aged, physical deterioration is accompanied by rapid and marked chemical imbalance. Our principles for supportive therapy are :

1. Food is preferable to parenteral therapy. A high-calorie, high-protein, and vitamin-rich diet is important. The edentulous should be given cooked ground meat.

2. The daily water requirement of 2.5 litres may have to be doubled, with additional sodium chloride, in patients who have been dehydrated.

3. The daily requirement of 1 g. of protein per kilogram of weight may have to be doubled or trebled after operation, or in depleting diseases or infection.

4. Starvation produces both nitrogen and potassium loss. Low blood potassium may produce asthenia, flaccid paralysis, respiratory distress, and ileus. Bodansky (1950) gives potassium as beef broth or meat juices, or potassium chloride, 2-4 g. daily. Randall *et al.* (1949) recommend a mixture of 1 g. each of potassium acetate, bicarbonate, and citrate in 8 ml. of water: 4 ml. may be taken three times daily. For intravenous use, 2-4 10-ml. ampoules of 15% potassium chloride may be given in 24 hours. Repeated blood potassium determinations are required.

5. Patients with diminished cardiac reserve tolerate best a hypodermoclysis of 2.5% glucose in 0.45% solution of sodium chloride. If diuresis is poor, 50-100 ml. of hypertonic (25-50%) dextrose solution intravenously is recommended.

6. In alkalosis Bodansky (1950) has used a 2% ammonium chloride solution intravenously.

7. A controlled diet and insulin are indicated for the diabetic. In emergencies 5% glucose in saline intravenously, with one unit of insulin for each 2 g. of carbohydrate, is recommended.

Other Problems

Heart Disease.—An ageing heart, coronary sclerosis with myocardial fibrosis, and valvular defects do not necessarily contraindicate operation. Pre-operative digitalization is advisable unless there is a definite contraindication. In 100 necropsies, 27% of the post-operative deaths were found to be caused by heart failure and 3% by coronary occlusion. All the necropsies revealed varying degrees and types of cardiac pathology. Master *et al.* (1950) have stated that "patients with severe heart disease tolerate even major operations if adequate precautions are taken to avoid anoxaemia and coronary insufficiency." Our experience supports these observations. We have used digitalis to strengthen the myocardium, unless there was a contraindication. Irregular cardiac action on the operating table can be controlled by the intravenous use of 5 ml. of a 1 or 2% solution of procaine for ventricular arrhythmias or auricular tachycardia; oxygen and digitalis for interference in the conduction system; intravenous quinidine for ventricular fibrillations; and adrenaline and cardiac massage for cardiac arrest (Collins, 1950).

Anaesthesia.—Improvement in anaesthesia is a major factor in the increasing success achieved by geriatric surgery. Recent advances in anaesthesiology have contributed to reduce morbidity and mortality. Anaesthetists plan the anaesthesia for the individual patient and supply supportive therapy during operation. Pre-operative sedation should be minimal. Cyclopropane is the preferable general anaesthetic. Intravenous sodium thiopentone is favoured for short anaesthetics, with curare as an adjunct for long procedures. Local analgesia, without adrenaline, is very useful in selected cases. Intratracheal anaesthesia is used in thoracic and some oral surgery, and in prolonged upper abdominal surgery. Our service has had but one anaesthetic death in ten years.

Psychological Approach.—Sick old people respond to kindness and understanding. A frank, tactful, and optimistic manner, patience, and kindness will help understand-

ing and inspire confidence. They can convert an unco-operative or frightened patient to a more reasonable and hopeful frame of mind. Ministers in the various religious groups have been most helpful. A proper psychological approach can mean the difference between co-operation and a will to live, and frustration and a hope to die.

Summary

With scientific advance, improved techniques and anaesthesia, and better understanding of the degenerative processes accompanying old age, it is possible for geriatric surgery to provide more comfort in disabling diseases and to prolong life when it is threatened.

Our mortality statistics show a decline (5%) in elective and emergency surgery when the years 1939-44 are compared with 1945-9.

In emergency surgery the mortality rate will be from two to two and a quarter times that of elective surgery.

Our clinical and necropsy experience has pointed to methods of reducing mortality. Some of them are briefly discussed.

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THERMAL COAGULABILITY OF SERUM PROTEINS AND THE DIAGNOSIS OF MALIGNANT DISEASE

BY

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The publication from a reputable source of any laboratory test which may be of value in the diagnosis of malignant disease is a matter to be examined seriously.

Huggins *et al.* (1949) published the results of their investigations on the altered thermal coagulability of serum proteins in malignant disease. They described a test involving the use of iodoacetic acid which was said to increase the sensitivity of the discrimination between the sera of patients with malignant disease and those of healthy individuals and subjects with non-cancerous diseases. While these authors stated that the deficiency revealed in the serum in malignant disease was not specific, and that similar results were obtained in pulmonary tuberculosis and some acute inflammatory processes, their results were striking enough to demand further investigation. Some other groups of American workers have recently described their experience with this test. A series of tests was carried out at the Christie Hospital during the last year, the results of which are given below.

