Ch.B.

SUBJECT

Miss A. B., aged 18. Right handed.

PRINCIPAL COMPLAINTS

Tremor, paraesthesiae, obesity, headache.

HISTORY

- (1) Tremor, impairment of fine movements and paraesthesiae of the right side, principally of the arm. The tremor worst at rest and exacerbated by concentration. Three months' duration and steadily deteriorating.
- (2) Increase in appetite and weight and excessive thirst for three weeks.
- (3) Frontal headache on rising in the morning for the past three weeks.
- (4) General medical and family histories negative.

GENERAL EXAMINATION

A tall, obese girl: otherwise negative: blood pressure normal.

NEUROLOGICAL EXAMINATION

1. Intellect not significantly impaired: no intracranial bruits: no papilloedema.
2. Slight slurring of speech.
3. Mild right facial weakness of central pattern.
4. Sensation depressed on right side of face and right arm.
5. Severe resting tremor of right arm and leg.
6. Increased tone of right limbs: equivocal right plantar response: drags the right foot on walking.
7. No inco-ordination or rombergism.

INVESTIGATIONS

Routine haematology and biochemistry normal; CSF pressure and protein normal.

Serum cortisols: (a) 11 p.m. — 8 $\mu\text{g}/100\text{ ml}$.
(b) 9 a.m. — 11 $\mu\text{g}/100\text{ ml}$.

- A. Where is the lesion and what is it likely to be?
- B. What neurological investigations are required?

FURTHER PROGRESS

After investigation a diagnosis was made and in view of her rapid deterioration the patient underwent craniotomy in an attempt to arrest the expansion of her lesion. During surgery there was marked venous oozing. Post-operatively she was slow to recover consciousness and suddenly deteriorated 18 hours later. Re-exploration showed an accumulation of clot from recurrent venous oozing. She remained deeply unconscious and some 24 hours later developed an intense jaundice: urobilinogen and bilirubin appeared in the urine. Prothrombin activity was 29%, S.G.P.T. 570 I.U., serum indirect bilirubin 2.5 mg/100 ml, direct 5.7 mg/100 ml. Bleeding time was 9 minutes: no increase in fibrin degradation products: direct and indirect coombs' tests negative: slight depression of vitamin K — dependent coagulation factors (II, VII and X). In spite of treatment including triple strength plasma and vitamin K, her condition deteriorated and she died 6 days after operation.

C. What was the cause of her jaundice?

(Answer on page 48)

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THE RECTAL EXAMINATION

John B. Dawson.

M.A., B.M., B.Ch., M.R.C.P.Ed.

Health Sciences Centre, New York

DIGITAL EXAMINATION

The use of the observer's eyes and forefinger with the initial chant of, "Now just turn over on your left side facing away from me and draw your knees up", so realistically caricatured by O'Grady (1963) is the first step in the "rectal".

Whatever the selected patient position, ensure that you have a good light on the perianal area and provide an intermittent commentary for the patient's benefit. Part the buttocks and make a thorough visual examination of the anal area for evidence of trauma, sore patches of skin, lichenification, ulcers, thread worms, blood or mucous, "piles" and skin tags, fissures and fistulae, pilonidal sinus, the highly contagious syphilitic condylomata (warts) or other signs of anal sexual contact, or a prolapse of piles, anal canal or uterus, and note whether the anus is withdrawn or patulous.

There are two methods advocated for inserting the finger as pleasantly as possible — covered in a soft fine rubber finger stall or similar two or five-fingered glove. The better method is to ask the patient to bear down, i.e. to increase his intra-abdominal pressure and thus cause a mild protrusion of his anal ring. As he does so, gently apply your examining forefinger with the long axis of its cross section in line with his anterior (12 o'clock) — posterior (6 o'clock) anal plane and allow your finger to be gently sucked inward as he releases his intra-abdominal pressure. The result is that your finger will find itself in the rectum almost unbeknown to the patient.

The second method is to place the pulp of

the distal phalanx of your examining forefinger flat against the anal ring and then gradually to pass it inwards, while at the same time slowly swinging the finger through a 90° angle until the tip points through the anal canal.

Whichever method you choose, never stab your finger at the anal opening because the suddenness will surprise your patient and the minor inevitable pain will produce your number one enemy — spasm.

You must now assess and make a decision upon:—

1) *The anal sphincter*

The integrity of this muscle mechanism is essential to man's well-being, for as Dr. Charles Mayo teaches:— "What other muscle in the human body has the exquisite ability to separate flatus from fluid from faeces!" You must objectively assess whether an increased tension of the anal sphincter is the result of your finger entry, through pain due to your inexperienced technique, or is maintained by an emotional overlay. If you suspect an emotional cause, pause and indulge in further conversation and explain your trouble to your patient and ask him to assist you by concentrating on a regular deep form of breathing and to relax as much as he can. Failure to achieve a reasonable relaxation of the sphincter at this stage may virtually nullify any further manoeuvres. A lax and toneless sphincter often associated with a patulous anus is an unusual condition and a cause such as rectal prolapse will usually be evident.

2) *The Anal Ring*

When all is settled, palpate the entire perianal ring between the pulps of the external thumb and internal forefinger, noting any lumps, cysts, foreign bodies, loculated pus, irregularities, pain-spots, etc. This practice is important and often passed over in the hurry to assess the rectum.

3) *The Temperature of the Rectum*

This is a very good indication of general body temperature. The Ancients, we are told, could detect early typhoid from a hyperpyrexia rectum.

4) *The Size of the Rectal Cavity*

The space in which your finger finds itself is very informative. It may be grossly ballooned as with a megacolon or from a longstanding condition of impacted faeces, it may represent the contracted rectum of longstanding ulcerative colitis, or the normal state in which the rectal walls are within easy reach of your fingertip.

5) *Faeces*

Some 50% of the time the rectum is empty, but if there are faeces present, decide whether they are hard (scybalae), indentable, soft, or fluid and try to make your findings fit the facts.

For Example: A rectum full of hard, "impacted" faeces is liable to occur in the elderly, those clinically confined to bed, patients in the tropics, those who drink insufficient fluids, and those very ill or with high temperatures. Such obstructions must be manually removed before you can hope to achieve maximal information from your examination. A proctoscope is often useful for this purpose.

6) *The Rectal Mucosa*

The condition of the rectal mucosa is very informative. The normal state has a characteristic feel and should be mobile. If it is bound down at any point, such as over the prostate, suspect active disease (cancer) or the fibrotic aftermath of previous affliction (gonococcal).

