fact, I have once seen a small longitudinal tear in the lateral sinus in a case of head injury without any fracture of the skull. In Case 2 there was a fracture on the right side of the skull, showing that severe stress must have occurred in the neighbourhood of the lateral sinus, and it seems to me probable that the dura forming the wall of the sinus was damaged by the same deformation as caused the fracture in the squamous bone.

In some, and probably all, of these cases there were abrasions or small lacerations of the scalp, and in one case a very large haematoma underlying it. In no case was there obvious infection. Thrombosis may have extended inwards from damaged small veins passing into the diploë, and thence the thrombus may have extended into the sagittal or transverse sinus. In some of the cases of Holmes and Sargent (1915) the outer table only of the skull was damaged, a gutter being left with diploë in its base, and it was evident that such wounds were sufficient to cause thrombosis in the sagittal sinus by spread from the vessels of the diploë. In Case 5 of this series the haematoma under the scalp probably arose from torn emissary veins, and the damaged vessels would afterwards become thrombosed. Such extension of thrombosis must therefore be taken into consideration. Moreover, we know that when infection is present this mode of extension of thrombosis is frequent and provides a potent vehicle for the transference of infection (Turner and Reynolds, 1931). In this way infection is conveyed from the mastoid cells into the substance of the brain, to give rise to a cerebral or cerebellar abscess, and in this way infection is conveyed from a pustule on the face, to cause thrombosis and infection of the cavernous sinus. If there had been any evidence of septic infection in our cases we would have had to admit this mode of spread, and possibly it may have obtained even though there was no sepsis. Non-septic infection may have been present, or the clot may have spread without any infection. If, however, extension of thrombosis by way of diploic vessels were an important factor in causing sinus thrombosis after trauma one would expect this complication of head injuries to be much more frequent than it is, since abrasions or lacerations of the scalp are seldom lacking.

On the whole, therefore, it seems likely that injury of the dura is the more important of these factors.

Summary

Five cases are described in which signs and symptoms attributed to obstruction of the superior longitudinal sinus occurred after closed-head injuries. In four of the cases the manifestations were closely comparable to those of otitic hydrocephalus: in the remaining case the full syndrome described by Holmes and Sargent developed.

Damage to the dura in the wall of a sinus and extension of thrombosis inwards from abrasions of the scalp or damaged emissary veins are probably the most important factors causing sinus thrombosis in such cases.

Since the superior longitudinal sinus usually turns into the right transverse sinus, a major importance, so far as this complication is concerned, attaches to injuries in the neighbourhood of the right transverse sinus.

ADDENDUM.—Foley, J. (*Brain*, 1955, **78**, 1) has described similar cases of benign hydrocephalus following head injury.

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CHLORPROMAZINE AND OPERATIVE STRESS IN A TROPICAL HOSPITAL

BY

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In Jamaican patients of the poorer classes the reaction to surgical intervention is excessive and therefore dangerous. Ill-judged or badly administered anaesthesia or inefficient resuscitation quickly leads to circulatory collapse; violent fluctuations in blood pressure are the inevitable result of moderate traction on abdominal viscera; and even the biochemical effects of anaesthesia and surgery are more pronounced than in the European patient.

Sudden circulatory failure may follow a long or short period of bad anaesthetic management, but it is more often due to a combination of slow haemorrhage and autonomic reflexes from the operation site. These reflexes may stall the heart by direct action through its control mechanism, or the main effect may be on the peripheral vascular bed, which becomes so expanded that the heart receives too little blood to carry on its own circulation. Prolonged anoxia due to undetected or uncontrolled bronchospasm, in an otherwise healthy patient, may cause death towards the end of a long operation. In none of these cases does the pathologist find a plausible cause of death. Malnourished elderly patients suffering from slow haemorrhage cannot withstand sudden peripheral vascular dilatation, nor can the effects of sixty years of undernourishment be corrected by two weeks in hospital and two pints (a litre) of blood.

