the supporting and the supported categories within a population, and with the increasing disparity between the number of mouths to be fed and the available food resources of the world, the problem that the *bouche inutile* creates gains in importance. In this country within the National Health Service it is already being found that the existing facilities cannot cope with newly discovered and enlarging needs. The authorities concerned are being forced to give serious consideration to the construction of a calculus of priorities. Great, therefore, becomes the need for the provision of the means whereby greater and more detailed knowledge concerning the variety and the needs of the public for those services can be secured. The changing age-structure and the changing pattern of morbidity are prominent among the factors that are creating the demand for the expansion of medical and hospital services at a time when the financial resources of the nation are strained.

It is to be remembered that in their beginning the medical services were encouraged because it was thought that such medical intervention would prove itself to be a sound business proposition. It would certainly seem that the reasons for the encouragement of medical research and of the practice of preventive and of curative medicine have changed, though not completely, since then. It would be difficult to maintain that the medical care of the old, permanently disabled by chronic illness, or of the idiot and imbecile beyond all human aid is economically desirable. Such matters are not to be considered in economic terms, for moral principles are involved. They do not create difficulties within the medical profession, for this is governed by an explicitly stated code; but they do constitute problems of profound difficulty and complexity for society as a whole. There is to be discerned a growing interest in such matters as the sterilization of the unfit and euthanasia, which can be regarded as an indication that the gravity of the problem is becoming recognized and that the search for a possible solution has begun. I refer to this matter only to attract your attention to the possibility that in the future the social ethic may come to be in conflict with the ethic that at the moment prevails within the profession of medicine.

Changing Needs

The medical ethic in its origin and development was associated with the development of the profession of medicine as a body concerned with the diseases of individuals. It regulates the relationship of physician and patient, often as intimate a relationship as that of the confessional. Like the Church, the medical profession would seem to claim that it is concerned with matters outside the province of the State, that its obligations are to the individuals that seek its aid, and that it is not in any way concerned with the social consequences of its benevolence. Concerning many matters of interest and importance to society—contraception, sterilization, euthanasia, divorce, for example—there are medical aspects. But concerning them there would seem to be no purely medical opinion, but merely the conflicting views of medical men and women whose attitude towards such matters as these is moulded by their sincerely held religious faiths, so that the opinions expressed derive their strength therefrom.

Yet it is with such matters as these that those medical men and women who serve in the field of population medicine, of medicine as applied to the affairs of the population as a whole, are becoming increasingly involved. They are required to present to the departments of government or to committees of local authority a purely medical opinion concerning them and to relate this to the action that is being considered. Such expert opinion commands the serious attention of those whose responsibility it is to consider and weigh all relevant knowledge and opinion and translate this into scheme and project.

It is not improbable that public opinion in this country concerning the value of the individual life, beginning at the moment of conception, will change. Indeed, there is plentiful evidence that both among the general public and within

the medical profession it is already changing fast. The social ethic, like the law that sustains it, is mutable. It may come to be regarded as ethical by the great majority of the general public to terminate the life that from birth is imprisoned in a body without a brain or to bring to a peaceful ending a life that flickers fitfully in a body that is tortured by agony beyond endurance. Should this happen, will the ethic of medicine remain inviolate or will it become modified as the social ethic changes?

If not, then it is not improbable that in the future the ethic of the medicine of the individual and that of the medicine that is applied to the affairs of society as a whole may come to differ, to make even greater the divergence in respect of their philosophies that even now distinguishes them. The ethic of the former belongs to an age that is swiftly passing and is becoming inappropriate to the circumstances of a world in which the major quest is for social amelioration rather than for personal continuance.

The major obligation of medicine in increasing measure will be towards society, and medicine will continue to be one of the most potent instruments that society will use for the achievement of its aims. It will be for medicine, along with the other social sciences, continually to examine and to define the changing and enlarging needs of socialized man, in respect of health conservation and augmentation, and for politics to design and to provide the means whereby society can be so shaped that these needs are satisfied.

But all such endeavour must remain barren unless the citizen, knowing its value, desires health and, seeking it, eagerly and intelligently makes use, in the conduct of his private and public life, of the knowledge and of the facilities thus made available.