7) *Suspicious Lesions Deep to the Rectal Wall*

If you have been using the lateral pos-

ition, rotate the patient into the supine position, keeping your examining finger in situ and proceed with a further manoeuvre. Bimanual palpation, by applying pressure with your remaining free hand firmly and gradually in the suprapubic region while you ask the patient to bear down and relax his abdominal wall in gentle succession, will force the lower abdominal and pelvic contents towards your examining forefinger and will remove many lesions from your diagnostic list of possibilities.

Individually palpate the four points of the internal rectal compass while the patient strains down, questioning at each cardinal site as to the presence of increased discomfort, tenderness and pain.

The normal fallopian tubes, seminal vesicles and often the ovaries will not be palpable, but the bimanual technique will allow you to assess the characteristics of any suspicious lump in terms of site, size, shape, surface, consistency, edge, the fascial level in which it lies, any associated pain, any related loss of function or presence of abnormal lymph glands draining the area — after Sir James Paterson Ross (Ex P.R.C.S.).

Your examination concluded, withdraw your finger, wipe your gloved finger on a piece of filter paper or keep the glove itself with its small surface complement of faeces and intrarectal contents for brief macroscopic examination and simple tests such as hematest, for occult blood.

Explain to the patient that you are finished and compliment him on his co-operation. Thoroughly tidy the patient's anal area, apply a pleasant cheap powder (Johnson's Baby Powder) from a plastic blower bottle and cover his exposed hindparts with a concealing sheet. There is nothing more unpleasant to a patient than of knowing the anal area to be covered in jelly, of having experienced the sensation of having passed a motion, or not being properly tidied up and of having his posterior "to human view displayed".

THE SIGMOIDOSCOPE

Should the previous proceedings detect anything that worried you, proceed immediately with a sigmoidoscopy.

This instrument need not be above 25 cm. in length for the normal adult (a smaller one for children), to visualize the hemorrhoidal area (10 cms.), superior hemorrhoidal area

cool. Make the volume up to 300 ml. with a 1/1000 solution of Mercuric Dichloride.

The knee-elbow position has been mentioned as the most suitable position for sigmoidoscopy, at least from the operator's point of view, because the abdominal contents fall away from the instrument and minimal internal upset is caused to the patient.

The routine for the lateral position approach follows:—

Take the sigmoidoscope and obturator which have been cleaned with a long bottle brush and running hot water, removed from the sterilizer and allowed to cool in a big plastic dish. Rewarm in body temperature saline, if desired, but nothing much is gained by so doing because the instrument is either of thin metal which soon warms up or of plastic which does not feel cold. Lubricate the

ends of the obturator and sigmoidoscope and insert them both under external visual control for 5 cm. Remove the obturator and apply the optical and air inflating attachments. With the left hand on the instrument and the left elbow on the patient's buttocks, apply your right eye to the proximal end of the instrument.

The position of the left hand and elbow is essential for ensuring that the instrument moves with the patient and does not independently wave around inside, a situation which is prone to cause pain and damage. The practice is akin to the firm placing of a thumb on the barrel of a hypodermic syringe and the fingers of the same hand around the arm of his patient, when the anaesthetist administers an ante-cubital I.V. injection. Advance the instrument only under visual control and use



Fig. II. A disposable Sigmoidoscope with power unit.



Fig. III. Equipment for the rectal examination.

just sufficient insufflation to distend the rectum, but not enough to cause discomfort to the patient or make loud backfiring flatus noises which cause him embarrassment. You will have to bypass an occasional faecal lump with minor movements, and will need to depress, lift and depress your end of the instrument as you proceed over the transverse rectal folds. As you progress, you may see the cause of the trouble and an estimation of its hardness can be assessed by prodding with the instrument. Continuing onwards you may then see, and feel, the iliac arterial pulsation transmitted through the rectal wall. For further progress you will require to move the proximal end and eyepiece posteriorly, with care as this may cause discomfort, in order to get around the sacral promontory, which will bring you to the region of the recto-sigmoid junction approximately 18 cm. up the alimentary canal as measured from the anal ring. Care must be taken in progressing further, some patients will permit the instrument with reasonable insufflation and judicious angling to pass beyond this point up to the full 25 cm., but about

25% will not submit no matter how devious is your approach and you must not force the issue. If you persist you run the grave risk of perforation with the rider of immediate reparative operation. It is far better to be satisfied with an 18 cm. traverse and see what you can discover with the aid of the radiologist beyond this point, putting the distance you actually achieved under observation on your x-ray request form along with the other relevant clinical information.

If during this process you wish to take a biopsy there are a few practical points to consider; but do not perform the biopsy yourself unless you know what you are doing. You may perforate the bowel wall when sampling above the recto-sigmoid junction or you may not bite deep enough and miss the all important basement membrane.

If the object is small, e.g. a polyp, it is worth removing the whole specimen. If, however, the lesion is a large ulcerated growth, the pathologist generally appreciates a full description with a snippet from the centre and one

from the margin as the centre may just disclose necrotic matter.

When you have procured the specimen with a minimum of trauma do not wipe it off the biopsy instrument with a piece of gauze and view it with a hunter's pride. Such a practice can cause a rapid dehydration of the peripheral cells with a resultant loss of many useful pathological diagnostic signs.

There is no need for hurry in these procedures, but quick and decisive movements are optimal if the specimen is being collected for histochemical enzyme or electron microscope studies. Normally it is quite sufficient to take your time and to put the end of the biopsy forceps straight into your plastic pot of Zenker's Formalin, shake off the specimen, label the container, and carry the specimen to the laboratory yourself or make sure a reliable and informed messenger has it in his charge. The specimen must be accompanied by a note designating your requests and supplying sensibly relevant information for the pathologist's benefit. Finally, and before doing anything else, describe your procedure and findings in a few well-chosen words in the patient's notes.

THE PROCTOSCOPE

This instrument has been left to the last because the indications for its use at the present time are becoming less numerous. It is accepted now that the digital, followed by the sigmoidoscope is the routine of choice. However, the proctoscope is still a very useful instrument for:

- 1) Reviewing lesions in the terminal 5 cm. of the rectum and for this a rotating grooved barrel instrument (Welch-Allyn) is a practical variant.
- 2) For the injection treatment of first and second degree "piles" using a tuberculin syringe (1 ml) and a 4" needle.
- 3) For the removal of excessive numbers of faecal lumps prior to a successful sigmoidoscopy.

The light for a proctoscope can also be supplied from power supplies in the pistol grip handle but in the interests of simplicity and expense, illumination from an angle-poise lamp, suitably held torch, or conveniently placed window is usually quite adequate. For future geographic anal reference purposes it is usual to use the clock terminology — that is,

12.00 is anterior between the legs and 6.00 is posterior. The classical position for hemorrhoids is that of 4-7-11 o'clock, a figure easily remembered by those who delight in "4711" Eau de Cologne.