Anaesthetic and resuscitation methods in this hospital do not differ materially from those in Great Britain except that low spinal or extradural blocks are more often employed in superficial operations.

For the past three years efforts have been made to develop anaesthetic methods which would not worsen the poor risk presented by the patient of 60 suffering from nutritional anaemia or nutritional cirrhosis of the liver, with alteration in the serum protein ratio and a systolic blood pressure fluctuating, even under resting conditions in the ward, by 40 mm. Hg. Spinal analgesia was tried in combination with light general anaesthesia, but it was not found effective in stabilizing the circulation—even in pelvic operations. The post-operative condition of patients given deep ether or cyclopropane anaesthesia would not be regarded as satisfactory by an anaesthetist, and in many cases their use during operation is precluded by the diathermy. The nearest approach to a solution of the problem was found in the employment of what is now a familiar technique: induction of anaesthesia with thiopentone and maintenance with nitrous oxide and pethidine usually combined with a relaxant. This has reduced but not abolished the incidence of dangerous vasomotor reactions. The appearance of a group of drugs which were claimed to abolish or at least damp excessive autonomic reaction to operative stress was welcomed.

Racial Reactions to Anaesthesia

It is unfortunate that little work has been published on the reactions of a population such as the Jamaican to surgery

and anaesthesia, for the clinical picture is sharp and the results of effective or ineffective treatment are unmistakable.

Barlow *et al.* (1953), in South Africa, state that race influences mortality from anaesthesia and that in the metropolitan countries the death rate for negroes during surgery is undoubtedly higher than for Europeans. Trent and Gaster (1944) report that in the United States a study of 54,000 anaesthetics showed that, while only 15% of the patients were negroes, 66% of the operating-room deaths occurred in them. Figures from South Africa indicate a death rate of 17.6 per thousand on the table, or non-recovery from anaesthesia, in Africans. This was reduced by careful resuscitation before and during operation and by better anaesthetic management to 3.9 per thousand (Barlow *et al.*, 1953). Meltzer (1947), also from South Africa, reports the death rate from anaesthesia in Africans as 7.45 per thousand, the corresponding rate for local Europeans being 1.6 per thousand. There is, however, some evidence that Europeans living in a tropical climate have a higher operative death rate than those in their home countries.

The original French reports on the phenothiazine group of drugs give the impression that the nitrous-oxide-pethidine-relaxant technique was not familiar there; moreover, the large number of drugs used in the "lytic mixtures," which include pethidine, arouses some doubt about which drugs were responsible for the alleged reduction in surgical shock. The common-sense treatment of haemorrhage is to replace the blood lost before the physiological balance of the body is upset and the "chain" reaction following the "alarm" has been set in motion. The prolonged ill effects of overaction of the sympathico-adrenal system is only now being appreciated by surgical and anaesthetic staff. It is not intended to discuss the genesis of operative stress in this report, but there is biochemical evidence that, in patients undergoing surgery here, there is excessive action of the sympathico-adrenal system, commencing shortly after incision and lasting long after the operation is over (Keating and Hill, 1955). It is well to point out that sympathetic activity does not always cause a rise in blood pressure, and the sudden fall in blood pressure due to traction and irritation of the sympathetic ganglia may well be due to action of the vasodilator nerves reported by Uvnäs (1954) to exist in the sympathetic system.

Properties of Chlorpromazine

Patients subjected to sympathetic ganglion block to reduce haemorrhage during operation appear to be in exceptionally good condition after operation—better than can be explained on the grounds of reduction of blood lost. In a few instances patients suffering from severe haemorrhage have been successfully treated by ganglioplegic drugs (Wyman, 1953). Overactivity of the sympathetic system decreases survival rates in animals subjected to stress, and they may be protected by sympathetic block (Goldstein *et al.*, 1952; Sawyer and Parkerson, 1953). Overactivity of the system also accelerates the onset of shock from haemorrhage or muscle trauma in intact dogs (Swingle *et al.*, 1938; Wiggers *et al.*, 1947). Anaesthetists have naturally been unwilling to put theories arising from these discoveries to the test in the human patient. French military surgeons did, however, use chlorpromazine to treat battle casualties in the Far East. This drug superficially resembles the ganglioplegics and possesses an anti-adrenaline action in animals (Courvoisier *et al.*, 1953). It has other useful effects in anaesthesia too: it protects the heart against chloroform-adrenaline fibrillation, potentiates the common analgesic drugs, depresses metabolism, and increases the survival rate in animals subjected to oligaemic shock; but those who have followed the published reports on cyclopropane since its introduction a score of years ago will appreciate the difficulty in estimating the value of new anaesthetic drugs and methods in the human subject.