TREATMENT OF POLYCYTHAEMIA RUBRA VERA*

BY

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The cause of polycythaemia rubra vera remains unknown; indeed, the very nature of the disease is still debatable, although perhaps a majority would favour its inclusion with leukaemia in the group of unexplained, and apparently purposeless, mesenchymal proliferations. Our ignorance limits treatment to the empirical and the symptomatic. In general the therapeutic aim has been to maintain a normal blood count. It is therefore pertinent to inquire whether its achievement relieves the patient's symptoms or prolongs his survival, and in what manner the disease terminates.

Associated Diseases in Polycythaemia Vera

There are symptoms, such as a sense of fullness in the head, vertigo, flushing, dizziness, and pruritus, which can be attributed without question to the changes in the blood and which disappear when the erythrocyte count falls to normal. They need to be separated from those of vascular degeneration, arterial hypertension, gout, peptic ulcer, renal calculus, and other common companions of polycythaemia vera. Videbaek (1950) has shown that the disease, as treated in the past, shortens the expectation of life; in his patients the mean survival from the time of diagnosis was six years for men and nine for women (Fig. 1). Whether maintenance of a normal erythrocyte count prolongs

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FIG. 1.—Percentage of patients with polycythaemia vera surviving at the end of each year compared with the survival for the general population of the same age (Videbaek, 1950).

survival is unknown, because no series of untreated cases is available and because satisfactory control has been exceptional. Videbaek's figures will provide a useful yardstick for measuring the efficacy of newer methods of treatment, but they show that a long period of observation is required before any conclusions are justifiable.

The causes of death in polycythaemic patients are relevant to this question of survival. It is a disease of middle and later life, and it is not surprising to find it accompanied by the degenerative states common in these epochs. Table I

TABLE I.—Associated Conditions in 36 Patients with Polycythaemia Vera

Arterial thrombosis:	
Cerebral	4
Mesenteric	3
Coronary	2
Limb	1
Thrombophlebitis	2
Peripheral arterial disease	2
Hypertension	8
Duodenal ulcer	2
Gastric ulcer	3
Intestinal haemorrhage	2
Renal calculus	2
Pylonephritis	1
Diabetes mellitus	3
Gout	1
Various	3

shows the frequency of complicating disease in the present series of 36 patients, and is representative of the larger experience of other authors. Vascular disease occupies the first position; but peptic ulceration, renal calculus, and gout are all more common than in patients of like age without polycythaemia.

The causes of death reveal the importance of these associations (Table II). It is rare for death to be immediately attributable to the progress of the polycythaemic process; perhaps the examples of leukaemia and the even less

TABLE II.—Causes of Death in Polycythaemia Vera (from Lawrence, 1949; Videbaek, 1950; Stroebel, Hall, and Pease, 1951)

	Not Treated with P ³²		Treated with P ³²		S.E. of Difference
	No.	%	No.	%	
Vascular accidents ..	56	52	17	39.5	8.87
Leukaemia ..	6	5.6	10	23.3	6.8
Other causes ..	46	42.4	16	37.2	—
	108		43		

common instances of secondary myelosclerosis fall into this category. More than half the deaths are due to vascular accidents, most frequently thrombotic; calculous pyelonephritis accounts for as many as 18% in one series (Videbaek, 1950), and leukaemia for 6%, while causes apparently unrelated to polycythaemia are responsible for the remainder.

Aims of Treatment

There is no evidence that vascular degeneration is more common in the polycythaemic patient than in others; it is logical, therefore, to attribute the frequency of thrombosis to the increased viscosity of the blood, and reasonable to hope that maintenance of a normal count will diminish, or at any rate defer, the incidence of such catastrophes. Renal calculus depends on the increased excretion of urates, a product of the bone marrow's overactivity, rather than on the elevated erythrocyte count; its control by measures which discourage this activity might be anticipated.

Restraint of the hyperplastic bone marrow seems, therefore, to be a rational treatment. It would control the erythrocyte count and relieve the "true" polycythaemic symptoms. The restoration of normal levels, both for erythrocytes and for platelets, might be expected to diminish the risk of thrombosis. Uric acid excretion, the increase in which is probably a function of bone-marrow hyperplasia, should fall to normal, lessening the danger of stone and renal infection. It must be stressed, however, that, although these effects can logically be anticipated, there is as yet no incontrovertible proof that, excepting the relief of true polycythaemic symptoms, they do in fact occur.

Methods of Treatment

From what has been said it will be clear that treatment of patients with this disease is often a matter of complexity: arterial or venous thrombosis, dyspepsia, gout, or renal calculus may dominate the picture, and the management of these disorders against a background of polycythaemia may call for many difficult decisions. This communication, however, concerns itself only with methods of controlling the polycythaemic process and not with these problems of general management.