The "take home message" is that a rectal examination is mandatory whenever there is:—

- 1) Bleeding from the rectum or evidence of melena.
- 2) Protrusion of mucosa from the rectum.
- 3) A change in the intestinal rhythm or content of the motions.
- 4) A "pile" (Hemorrhoid) present.
- 5) Pain in the lower abdomen and backache.
- 6) A discharge of pus or mucous P.R.
- 7) Pain in the ano-rectal area.

However, whatever the indication — digital rectal, proctological and sigmoidoscopic examination is neither burdensome nor difficult and for the patient, may be life-saving.

Finally, and before you leave the patient, explain to him what you have found and see that he is once again decorously dressed and comfortable. This last refinement is most essential because the majority of your patients will not have been so treated previously, and may mildly resent your assault — not appreciating the vital importance to you, the doctor, of such an examination. Handle the whole situation from start to finish with decorum, good manners and employ a matter-of-fact form of grace that will spare him any form of embarrassment. If you can accomplish this successfully you will find that the mental reaction within the patient will not be one of resentment but will be one of a grudging, but friendly, "Well this man is at least thorough."

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The first part of this article appeared in the last edition of Res Medica.

GRAPHOLOGY

Malcolm Macnicol, B.Sc.

Personality assessment is serious business. It goes on all the time and involves everybody from the Prime Minister to modern Miss Telephonists of 1969. Because of its intangible nature people search for tangible systems to define it. The way a woman wears her face, a man his laugh, the way we act, talk and write, help to form some sort of register, permanent or hopefully immutable. People like to know most things about most other people. I just don't understand you, sighs a puzzled lover; a disillusioned contemporary looks to the bottom of his beer mug for support. Both clutch at any technique that offers to crack the code of those that matter to them.

Graphology has struggled hard with its metamorphosis from art to science. If the ecdysis is not yet complete it is not for want of trying. The approach in graphology has been modified from an artificial and laboured point by point analysis of handwriting, the "school of fixed signs" of Michon, to a wider assessment of the traits and general forms inherent in writing. Pulver, Kraeplin and Klages, Allport, Vernon and Saudek, Roman, Lewinson and Zubin, these are the names that have introduced a commonsense, rhythmical and balanced line to handwriting analysis. While not entirely acceptable, it is intriguing and full of promise. Inevitably the subject finds itself variously ascribed to a booth along with Mme. Lizandra and her magic ball, phrenologists, homeopaths and cocktail party astrologers, or to the laboratory with psychometrists, forensic scientists and employers. It is not an entirely happy resonance.

BEYOND THE TRACES

Any tracker will be able to tell you a deal about preceding events by observing scuffs in the sand, footprints, spent matches and so on. Handwriting is a similar spoor or tracing, representing the focused activities of a person as thought follows thought and is relayed. Some claim, like the tracker, to be able to assess the reasons behind the marks, and then by further study to gain insight into the personality and workings of the writer's mind. They maintain that writing style is a product of personality, as is any observable behaviour, so long as some control can be imposed on the environmental situation. Thus traits, recognisable in any script (and different cultural forms pose the usual problems here), tally with definable traits in personality. Others do not make this extended claim with graphology but feel it has great use in monitoring the changes in a person's character, whether from experience, drugs or therapy. No claims are made that it allows greater insight into a certain personality than one or two interviews would afford, but its projective permanence is extolled.

*"The Moving Finger writes; and,
having writ,
Moves on: nor all the Piety nor Wit
Shall lure it back to cancel half a
line,
Nor all thy Tears wash out a Word
of it."*

(from the Rubaiyat of Omar Khayyam)

DIRECTION OF FLOW

The earliest form of symbolic and permanent communication utilised the knotting of reeds and twine, followed eventually by the engraving of designs on wood or stone. These markings were necessarily effected by hand. Then came the pictorial techniques of ancient writing, the hieroglyphics of Egypt and the ideograms of China, still in use today. The direction of flow of these pictures was variable with different cultures, or could be read across or from top to bottom as with the Cartouche of Cleopatra on the Rosetta Stone. It was not until simplified symbols began to be strung together, like replicas of articulated sounds, that writing developed a fluency of line.

Ancient Greek and Hebrew maintain a backwards and forwards movement with successive lines, rather like the plowing of a field. The gradual predominance of left to right flow has been attributed to the greater proportion of people born right handed, it being easier to write in a direction away from the body. The explanation may be more complicated however. In his studies of the right to left writing of the Szekely tribe of Transylvania, the Hungarian anthropologist Sebestyen observed how one of the last adherents to this language wrote in vertical columns from top to bottom, but beginning at the left; then to read the message the inscription was turned in a clockwise direction till the lines were horizontal. The newly aligned writing was of course read from right to left, apparently against the rules of predominant right handedness, though the actual writing had been from left to right in columns.

SLANTS AND SLOPES

The slant of handwriting is one of the first features to strike the eye. A rightward slant is one that leans more than five degrees from the vertical in its upper zone. This is meant to depict the self reliant, feeling personality and only when it becomes significantly tilted, 45 degrees or more, does it indicate someone with an over-excitable and sentimental temperament. The alcoholic is reputed to manifest this excessive slant, along with unsteady, tremulous strokes of the pen and a tendency to write lines that slope downwards towards the right. Hitler's nearly prone signature is likewise looked on as revealing severe pathology.

Erect writing, within 5 degrees of the

vertical, indicates the person governed by reason. It is certainly a more controlled variety of script and it is interesting that an academic training often induces a straightening of the script. Much will depend on the writing school of the person when young and on his compliance with scholastic strictures. Leftward sloping writing, so called backhand writing, characterises the defiant individual, and if extreme often indicates previous childhood conflicts and unresolved tension with the parents. Some graphologists have suggested that the leftward slant shows up "mother fixation", finding the slant commonly in matriarchal societies. Writing that varies in slope represents the individual with pronounced ambivalence of response, varying between fixation and protest, love and hate. In passages of expressive writing, as in letters, emotional pieces of news are often written in a more pronounced slant to the right than relatively innocuous sections.

LEFTHANDERS

The leftward slant is in fact the more natural tendency of the left hander, and in order to compensate for this the paper is often held skew so that the resultant hand is acceptably sloped to the right. That the leftward slope is more convenient for the left hander has been shown in the cases of those who lose the right arm, like Nelson, and subsequently change from right to left slope while maintaining most of the other characteristics of their handwriting. Left handers also show a greater facility at writing reverse image or "mirror" writing than right handers; furthermore, latent left handers writing with their right hands are far more able to perform mirror writing than their truly right handed fellows. Leonardo da Vinci, equally adept with either hand, wrote a conventional right handed script for general communication, and mirror handwriting for his diary.