Numerous favourable reports and reviews concerning the actions of chlorpromazine have appeared in the more widely

read journals, and it is no longer necessary to enumerate all its pharmacological actions in a clinical report. That it has an important depressant action on the hypothalamic nuclei controlling the neuro-vegetative system appears probable (Laborit, 1954), and it is interesting that damage to this area of the brain can produce acute or chronic dysfunction of the lungs, liver, kidneys, and coronary circulation (Mosinger, 1952), hence its use in the treatment of neuro-vegetative diseases of these organs. The sudden peripheral failure of the circulation occurring in patients is familiar to the anaesthetist working with a neurosurgical team. This effect is not produced by chlorpromazine, but it does appear in a modified form if a relative overdose of the drug is given.

Chlorpromazine hydrochloride ("largactil") has been used in this hospital for nearly two years, mainly in patients in whom violent blood-pressure fluctuations might endanger life. To avoid the confusion of polypharmacy and to determine the value of the drug, chlorpromazine alone was used as a supplement to the standard anaesthetic sequence, the precise action of which has by now become familiar.

As the reactions of our patients cannot be predicted on the basis of reports originating in Europe, it was decided to begin with small doses of chlorpromazine given intravenously half an hour before operation. The amount was gradually increased in the course of several months. If accidents are to be avoided the dosage of new drugs should be evolved for the local population slowly and by careful trials. No deaths which could be attributed to the anaesthetic or chlorpromazine occurred, although most of the patients were poor risks, few had a normal haemoglobin or blood protein level, and many showed biochemical or macroscopic evidence of liver damage. Special care was taken to avoid anoxia and to replace immediately all blood lost.

Present Investigation

This report is mainly concerned with a series of 150 patients given chlorpromazine as a supplement to nitrous-oxide-pethidine-based anaesthesia. The Table shows the type of operation and the number of patients in each group. In addition, 12 patients were given chlorpromazine as a supplement to spinal block administered for hernia operations. All were low- or medium-level blocks.

Type of Operation Performed in 150 Cases

Cholecystectomy	6	Excision of melanoma ..	2
Abdomino-perineal resection of rectum	8	Partial cystectomy	2
Abdomino-sacral excision of rectum	1	Gastro-enterostomy	7
Oesophagectomy	3	Laparotomy	12
Thoracotomy	5	Amputation of penis	2
Hysterectomy	5	Suture of perforated stomach ..	1
Wertheim's hysterectomy ..	3	Total gastrectomy	2
Partial gastrectomy	29	Amputation of leg	1
Resection of colon	4	Reconstruction of urethra ..	2
Resection of mandible	5	Elephantiasis of scrotum ..	
Thyroidectomy	8	(plastic repair)	2
Anastomosis of bowel	2	Spinal fusion	4
Radical mastectomy	11	Pneumonectomy	3
Prostatectomy	14	Lobectomy	4
		Thoracoplasty	2