Until recent years the two therapeutic measures in common use were venesection and the haemolytic agent phenylhydrazine, either alone or in combination. By these means many patients have been kept free from symptoms for long periods, but both methods have practical and theoretical disadvantages. Repeated bleedings and the haemolysis occasioned by phenylhydrazine are bone-marrow stimulants, and, although the erythrocyte count may be kept within bounds, there is no like effect on the leucocytes or the platelets. The dosage of phenylhydrazine is difficult to control and its action is sometimes unexpectedly abrupt. More important is the iron deficiency which results from continued venesection: in many patients treated in this way chlorotic polycythaemia (Rosenthal and Bassen, 1938) appears, the haemoglobin reading falling below normal although the erythrocyte count remains high. An impasse is reached in which the increased viscosity of the blood and its attendant perils demand further bleeding, which will inevitably reduce the haemoglobin level enough to cause anaemic symptoms.

During the past decade, chemical and radiotherapeutic methods of treatment have been devised which meet our theoretical requirements better than the two already discussed, in that they aim to abolish the bone-marrow hyperplasia. Nitrogen mustard is representative of the first group and will certainly procure remission in many patients. Its action is short-lived, and relapse usually occurs within six months (Spurr, Smith, Block, and Jacobson, 1950); moreover, its side-effects are often unwelcome. The folic acid antagonists have been used, but results are indifferent (Bell and Davis, 1950). Radiotherapy is undoubtedly more satisfactory. It is best applied by total body irradiation (Richardson and Robbins, 1948), and the results are excellent. Only three patients of the present series were treated

FIG. 2.—Polycythaemia vera in a woman aged 50. Satisfactory control with venesection and radioactive phosphorus.

in this manner, and good remission was obtained in all; one of them remains well after more than three years. The method is, however, cumbersome, and treatment may take several weeks.

Radioactive Phosphorus

A more convenient means is by the administration of the radioactive isotope of phosphorus, P^{32} . This was first employed in 1940 by Lawrence, and the results in several large series have been published in the United States (Erf, 1946; Reinhard, Moore, Bierbaum, and Moore, 1946; Lawrence, 1949; Stroebel, Hall, and Pease, 1951; Wiseman, Rohn, Bouroncle, and Myers, 1951). The following remarks are based largely on these reports.

P^{32} is prepared from red phosphorus by one of several methods; it decays at a constant rate, emitting only beta rays, and has a half-life of 14.3 days. Its radioactivity is measured in millicuries, one millicurie being that amount of radioactivity produced by the disintegration of 37,000,000 atoms per second. When administered, P^{32} is incorporated in the nucleoproteins, particularly of rapidly dividing cells, and finds its way mainly to the bone marrow, liver, spleen, lymph nodes, bones, and teeth. Given intravenously 5–25% is excreted, chiefly in the urine; by mouth the loss is 15–50%, largely in the stool. About 75% of an oral dose is absorbed. In the average adult, 1 mC of P^{32} emits on the first day radioactivity equivalent to about 0.6 roentgen unit given by total body irradiation, or 12 roentgens during the time required for complete decay. In healthy monkeys its effect is shown by a reduction in the number of circulating leucocytes, with a lesser fall in the erythrocyte count; the lethal dose is about ten times that judged to be the equivalent of the human therapeutic dose (Scott and Lawrence, 1941).

The results of the American workers are all in close accord: in 80% of patients satisfactory remission, lasting for at least a year, is obtained; in about 20% the result is

poor or treatment has to be abandoned because of a precipitous fall in platelet or leucocyte count. These last haematological complications are rare, and fatal in less than 1%. Remission does not, of course, imply more than restoration of a normal blood picture and freedom from true polycythaemic symptoms; insufficient time has elapsed to know whether patients receiving P^{32} live longer than those treated by other methods.

There is little doubt that acute myeloblastic leukaemia occurs more commonly after the use of P^{32} . The incidence of chronic myeloid leukaemia remains the same, and may perhaps be regarded as one normal termination of the polycythaemic process. The figures in Table II include patients dying of both forms. Even so, the increase is unlikely to be due to chance; if only the acute variety is included the increase is undoubtedly significant. In one paper reports of 453 patients treated with P^{32} were reviewed, of whom only 40 (8.8%) had died; yet of these deaths, 12 (30%) had been due to acute myeloblastic leukaemia (Wiseman *et al.*, 1951).