THE THREE ZONES

Another graphological technique is the dividing up of the script into zones. Thus unizonal letters like 'a' and 'n' occupy only the middle zone, whereas bizonal letters occupy additionally the upper zone, like 't', or the lower zone, like 'g', and trizonal letters like 'f' encroach upon the full writing space. The middle zone is considered to represent the sphere of actuality, so that when it is well de-

veloped the writer is considered to be well in touch with reality and able to relate with his personal and material surroundings. The upper zone is the sphere of abstraction where the interests and aspirations of the mind and spirit find expression. Artists and creators show pronounced excursions into this zone, though excessive flamboyancy or over-extension above the normal limits into what is termed the "stratosphere" shows up the person who is apt to over-indulge his imagination or to day dream.

However if the other zones are also well developed the handwriting may be perfectly compatible with the highly creative mind. Dotting the 'i' and crossing the 't' are both functions within this zone; when the procedure is carried out well above the parent stem this suggests flightiness and fantasy, while if the 'i' dots and 't' strokes are carried considerably to the right the writer is probably full of verve and even slapdash. It has also been said that crossing a 't' is a decisive action while dotting an 'i' is a self conscious movement.

The lower zone represents the instinctual drives of self preservation and sex. Large closed loops in the zone indicate the sensuous person, while such features as breaks in the loops, blotchiness, and flowery appendages show up the person preoccupied with the sexual or sensual. When the loops are reduced to single vertical strokes the person is either cold or finds himself in a position where his sexual life has to be well governed. In many ways these three basic zones are analogous with the primordial metaphysical concepts of a mind, soul and body, or the psycho-analytical division of superego, ego and id.

Persons of limited education and culture, children and the old show proportionally enlarged middle zones. Those with a facility for words show longer stems and loops, the middle zone often reducing to less than the three millimetre average. It is found that loops elongate at puberty, while before exams they tend to lengthen, perhaps as pent up emotions and instincts are released. A monotonous regularity of loop size indicates a dull temperament or over-control, whereas marked irregularity is a sign of extreme excitability and lack of control.

CONNECTIVE FORMS

By connective form of writing is meant the predominant linking pattern within words. The garland appears like 'u's joined together

with the angular links pointing upwards. The arcade is the reverse of this, like a series of 'n's. Mixed writing occurs when neither connection is dominant, and angular writing gives the impression of a general lack of curves in the middle zone. The garland, like the open hand, is used by the person with an open and liberal mind, a person of frank disposition. The arcade, held to represent the grasping hand, is the connective form of the more formal and aloof personality. Mixed connective forms betoken the person with intermediate traits while the sharp angular connective form signals the sharp intellect given to nonconformism or aggression; thus regular angles denote the theoretician but irregularity shows up the obstinate personality.

Attention is also paid to the linking of letters in a word, some claiming that the more connected the letters the more logical is the writer. Conversely, separation of letters is a sign of the intuitive mind. Most handwriting incorporates both forms, but occasionally the script may be remarkable for its degree of connectedness, including even the linking of whole words, or vice versa. Words that "die out" into a thread at the end, commonly those ending in 'n', 'm', or 'ing', are the property of intuitive people who may possess a sinuous dexterity in handling of others.

VALIDITY AND SIGNIFICANCE

There are many other cues that have been used to assess personality from handwriting. Pen pressure, expansiveness, fluency and speed, the size of capital and the degree of closure of such letters as 'o' have all been persuasively argued as indicators of certain traits. The validity of graphology is constantly questioned, and certainly in controlled trials where panels of psychiatrists have assessed the personality of patients and compared their results with the graphologists there has been poor correlation. But although graphology by itself may never furnish the full answer regarding personality, neither would one expect a single clinical sign to provide the diagnosis of a disease. Taken in conjunction with interviews, questionnaires and behavioural observations, graphology may indeed be of help to some professional workers, and as a projective test it is sometimes preferred to techniques like the Rorschach ink blot test.

Greater reliability is afforded in cases where a subject is being monitored before and after drugs or therapy. The writing of depressives

is often found to expand after successful therapy, changing from a hand that was originally cramped away into the corner of a page. Schizophrenics write with a tidier, reduced hand after improvement in their condition and it is interesting to note that some subjects who respond with pronounced psychical and physical symptomatology to hallucinogenic drugs, the so-called "strong reactors", show a significant increase in script size, as measured by planimetry, during the period of drug effect. "Non reactors" show no significant change in size. Other fields that engage the graphologist are forensic medicine and the detection of forgery, but these are subjects in themselves.

SIGNING OFF

Signatures are very important and represent what we wish to be remembered by. Everyone is conscious of a signature and many have practised their own for hours. Personal embellishments and subtleties of stroke are in-

corporated until "improvement" is established, often at the expense of legibility. Change in a signature is nowhere better seen than in the evolution of Napoleon's signature which was at first simply written and unremarkable, then became forceful, heavy and slashing at the height of his power, and confused, narrowed and manifesting self-covering strokes after the retreat from Moscow.

Placing of the signature is conventionally to the lower right hand section of a page. Extreme rightward shift indicates the impatient person while leftward placing is taken as an indication of anxiety. Dejected or depressed people drop the signature low down on the page, the signatures of suicides being often found towards the bottom left hand corner of the page. With all this said, it is as well that the only writing we have to contend with is our own, our friends' and our colleagues' (including the "Dear Dr." brigade), and that the only people who have to grapple with our signatures when it matters are officials and bank managers, who hold the keys to our anxiety, impatience and depression anyway.

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STUDENT RESEARCH

CLOSTRIDIUM OEDEMATIENS

Certain types of *Clostridium oedematiens*, a demanding anaerobe, are difficult to subculture on to solid media. A recent significant advance has been made in the observations that development of colonies of *Cl. oedematiens* types B and D, on human blood agar media, is reliably enhanced by the presence of iron filings at the surface of the medium. The incorporation of metallic iron in laboratory cultures of anaerobes has been described by several workers, but its use has been limited to fluid or semi-solid media. It is suggested that iron filings make conditions suitable for proliferation of viable particles in the inoculum by lowering the oxidation-reduction potential at the surface of the medium.

G. G. Coleshill

N.H.S. WIGS

Normal male type baldness does not qualify for a wig under the N.H.S. and a patient must suffer total alopecia to justify prescription. No woman, however, can be expected to wait until her last hair disintegrates before qualifying, and thus the Consultant Dermatologist often provides a prescription before complete baldness occurs.