Dosage of Chlorpromazine

The trial period showed that the pre-operative dose of chlorpromazine should lie between 50 and 100 mg. and that it was best given intramuscularly about two hours before the arrival of the patient in the theatre. The smaller dose was used in the elderly or hypertensive patient. When the effect was considered to be insufficient a further 25 mg. was given slowly intravenously, if possible half an hour before operation. Atropine, scopolamine, and narcotics were not found necessary after the preliminary trials. However, patients did vary appreciably, and to a great extent unpredictably, to this dosage, especially those suffering from hypertension. If, as is possible, the drug is altered in some way in the body before producing its characteristic effects, the high incidence of liver disease may account for the varying effects on the blood pressure. Patients under 45 were often alert though not nervous before operation, and psychic depression did not appear to be closely related to the blood-

pressure changes. No obvious reduction in the quantities of analgesics required to maintain anaesthesia was noted, but patients vary widely in their requirements of these drugs during surgery. If supplementary chlorpromazine is needed during operation it should be given intravenously, and a minimum period of at least fifteen minutes is essential between successive injections if marked post-operative depression of blood pressure is to be avoided.

Blood Pressure

A fall in blood pressure is the rule after premedication, especially in hypertensive patients, who show this effect with very moderate dosage of narcotics. The average pre-operative blood pressure in our patients before being given premedication was 135/75 mm. Hg.; half an hour after premedication the average systolic blood pressure was 25 mm. Hg. lower. In this group the pressure-drop from chlorpromazine did not exceed this figure. In 23 elderly hypertensive patients given atropine, 1/100 gr. (0.65 mg.), and morphine, 1/6 gr. (11 mg.), the average fall in systolic blood pressure was 51 mm. Hg. Sixteen hypertensive patients given chlorpromazine did not show a greater fall than this figure, but two had what was regarded as a dangerous fall in pressure and required L-noradrenaline to restore it to a safe figure. It is difficult to estimate the dosage for this group: too little allows the patient to reach the theatre in a nervous state, while a slightly increased dose produces severe hypotension.

This study has directed attention to the effects of narcotics on the immediate pre-operative blood pressure. It is, of course, well known that they cause a fall, but the extent of this fall in the hypertensive patient is not always appreciated. In most patients the blood pressure returned to a safe figure within thirty minutes of the beginning of operation. In the dosage used chlorpromazine did not show a clear advantage over pethidine in equal dosage in stabilizing the blood pressure, and sharp changes in an upward direction still occurred.

Eosinophil Count

It has been stated that the eosinophil count is a useful indication of adrenocortical secretion during surgery (Dougherty and White, 1944; Hills *et al.*, 1948; Thorn *et al.*, 1948; Almy and Laragh, 1949; Roche *et al.*, 1949). A fall of 50% in the absolute eosinophil count is regarded as evidence of cortical activity. Estimations of the uric acid/creatinine ratios in the urine were not done, and it must be admitted that the eosinophil count alone is not a reliable index of cortical function (Best *et al.*, 1952; Meyer, 1953). Total eosinophil counts were carried out during operation in 25 patients. In 15 no fall in the count occurred, in five the fall was less than the critical 50% and only in five did a 50% or greater fall occur. In 32 controls a fall in the total eosinophil count of 50% or over occurred, but this was delayed in 17 for up to two hours after operation. It is not possible to carry out biochemical estimations of the blood or urinary cortical hormones here. In all patients the white-cell count rose during operation. Haematocrit readings did not appreciably affect the results. Further investigations into the effects of chlorpromazine on adrenocortical function are required.

Effect on Blood Sugar and Pulmonary Activity

The blood sugar in Jamaican patients rises sharply during operation even when ether and similar volatile anaesthetics are not used. This effect is much more marked than in European patients undergoing similar operations under the same anaesthetic. The effect is certainly mediated through the sympathetic system, for it can be prevented by high spinal block or by ganglion-blocking drugs like hexamethonium or "arfonad." It is not suggested that chlorpromazine has a similar action as these drugs, but it was thought that it might have a similar effect on the blood sugar. Estimation of the blood glucose levels was made in 21 patients undergoing major operations in this series. In two only was there no significant rise in blood sugar; in 12 it rose to over double the pre-operative level; in five the rise was 50% above

the fasting level, while two showed a 30% rise. These figures may be regarded as usual for our patients undergoing major surgery. Chlorpromazine itself causes a slight rise in blood-sugar. We have not found that chlorpromazine prevents the rise in blood sugar resulting from operative stress.