The iodoacetate test consists in exposing a given concentration of serum to increasing concentrations of iodoacetate in buffer at pH 7.4 and heating to 100° C. for 30 minutes. Iodoacetic acid reacts with certain linkages in the protein molecules and interferes with the coagulative process which normally occurs on heating. The end-point is found by estimating in which of the series of tubes the contents have just failed to remain fluid, and the quantity of iodoacetic acid thus required is related to the amount of protein present in the serum as an "iodoacetate index." Huggins and his co-workers at first described a certain technique; from this they later evolved a modified test in which the estimation of the end-point did not depend so much upon the personal opinion of the observer.

A trial of this later method (55 cases) convinced us that it was unreliable, and so in most of our tests their original technique has been used.

Blood for the tests was run into sterile tubes, allowed to clot for an hour or so, refrigerated overnight, and the serum removed aseptically and kept in the refrigerator for use. Each test was carried out in duplicate—the second test being made either concurrently or in the course of a few days. The interpretation of the end-point was made by one individual throughout, working entirely in ignorance of the origin of the serum. With few exceptions the duplicates gave reasonable correlation—either complete agreement or differing by one tube. The mean results were calculated when differences between duplicates occurred. In some tests the end-point was difficult to ascertain and in a few quite impossible (seven tests out of a total of 224). These latter occurred in individuals in whom the serum protein was high (8.2% or more) and the coagulation took place in flocules interspersed with clear fluid. The total serum proteins were calculated from the total nitrogen figures estimated by the micro-Kjeldahl technique.

All cases of malignant disease examined were new and untreated, and the pathology was confirmed histologically except in a few instances in which there was no doubt on clinical examination. No attempt has been made to relate the test to the clinical stage of the condition.

Results

The collected figures from our tests are shown in Table I and in histogram form in Fig. 1. In addition, a group of cases have been chosen to illustrate the relationship of

TABLE I

	Normals		Non-malignant Pathology		Cancer	
	No. of Cases	Test +ve(%)	No. of Cases	Test +ve(%)	No. of Cases	Test +ve(%)
Huggins <i>et al.</i> (1949) ..	100	0	95	16	85	100
Bodansky and McInnes (1950) ..	68	0	68	6	137	26
Homburger <i>et al.</i> (1950) ..	47	27.5	108	70	102	93
Homburger (modified technique) ..	46	0	30	23	51	78
Clifton (1949) ..	42	23	99	65	54	83
Jackson ..	38	26	63	80	61	64
Jackson (modified technique) ..	27	59	0	0	28	57

the test to various clinical conditions (Table II). The distribution of the total serum proteins in the three groups—normal, malignant, and non-malignant pathology—is shown in Fig. 2. It is commonly stated that the serum proteins diminish in malignant disease, but in the individuals we have studied the general distribution pattern is normal.

FIG. 1.—Serum coagulation test.

TABLE II

	Test Positive in
Carcinoma of tongue	3/5
Basal-cell carcinoma	1/6
Carcinoma of breast	4/11
Carcinoma of cervix	2/3
Leukaemias	6/7
Hodgkin's disease	3/4
Carcinoma of lung	8/9
Tuberculosis of lung	8/8
Pneumonias	10/10
Non-malignant pathology associated with haemorrhage ..	8/8
Total	53/71

FIG. 2.—Total serum proteins.

Discussion of Results

Huggins *et al.* (1949) selected an iodoacetate index of 8.99* as a dividing-line between normal and abnormal. Not one of their series of 100 normal sera gave an index less than this figure. Of 85 cases of proved malignant disease all except three were found to have an index of less than 8.99. The three exceptions were patients with carcinoma under treatment, stated to be apparently well controlled. Of the group of non-malignant pathology, 16 out of 95 cases gave a "cancer positive" test (Table I). All these "false positives" were stated to have serious disease. No further information was given of the types of malignant disease tested or of the varieties of non-malignant pathology included in the group, except that there were seven cases of pulmonary tuberculosis, all of which gave a positive test.

*A difference in end-point of one tube makes an alteration of 1 unit in iodoacetate index.

Clifton (1949) compared the results he obtained using three "cancer tests"—namely, an antiproteolytic reaction and thermal coagulation tests. Using the iodoacetate test, he found no significant difference in results whether the original technique of Huggins *et al.* or their later modification was applied. These results are shown in summarized form in Table I. In his entire series (235 cases) the overall accuracy in cancer diagnosis was only 55.5%.