A survey to discover the reasons for the recent increase in the number of wigs issued, was carried out using the records of the R.I.E. Dermatology Department. Age, sex and cause of alopecia were noted for all cases in which wigs were prescribed from January 1962 to July 1968.

An increase due to increased numbers of patients was discounted for although patients rose in 1963-64 when one more Consultant was appointed, the number has since been constant. Analysis of specific causes of alopecias by age and sex showed no significant fluctuations for those due to myxoedema, trauma, drugs or other specific causes but senile and post-irradiational alopecias have shown an increase.

Post-irradiational alopecia is mostly the result of *Tinea capitis* therapy as a child but occasionally has followed irradiation of tumours. Close study of senile hair loss showed that while 52% of patients in 1962 were under 70 years, 63% fell into this category in 1966 and 68% in 1968.

A last fact to be considered is the abolition of the £2 10/- prescription charge per wig in February 1968 and it will be of interest to see if any decrease in the upward trend follows its reintroduction this year.

The conclusion is that the main reasons for the increase in wig prescription are increased frequency of diffuse alopecia in younger women with consequent increase in renewals.

Angela R. Miller

VASCULAR DISEASE

Investigations of factors controlling the blood lipids, and in particular, blood cholesterol, may have a bearing on theories pertaining to the aetiology of vascular disease, since elevations in blood lipoprotein levels appear to precede the development of atheromatous plaques and thrombi. Such investigations are

thus of prime importance in the development of drugs, both therapeutic and prophylactic, to minimise vascular lesions of this type.

It is known that the main quantitative reaction sequence for cholesterol catabolism is the hepatic production of bile acids. It is now established that the first step in this sequence is 7- α hydroxylation of the cholesterol molecule by a virtually irreversible "mixed function oxidase" occurring in the microsomal fraction of liver cells. This enzyme is thought to represent a central site, as 7- α -hydroxy-cholesterol has no other metabolic fate than further conversion to the primary bile acids — chenodeoxycholic and cholic acids.

This project under the supervision of Dr. G. S. Boyd consisted of the investigation of this oxidase in hepatic tissue. A series of rats was fed 1% cholesterol for five days, and then their livers were assayed for cholesterol-7 α -hydroxylase activity, and compared with those of a control group. The assay consisted of isolating the microsomal fraction from a known amount of liver by homogenisation in sucrose solution and centrifugation in two stages, i.e. an initial stage, to remove cell debris, and a later stage to isolate the microsomal fraction itself. Each fraction was incubated with C¹⁴ cholesterol, the products being estimated later by thin-layer chromatography and scintillation counting of each derivative.

The final results, after calculation of biological variation, tended to show an increase in cholesterol-7- α -hydroxylase activity in the best group, with a decrease in the amount of autooxidation products normally formed during *in vitro* incubations. It could therefore be tentatively concluded that increased cholesterol intake results in increased catabolism of the sterol to bile acids; this sequence of events would tend to control the net size of the cholesterol pool.

M. Braithwaite

SGOT LEVELS IN TUBERCULOUS PATIENTS TREATED WITH PAS AND ISONIAZID

Hepatic toxicity in patients receiving anti-tuberculosis chemotherapy may be due to a direct toxic effect of the drug employed or to drug hypersensitivity. Certain drugs are notorious for their potential hepato- toxicity

(e.g. pyrazinamide, ethionamide, etc.) and regular monitoring of hepatic function is necessary to detect and avoid serious liver damage. All of the increasing number of antituberculous drugs are capable of causing hypersensitivity and in this context hepatic dysfunction may be only one of the features of systemic upset. Experience has shown that the most subtle of the hepatic function tests are the transaminases (SGOT and SGPT) and estimation of one or other of these is the standard test when drugs such as pyrazinamide or ethionamide are used.

The present pilot study undertaken in Yale-New Haven Medical Center under the aegis of the Connecticut Thoracic Society and supervised by Professor Nicholas D'Esopo is concerned with SGOT levels in tuberculous patients treated with PAS in combination with isoniazid.

One hundred and seven patients receiving treatment for the first time for pulmonary tuberculosis were given PAS (12 G. daily) and isoniazid (200 mg. daily). Thirty three of these (30.8%) had significant elevations of SGOT (greater than 50 Reitman-Frankel units) during the first three weeks of treatment when hypersensitivity is most likely to occur. Of these 9 (<10%) had clinical evidence of hypersensitivity but only 5 had proven hypersensitivity to PAS. It is, of course, feasible that isoniazid was the offender in the 4 cases without PAS hypersensitivity but it is common experience that isoniazid hypersensitivity is relatively rare and scarcely ever occurs singly, i.e. it is usual to find associated hypersensitivity to the companion drug. The problem of isoniazid hypersensitivity was not studied in the present series.

The elevated SGOT values unrelated to drug hypersensitivity might be explained by a toxic effect on an already damaged liver. For example 26 of the 107 patients were alcoholics and may have been predisposed to drug toxicity which might not have occurred in normal subjects. Nevertheless, only 11 of the 26 alcoholics had raised values for SGOT and 9 of these had continued treatment with PAS and isoniazid without ill effect. Of all the cases with raised SGOT one quarter showed other biochemical indications of hepatic dysfunction (Bromsulphthalein Excretion, Serum Bilirubin, Thymol Turbidity, etc.). In 4 patients liver biopsy was performed and showed the features of drug toxicity in two, viral hepatitis in one and no abnormality in the fourth.

Hyposensitisation to PAS was successfully

achieved in 5 patients with proven hypersensitivity. A lower (but still effective) dosage of PAS was tolerated in 6 others.

It was concluded that a more extensive study of SGOT values in patients having standard antituberculous chemotherapy might indicate minor and clinically undetectable hepatic dysfunction not attributable to PAS hypersensi-

tivity. This is especially likely as pulmonary tuberculosis in developed countries now has its highest incidence in the older age groups (particularly in the male), in which hepatic function may, for several reasons, be already impaired.

C. F. J. Grindle

THE CONTRIBUTORS

DR. HENRY WALTON is the consultant in administrative charge and director of the University Department of Psychiatry at the Western General Hospital. His article, of which the first part appears in this issue of RES MEDICA, gives us a great deal of insight into the way in which the Psychiatrist obtains his information from the patient.

DR. JOHN CLARK is a Senior Registrar in the Department of Surgery at the Royal Infirmary, and an ex-president of the Royal Medical Society. His research in tissue transplantation and antilymphocytic globulin makes him well qualified for his excellent article on this subject.

DR. JOHN DAWSON is an ex-president of the Oxford University Medical Society and gained his early clinical training at St. Bartholomew's Hospital, London. He also worked under Sir Stanley Davidson and is a member of the R.C.P.E. He is conversant with medicine in Australia and the U.S.A., and we welcome his contribution to the Journal.