The effects on pulmonary activity under anaesthesia are well marked. Only two patients in the series developed severe bronchospasm, but one was a "wet lung case" in which chlorpromazine alone was used as premedication. A subsequent operation in the same patient with an increase in the dosage was not attended by bronchospasm. A period of depressed respiration or apnoea requiring respiratory assistance is common after induction with thiopentone and pethidine. This was not usual with chlorpromazine. The stimulant effect on respiration attributed to the antihistamine group of drugs may be due to a local anaesthetic effect on the stretch receptors in the lungs (Dawes and Comroe, 1954), and certainly a lack of resistance to manual inflation of the lungs is well marked. None of the patients developed post-operative pulmonary complications, but these are uncommon in this hospital irrespective of the anaesthetic used. Atropine was not used with chlorpromazine after preliminary trials, as the drying effect of the latter drug is sufficient in itself.

Other Effects

The bright red colour of the wound or operation field is characteristic and may be due to a reduction in the vasoconstriction common after injury to tissue. There were no complaints of excessive bleeding. After the initial fall in blood pressure due to premedication, a return to normal began within fifteen minutes of the incision. Although a rise above the immediate pre-operative level followed the incision, in elderly hypertensive patients it never reached the norm for the patient, and indeed remained low for up to forty-eight hours.

In two such patients who had not lost blood it was considered that the pressure was too low for safety and they were treated with L-noradrenaline ("levophed") successfully. No instance of failure of the blood pressure to respond to noradrenaline occurred, nor were excessive quantities of this powerful drug required. The pressor response inversion to noradrenaline, reported by Melville (1954), was not encountered.

Spinal anaesthesia below the level of T8 was supplemented by chlorpromazine in 12 instances. The fall in blood pressure due to the spinal block was aggravated by chlorpromazine, but not to an extent requiring treatment. The nausea occasioned by traction on peritoneum did not occur, and the patients slept throughout operation. The dose was 25 mg. given intravenously.

Intubation with the aid of succinylcholine was easy, but no reduction in the incidence of coughing or bucking from the foreign body in the trachea was noticed.

The effects of anaesthetics on the heart are naturally of concern to the anaesthetist, especially as pethidine and chlorpromazine belong to a group of drugs with similar action on the myocardium. The synergistic toxic effects of this family of drugs are of importance in cases where the heart muscle is already diseased (Calesnick *et al.*, 1952). Finkelstein *et al.* (1954) point out that in the cat heart papillary muscle preparation of Cattell and Gold chlorpromazine in a concentration of 0.1 to 0.5 mg. per 100 ml. in the bathing solution causes a negative reversible inotropic effect with a 40-60% reduction in the contractile force and decrease in the irritability of the muscle. Courvoisier (1953) found no electrocardiographic evidence of cardiac damage with clinical dosage in animals, but the existence of a normal E.C.G. does not necessarily prove that a drug is not a cardiac poison. Six patients had E.C.G. records made before and after the intravenous injection of 50 mg. of chlorpromazine. In one no abnormal effects occurred; four showed a slightly prolonged Q-T interval, but in one patient who was hypertensive the

Q-T interval was markedly reduced. I am indebted to Dr. Bunjé, lecturer in medicine, for reports on these.

The post-operative condition of the majority of patients was satisfactory, but they tended to lie still for prolonged periods and required careful watching to ensure a clear airway. Recovery is not so rapid as after nitrous oxide and pethidine, but less sedatives are required post-operatively.

Summary

Chlorpromazine has been used before and during induction of anaesthesia in 150 serious-risk patients in a tropical hospital with a view to reducing the incidence of sudden alterations in blood pressure due to over-sensitive autonomic reflexes occurring during major operations. It was not found possible to obtain figures which would show an obvious improvement over the standard technique using nitrous oxide and pethidine, and premedication with the opium alkaloids and scopolamine. Nevertheless, the drug is still being used, especially as a premedication before chest surgery. Overdosage is associated with hypotension and responds readily to a L-noradrenaline (levophed) infusion.