Bodansky and McInnes (1950) found the original technique recommended by Huggins *et al.* unreliable and adopted their own modification of the second method described. Their results are summarized in Table I.

Homburger *et al.* (1950) published an account of their investigations and included a detailed list of cases. They used both techniques described by Huggins *et al.*, and, as we have done, made an attempt to assess the reliability and reproducibility of the test. They condemn the original method of Huggins *et al.*, maintaining that reproduction of the test by different investigators is impossible. They consider the modified method easier to reproduce and less complicated, but find the results so obtained at considerable variance with those from the former method (Table I).

Finally, Kiefer *et al.* (1950) carried out the modified technique of Huggins *et al.* on 700 apparently healthy men and women. All except six gave values higher than 9.3. These latter were found to give figures greater than 9 on repetition. Of 25 cancer cases run as controls, 76% gave a positive test. According to these workers "the thermal coagulation end-point is striking and reproducible," and "in no instance did multiple determinations of the end-point upon the same specimen vary more than one tube."

The results of the six groups of investigators clearly show no consistent correlation, so that the conclusion is inevitable that the test as such is valueless. The figures obtained by Clifton (1949), Homburger *et al.* (1950), and ourselves, all using the original technique, are directly comparable, and contrast sharply with the results quoted by Huggins *et al.* (Table I).

We had hoped that the test might have some application in the diagnosis of malignant disease in the chest or abdomen. In our experience, however, strongly positive tests were nearly always obtained in acute and chronic inflammatory lesions of the chest and in haemorrhagic states in the alimentary tract not associated with malignancy (Table II).

The conclusion, therefore, is that the change in serum proteins manifest as altered thermal coagulability is not invariably present with malignant disease, even in clinically advanced lesions, and also occurs in a high proportion of cases with non-malignant pathology and even in apparently healthy individuals. The cause of such a change is not necessarily related to an alteration in the total serum proteins. The nature of the change is as yet obscure.

Summary

The thermal coagulability of serum proteins in the presence of iodoacetic acid has been examined in 65 normal individuals, 89 cases of malignant disease, and 63 patients with other diseases.

An "iodoacetate index" has been calculated for each serum; this has been used to assess changes in the coagulability of serum proteins in relation to disease. The distribution pattern of the figures so obtained leads to the conclusion that the determination of such an index is useless in the diagnosis of malignant disease. Not only may serum from apparently healthy individuals furnish iodoacetate figures falling into the index range suggested for cancer cases, and vice versa, but most cases of non-malignant disease gave values in the "cancer range."

The test also reveals no consistent correlation between "iodoacetate index" and the severity of the malignant condition; even advanced cases of cancer may give figures in the "normal range."

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KELL-CELLANO BLOOD GROUP SYSTEM IN PREGNANCY AND TRANSFUSION

BY

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Coombs, Mourant, and Race (1946) described a new antigen-antibody system (Kell) unrelated to the Rh system but nevertheless capable of producing haemolytic disease of the newborn. More recently, Levine *et al.* (1949) found another antibody (Cellano) which also caused haemolytic disease of the newborn, and showed that the Kell and Cellano genes are alleles. They suggested that the symbols K and k, previously employed to represent Kell-positive and Kell-negative, be used to indicate the presence of the Kell and Cellano genes respectively, and calculated that the three genotypes, KK, Kk, and kk occur with frequencies of 0.2%, 8.6%, and 91.2% respectively among white Americans.

Six examples of anti-Kell are noted in their paper and at least a dozen others are known at the present time (R. R. Race—personal communication). The Kell antibody in the case described here was discovered at the Sheffield Blood Transfusion Centre in 1948 (Dunsford, 1949), and is exceptional in reacting in saline but not in human serum or bovine albumin.

Case History

The patient, aged 38, was first seen on March 12, 1948, when she was admitted to hospital at the 33rd week of gestation in her third pregnancy, on account of intrauterine foetal death. Her previous obstetrical history, which was somewhat chequered, was as follows.

1. On March 1, 1929, she gave birth in her own home to a living female mature infant weighing 9½ lb. (4.3 kg.). Post-partum haemorrhage occurred and she was removed to a non-obstetrical general hospital, where two blood transfusions were given on the day of admission, each transfusion apparently of one pint (570 ml.) and each from a separate donor. Septicaemia supervened, but full recovery occurred after four weeks, when she was discharged. Unfortunately the transfusion records could not be found and so the donors could not be traced.

2. A stillborn male mature infant was born at home on January 21, 1932; weight unknown. Foetal movements were not felt by the patient for six weeks before delivery. No investigations were made. She divorced her husband in 1936, but remarried in June, 1947. The first husband, unfortunately, cannot be traced, and so no investigations on his blood are possible.

3. On March 16, 1948, a stillborn macerated male foetus was delivered; gestation 34 weeks. She had booked for home