MALCOLM MACNICOL is an honours graduate in pharmacology and is now in his final year at Edinburgh. His interests are spread widely, both inside and outside medicine, and he has first hand experience of medical services in both Russia and America.

GORDON LEITCH graduated in honours physiology and is now in fifth year. His article on Cardiogenic Shock is based upon the prize winning essay which he submitted to the essay competition organized by the Scottish branch of the Chest and Heart Association.

Cure of Epilepsy

In the case accompanied by the Aura Epileptica, the fit may be prevented by compression of the part; or when we perceive the sensation proceeding from the extremity of any particular nerve, dividing (if possible) that nerve in its course. Amputation is the most effectual mode of putting a stop to it. Blistering and keeping up a discharge on the part by means of Issues, has been recommended.

—from Society case records, 1798.

REVIEW

● For many years, the R.M.S. has attracted a membership of only 10% of medical students between 2nd and 6th years in this University, and has had very variable (and often disappointing) turn-outs at both public and private meetings. A questionnaire was put out to students last Summer Term to determine what proportion of medical students might be attracted to joining the Society.

This showed that 30% of students were 'regular' attenders at extracurricular lectures, societies, symposia, etc., i.e. attended more than twice per term; 30% did not attend any such meetings, the remainder (40%) being 'occasional' attenders. Comparison showed that twice as many students attended Edinburgh Medical Group meetings as R.M.S. meetings; why this should be we could not definitely ascertain, but it is significant that 72% of medical students felt that they were insufficiently informed about R.M.S. activities.

In attempting to define the reasons for the Society's small membership over the years, an opportunity was provided for students to voice their criticisms of the Society's affairs, and indicate why they had not joined:

(a) 55% of students suggested that Friday night was unsuitable for meetings, for various reasons; Wednesday stood out from other weekdays as the most suitable alternative.

(b) 40% indicated that they had never been approached with regard to joining; indeed, a surprising number did not know of the existence of the Society!

(c) 33% suggested that the 2 guinea subscription was prohibitive; this was a particular criticism of the 2nd-4th years.

(d) 20% objected to the 'formality' of the Society's proceedings, though very few took the opportunity to elaborate on any particular aspects of this; furthermore, 50% of these had not been to any meetings, and so could not authoritatively comment on this point.

(e) 28% felt there was no feeling of welcome in the Society.

(f) 27% thought the Society's business too similar to the medical school curriculum.

Finally, 42% of students said that they would join the R.M.S. if changes were made along the lines suggested; 11% said they would not join, the remainder being undecided.

In view of the above figures, but bearing in mind the history and essential traditions of the Society, it seems reasonable that the Society's membership could be at least doubled (to 20% of the medical school) if public relations were improved and some meetings held on Wednesdays; and with better publicity and more imaginative topics, larger audiences could be assured at Public meetings.

Action is being taken on these lines, and there are already very promising signs of substantial improvement in membership and attendances.

● Maintaining a neutral attitude to Professor Christian Barnard is beset with the same difficulties as watching a Rangers-Celtic match without taking sides. Professor Barnard's address to the Society, which filled the George Square lecture theatre to capacity, was a victory for his supporters, and I suspect won over a few of his critics as well. His technique is not so much one of initially breaking the ice with his audience, as of causing complete liquefaction, using his charm as a catalyst and poetry and anecdote as his stage-props.

After a justification of heart transplantation, with an admission that the first operation was something of a step into the unknown, as all medical advances are to a greater or lesser degree, the real meat of the talk followed. Here we were told about the techniques employed

in replacing the recipient's heart muscle with that of the donor and the methods used for maintaining the circulation during this manoeuvre. Professor Barnard then discussed the rejection phenomena, the way in which this had been combated with a combination of Azathioprine, prednisone and A.L.G. and the extensive search that the South African team had made for a reliable indication that rejection was taking place.

A few photographs of recipients and of the hospital at Cape Town followed by one last poem, revived the men from Grampian, who had seemed a little bemused by all the technical jargon and saw Barnard bowing out to rapturous applause. And if one questioner did have the audacity to suggest that the Professor's experiments in heart transplantation with dogs had not met with 100% success, the audience were in no mood to swallow their angostura after the feast.

● Starting the 232nd. session with the chains of tradition falling from all parts of its body, the Society can be excused if at its first meeting it acted a little like a cat with two tails. The lady presidents were showered with bouquets and professor Perry, by combining his Inaugural Address with his dissertation to the Society earned himself a tankard of beer. The owner of the femur, which is still punished twice nightly under the hand of the Senior President, would no doubt be proud that the bone which served him (or was it her) for so long, is still in use. Perhaps the person who pinched the silver gavel will, even yet, one day return it.

Professor Perry in his address on "Trends in Medical Education", placed himself more in the camp of the radicals than the conservatives in this field, although he recognised the necessity for compromise. His lucid explanation

of the rationale behind the way in which the present Edinburgh medical course was constructed makes it easier for the student to accept those aspects of it which at first sight appear incongruous. The compromise in this case, it was explained, is a resolution of the need to provide the scientifically trained professional man and the immediate doctor. Perhaps the first of us through the mill will be more tolerant of teething troubles and Professor Perry's admission that the ideal has not yet been fully achieved, helps us to realise that much thought is still being given to the problem.

Let us hope that from his new job with the University of the Air, he will find time to return to Edinburgh. He will certainly not be soon forgotten.

SYLLABUS FOR THE SPRING TERM

January

- 10 Address: Professor Henry Millar, "Head-ache" (in Surgeon's Hall).
- 20 Talk: Dr. Ian Oswald, to be announced.

February

- 14 Address: Dr. C. A. St. Hill, "Suspicious Deaths".

March

- 5 Annual Extraordinary General Meeting.
- 7 President's Valedictory Address.

Member's Dissertations will be announced during the term and Business Meetings will be announced weekly.

The honorary editorial board and Miss Harkins and Mrs. Thompson once more deserve undying gratitude. We thank them again for their help and advice which they are always willing to provide.

OFFICE-BEARERS FOR THE 232nd SESSION

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BOOKS

Auscultation of the Heart (3rd. Edition) by R. W. D. Turner. E. & S. Livingstone Ltd. 6/-.

This is the third edition of a popular pocket-sized handbook, which originated from three articles written by Dr. Turner for *Res Medica* in 1960. The expansion of the text has greatly enhanced its comprehensibility, though the changes in the diagrams have not significantly elevated them beyond their former mediocrity. Dr. Turner once again emphasises the need for a methodical approach to auscultation, entreating that the student listen to only one thing at a time. He underlines the point by considering the events of the cardiac cycle in turn, passing from heart sounds to systolic and then to diastolic murmurs. Nevertheless, a short appendix systematically describing the auscultatory features of the various cardiac lesions in turn, would add to the value of the book. It is a volume which every clinical student must possess.