I am indebted to Messrs. May and Baker for initial supplies of largactil.

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The assistance which the World Health Organization gives to educational institutions, particularly to medical schools, is reviewed in the *Chronicle of the World Health Organization* for May (Geneva, 1s. 9d.). Political and economic changes resulting in a sudden shortage of senior teaching personnel, or recognition of academic insufficiency in their institutions, may induce governments to ask W.H.O. to assign them a visiting professor. During 1954 thirty-eight such assignments were made and a total of 515 "professor-months" spent on the project. Short visits by eminent scientists to underdeveloped countries were also arranged. The aim of the visiting professor is to help develop the local staff and to train someone to succeed him. The greatest deficiencies have been in the medical schools, where during 1952-4, 227 "professor-months" have been spent. A card index of experienced teachers willing to go abroad under W.H.O. auspices has been prepared, as well as an inventory of equipment needed for teaching medical subjects, in which the cost of each article is indicated. Where needed, medical literature, laboratory apparatus, and diagnostic and therapeutic instruments are sent with the professor, who trains the local faculty to use them. In Burma, Ethiopia, and Nepal institutions have been set up for training auxiliary staff to help in health work.

DESENSITIZATION OF NURSES ALLERGIC TO PENICILLIN

REPORT OF A CASE

BY

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"The position with regard to desensitization is confused. Some dermatologists state roundly that it is useless" (Ministry of Health, 1953). The chief object of the present article is to prove that nurses can be desensitized to penicillin—although desensitization of a nurse may be somewhat more difficult than desensitization of a patient.

When penicillin was first used for treatment it was thought to be completely non-toxic. Although time has on the whole justified this assumption, it was soon found that some patients are already, and that others become, hypersensitive to the antibiotic. The Ministry of Health report shows that many nurses have had to abandon their career on account of sensitivity to penicillin.

Review of the Literature

O'Donovan and Klorfajn (1946) successfully desensitized a patient by giving repeated doses of penicillin by mouth. Peck et al. (1947) evolved a technique for desensitization by giving progressively larger subcutaneous doses of penicillin. Garai (1949) found that a patient who was sensitive to sodium and potassium penicillin was insensitive to the calcium salt, and desensitized him with gradually increasing subcutaneous doses of calcium penicillin. Kalz and Prichard (1952) published reports of cases of penicillin sensitivity that were relieved by antihistamines. Maslansky and Sanger (1952) found that penicillin is less likely to cause reactions when it is mixed with an antihistamine. They believed that the addition of the antihistamine rendered the penicillin less prone to cause reactions. Beck (1953), however, showed that an antihistamine is as effective in preventing reactions to penicillin when it is given intramuscularly before the penicillin as when it is given mixed with it.

Roberts (1953) desensitized three workers in a penicillin-manufacturing plant with increasing doses of penicillin, using antihistamines to control the reactions and continuing the maximum doses for several months at decreasing intervals. Crofton (1953) showed that the antihistaminic action of diphenhydramine hydrochloride ("benadryl") did not interfere with the desensitizing property of streptomycin. Balme and Dormer (1954) were similarly able to eliminate the antihistamine from a mixture of mepyramine maleate ("anthisan") and penicillin when they had given maximum doses of the antibiotic to a penicillin-sensitive patient.

Case Report

On February 19, 1954, a nurse aged 24 was referred for treatment because her face swelled every time she came near penicillin.

She started training in April, 1949. One year later her eyelids swelled occasionally. Some months after this her eyelids swelled immediately she took penicillin tablets for a sore throat, and the swelling lasted for some days. It was then she noticed that the swelling of the eyelids always occurred after she had given penicillin injections. Consequently she avoided giving penicillin, so far as possible, during the remainder of her training. When she had qualified as a general nurse she did her midwifery training. During that time she never handled penicillin and her face never troubled her. In February, 1953, she took up duty in a nursing-home. Two weeks later her eyelids began to swell, and in a further