D.McL.

A Dictionary of Microbial Taxonomic Usage by S. T. Cowan. Oliver & Boyd. 42/-.

Microbial Taxonomy is a subject that few people show any inclination to venture into very deeply. Those who do are faced with outstanding problems in the classification, nomenclature and identification of micro-organisms. S. T. Cowan has actively participated in the International Committee on Bacteriological Nomenclature which was formed to discuss the problems involved in taxonomy.

In this text 'A Dictionary of Microbial Taxonomic Usage', he has contributed further with a concise account of taxonomic study as

it is today. The book brings to the forefront the difficulties and pitfalls of bacteriological taxonomy and includes explanatory notes on the various attempts to design a successful taxonomic scheme. Moreover, Cowan has defined principles that require to be followed in the laboratory and particularly in the literature, stressing these in respect of rules formulated at the meetings of the International Committee. A unique and sensible presentation that brings to one's attention the attempts being made to bring order to the chaos of bacteriological taxonomy.

G.G.C.

Acute Myocardial Infarction. Eds. D. G. Julian and M. F. Oliver. E. & S. Livingstone Ltd. 50/-.

This is a series of forty short papers, by cardiologists from all over the globe, presented to a symposium on Myocardial Infarction held in Edinburgh in September 1967.

These articles are concerned with the many aspects of the treatment of acute infarction, ranging from artificial pacing and specialised coronary care units, to digitalis and diuretics. Particularly interesting are those papers in which cardiac arrhythmias are considered. In the discussions, which are liberally interspersed among the proceedings, other participants in the symposium have an opportunity to air their views; many old questions are answered, while new ones are posed and considered.

One would require more than a casual interest in the subject to get very much out of this book.

D.McL.

Textbook of Medical Treatment. Eds. Dunlop and Alstead. E. & S. Livingstone Ltd. 75/-.

Sir Derrick Dunlop was one of the most well-known of teachers in the Edinburgh Medical School, and his active days as Professor of Therapeutics here are remembered with affection and gratitude by his students. We rarely see him in person now, but he still contributes to our medical lives to a significant degree, in print.

The well-known textbook of Medical Treatment, edited by Sir Derrick and by Professor Stanley Alstead now reappears two years after the old edition, in a retread version. The old layout has been abandoned in favour of a double-column page, giving Livingstone's a new, transatlantic look.

The vast knowledge of its team of Scottish contributors guarantees that the book remains as comprehensive and as authoritative as ever, new sections on anti-coagulants and iatrogenic effects, and a glossary of drug names, having been added. The whole thing is as up to date as a textbook can be.

The book is recommended to anyone with aspirations in medicine, and upholds the very fine standard set by previous editions.

J.E.H.

Medical Aspects of Fitness to Drive Vehicles. A Report by the Medical Commission on Accident Prevention. 5/-.

This monograph, designed for medical practitioners, contains nine chapters, each dealing with different aspects of disease in relation to driving. It also includes an appendix on 'Unwanted and dangerous interactions between drugs'.

Of particular interest are the chapters concerned with cardiac conditions and with ageing, problems which affect a sizeable proportion of the driving population. Professor Mary Pickford is the principal author of the chapter on fatigue and boredom, a factor of increasing importance in these nomadic days of mechanised transport. Particularly good are the sections on 'Suggestions and advice to patients' for they provide, in considerable detail, a well reasoned approach to this often neglected aspect of patient care.

The little time spent in studying this pamphlet would not be wasted for either student or practitioner.

J.W.

Modern Trends in Toxicology I. Eds. Boyland and Goulding. Butterworth & Co. 75/-.

Though this book is definitely for the specialist, it leaves the non-specialist reader with an uneasy awareness of the chemical hazards in the environment. Most of us live with the suspicion that the surfeit of new substances around us may include molecules mitching mallecho; bestowing ills tumours and monsters. These review articles summarise what is known in this gloomy area of biology. Toxic substances, their access to the human organism, their immediate or delayed effects and their visitations upon our children and upon our children's children, are reported with detached scholarship. The scope is wide, ranging from the dangers of food additives ('all will agree that cancer-causing agents should be avoided in foods wherever possible'), to the inevitable self-inflicted tobacco injury ('the most potent known carcinogen operating on man at the present time is cigarette smoke').

Read it, and scare your friends!

C.T.C.

Vascular Diseases by M. J. Tsapogas, V. V. Kakkar & E. N. Gleave. H. K. Lewis & Co. £2 10/-.

The authors of this excellent book have culled their extensive experience from many years of research in the field of vascular disease; including work at King's College Hospital and at the research establishment of the Royal College of Surgeons of England. They have now published a textbook on this subject, which is both lucid and interesting. It covers all aspects of vascular disease, and includes an introductory chapter on the assessment of the vascular patient which is enormously helpful to medical students, especially to those approaching clinical medicine for the first time. Diagnosis, special investigations and the indications for conservative or for surgical treatment are made abundantly clear and reasonable. The presentation of the book is, on the whole, a clinical and practical one which many of its student readers will appreciate.

The illustrations and diagrams are very good, appropriate and illuminating and the style is crisp, concise and readable. From this book one may painlessly absorb a great deal of knowledge, and yet read it with pleasure and enjoyment.

M.F.O.

Principles of X-Ray Diagnosis by D. H. Trapnell.
Butterworth & Co. £6 10/-.

This well planned and explicit publication must be of interest, and of substantial value, not only to the postgraduate for whom it was primarily produced, but to a greater proportion of senior medical students than was initially envisaged.

The introductory chapters are informative and interesting, and those following present a logical and very complete discussion of the evaluation of the information available from radiographs. Many senior students might benefit from such a concise introduction to the subject and the more advanced information follows very readily for those pursuing post-graduate courses of study.

It is to be hoped that the daunting cost of this book does not limit the circulation, placing it on the shelves of reference libraries only and thus rendering it less easily available to the readership it properly deserves.

M.J.R.

Elements of Medical Genetics by Alan E. H. Emery.
E. & S. Livingstone. 35/-.

Little more than a decade ago it was shown for the first time that the normal human cell contains not 48 chromosomes but 46. The M.R.C. unit in Edinburgh is today thinking in terms of karyotyping whole populations at birth by a fully automated system utilizing advanced techniques and sophisticated computer programming. This is a measure of the explosion which has occurred in genetics in recent years and an indication of the likely impact on medicine in the future.

Hand in hand with cytological advances have gone those in biochemical understanding and Professor Emery has attempted to relate the altered position in genetic knowledge to the needs of medical practice today. In this he has met with great success and both student and physician are provided with a comprehensive account of the fundamental changes in understanding which have occurred in relation to individual, family and population.

It is a tribute to the author that he has been able to cover the wide field of medical genetics whilst keeping technical terms to a minimum. The result is both readable and instructive and extensive references at the end of each chapter enable topics in which especial interest has been created to be easily pursued further.

P.D.B.

The Principles and Practice of Medicine (9th. Edition) by Sir Stanley Davidson. E. & S. Livingstone Ltd. 45/-.

Thomas Fuller's dictum that "Learning hath gained most by those books by which the printers have lost" is sure to be refuted once more by this latest edition of *The Principles and Practice of Medicine*. The ninth edition is similar in style to the eighth, emphasis being on those common disorders encountered in practice with preceding summary of the anatomy and physiology relevant to each section. Useful additions appear in the chapters on Nutritional Disorders, Diseases of the Pancreas and Diseases of the Liver and Biliary Tract.

Professor Carstairs' rewriting of the Psychological Medicine section is directed towards the neurotic and psychosomatic symptomatology likely to be encountered by the non-specialist physician in day to day practice. A short resumé of psychotropic drugs is an addition which recognises that both medical and illicit use of these agents should be familiar to every practitioner.

The updating of all sections has not led to any increase in length and despite the slight price increment this is a book which must have high claim to being perhaps the best value amongst general medical texts now available.

A.D.D.

Development of the Brain by W. A. Marshall.
Oliver & Boyd Ltd. 7/6d.

Most medical students quail at the thought of learning neuroanatomy after having spent a year studying systematic anatomy in their second year. Consequently all new texts on this subject are eagerly awaited, scanned, and then usually rejected. Let there be no doubt that this is not an examination-cramming book; rather a lucid volume purely for leisure reading — it does not even have an index. It does however succeed in what it sets out to do. It provides a very elementary picture of brain development and includes a consideration of brain-waves, neurobiochemistry and the influence of the endocrine system on cerebral development and metabolism.

For the aspiring neurophysiologist this work is not adequate; for the average medical student it is a useful little book.

A.K.T.C.

In this monograph Professor James attempts to assist the young orthopaedic surgeon by presenting a careful review of the confused literature on scoliosis. Assessing his subject with the authority gained from twenty years of practising interest and drawing on research from the Edinburgh Orthopaedic Service, he first defines the terminology of scoliosis, aided by well-chosen radiographs and by clinical photography. He then proceeds to consider the differential diagnosis, aetiological evidence, classification and treatment. Included also are notes on the inheritance of scoliosis and on its medical aspects. The treatments discussed are those which involve special immobilisation and traction and also the definitive surgical correction. Throughout the book stress is laid on the importance of the surgeon's relationship with both the patient and the parent, in what may be a protracted period of orthopaedic supervision.

Progressive idiopathic scoliosis deforms cruelly and shortens life by its cardio-respiratory consequences. Early recognition is thus paramount and the undergraduate will find it valuable to read the earlier chapters. He will not regret the time spent and will enjoy a book which is marked by its clarity of language and organisation, and by the quality of its illustrative photographs, which are well integrated with the text. Professor James' style is attractive and dogmatic, though always supported by evidence. His book should arm well the postgraduate who progresses to the wider literature on scoliosis, to which he will find full references are given.

W.L.C.

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ANSWERS TO DIAGNOSTIC PROBLEM

(See page 27)

A. The lesion lies in the left basal ganglia and neighbouring structures: the left corticospinal tract at the level of the internal capsule, the somatic sensory system in the region of thalamus and the hypothalamus (change in appetite, weight gain, excessive thirst). The most probable lesion is neoplasm.

B. The ventricular system would be distorted by a mass lesion in this region, and lumbar air encephalography is therefore indicated. This confirmed the site of the lesion, but suggested that it might arise from the brain stem. Vertebral angiograms were therefore taken, and showed an aneurysm on the trunk of the left posterior cerebral artery. The region which filled with dye was not large enough to produce the distortion seen in the encephalograms and it was therefore concluded that the aneurysmal sac was large, but mainly filled with thrombus.

C. Acute hepatic failure.

At autopsy the liver showed a gross macronodular cirrhosis, most probably due to previous subclinical virus hepatitis. Nothing in her history or examination suggested the presence of cirrhosis, and the earliest development raising the possibility of liver disease was the abnormal bleeding tendency noted at the first operation.

A large aneurysm was found arising from the trunk of the left posterior cerebral artery and extending upwards and backwards into posterior hypothalamus, left basal ganglia and brain stem: there was extensive destruction of brain tissue and such a lesion would inevitably have carried a fatal prognosis, without the additional problems arising from her liver disease.

Thus although neoplasm is the commonest lesion in this site the possibility of vascular lesions such as aneurysm or angioma should also be considered.

Acknowledgment

This patient was under the care of Professor F. J. Gillingham and his permission to report this case is gratefully acknowledged.

Speech and Hearing Science by W. Zemlin. Prentice Hall International. 102/6d.

Assuming no previous exposure of his readers to the biological sciences, Professor Zemlin aims to provide "a manageable overview of the field of speech and hearing".

Man, anatomy and physiology are defined and the cell, basic tissues, organs and body systems are described in Chapter One, which features Gray's Anatomy in its selective reading list. A lengthy discourse on the mechanism of breathing must be negotiated before basic structure and the mechanism of phonation is reached. The section which might be expected to provide a review of the nervous mechanisms in speech and hearing, proves to be a revision course for consultant neurologists. One would expect the potential readership of this book to be relatively small, anticipating that most medical students and specialists in this field would already have had considerable contact with biological science.

J.M.R.

Industrial Dermatoses and The Industrial Injuries Act by J. T. Ingram. J. & A. Churchill Ltd. 10/-.

This monograph by the Emeritus Professor of Dermatology, Newcastle upon Tyne, deals mainly with the complex problems of industrial diseases and injuries affecting the skin. Attention is focussed on the relation of these injuries to the Industrial Injuries Act. Procedures under the Act and Medical Board and Appeal Tribunals are explained and clarified. Scheduled Prescribed Diseases are succinctly classified and non-infectious dermatitis of external origin is described in the following chapter.

As the Act has in the past led to much confusion, a section is devoted to "Suggested Modifications" in which clarification of several aspects are considered. To complete this forty page booklet, management, diagnosis and treatment is reviewed from the point of view of the Industrial Injuries Act and fifty or so illustrative cases put the numerous points discussed in their true perspective. E.A.H.

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