The present series is so small compared with those from America that detailed analysis would be impertinent. Of 35 patients seen during the past five years, only 20 were treated with P^{32} ; of these, 16 have been observed for more than a year. In 13 patients (80%) satisfactory remission lasting a year or longer followed treatment; one of the treated patients has died from calculous pyelonephritis.

The technique employed has been developed with Mr. I. G. Williams, Director of the Radiotherapeutic Department at St. Bartholomew's Hospital, and closely follows those described by other authors. The initial erythrocyte count is reduced to 6,000,000 per c.mm. and the haematocrit reading to 55% by daily venesections, not exceeding 1,000 ml. in volume; patients have been bled of as much as 6,000 ml. in a week without ill effect. After venesection P^{32} is given intravenously in doses varying from 3 to 5 mC; the dose is judged by the initial erythrocyte, leucocyte, and platelet counts and by the size of the patient. Patients are seen at intervals of six weeks, and no further P^{32} is given for at least two months; further venesection is avoided. Few patients have required a second dose. A leucocyte count below 5,000 per c.mm. or a platelet count below 150,000 per c.mm. has been taken to contraindicate this form of treatment (Figs. 2 and 3).

FIG. 3.—Polycythaemia vera in a man aged 36. Unsatisfactory control with nitrogen mustard, followed by venesection and radioactive phosphorus. Further treatment with radioactive phosphorus was withheld because the platelet count fell to 90,000 per c.mm.

Conclusion

Our experience, although diminutive, has confirmed the published opinions that radioactive phosphorus offers the most convenient means of controlling the haemopoietic exuberance of polycythaemia rubra vera. In 80% of patients the blood count is restored to normal for at least a year, and the symptoms immediately attributable to its previous perversion are relieved; the remainder are either resistant to this form of treatment or show leucopenia or thrombocytopenia sufficient to make it dangerous.

Acute myeloblastic leukaemia is a more common termination in those given P^{32} than in those not so treated. The size of this risk remains to be assessed, and it will be some years before we can be certain that the mean survival is increased or the incidence of vascular and other complications lessened by treatment with radioactive phosphorus.

REFERENCES

- Bell, E. C., and Davis, P. L. (1950). *Amer. J. clin. Path.*, **20**, 839.
 Erf, L. A. (1946). *Blood*, **1**, 202.
 Lawrence, J. H. (1949). *J. Amer. med. Ass.*, **141**, 13.
 Reinhard, E. H., Moore, C. V., Bierbaum, O. S., and Moore, S. (1946). *J. Lab. clin. Med.*, **31**, 107.
 Richardson, W., and Robbins, L. L. (1948). *New. Engl. J. Med.*, **238**, 78.
 Rosenthal, N., and Bassen, F. A. (1938). *Arch. intern. Med.*, **62**, 903.
 Scott, K. G., and Lawrence, J. H. (1941). *Proc. Soc. exp. Biol., N.Y.*, **48**, 155.
 Spurr, C. L., Smith, T. R., Block, M., and Jacobson, L. O. (1950). *J. Lab. clin. Med.*, **35**, 252.
 Stroebel, C. F., Hall, B. E., and Pease, G. L. (1951). *J. Amer. med. Ass.*, **146**, 1301.
 Videback, A. (1950). *Acta med. scand.*, **138**, 179.
 Wiseman, B. K., Rohn, R. J., Bouroncle, B. A., and Myers, W. G. (1951). *Ann. intern. Med.*, **34**, 311.

OBSERVATIONS ON PROGNOSIS IN HYPERTENSION

BY

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Lumbo-dorsal sympathectomy for hypertension is no longer a novelty, although in this country experience of this method of treatment is perhaps only now maturing. Reports of success from this operation have been criticized by Platt and Stanbury (1950) on the grounds that the prospects of many of the patients chosen for operation may well have been favourable in any case. Such criticism, indeed, cannot easily be refuted, since it exposes an unfortunate gap in our knowledge.

Follow-up studies such as those of Janeway (1913), Blackford, Bowers, and Baker (1930), and Bechgaard (1946) have helped to give us a fair conception of the overall prognosis in hypertensive disease, yet probably most of us would agree that, though we could recognize the malignant type of case and perhaps the obviously benign case, we are seldom in a position to predict with any confidence the future of a hypertensive patient, at least at the first examination. So long as we lack this facility unnecessary operations may be inflicted upon hypertensive patients, while in others the decision to operate may well be left too late. It seemed that this situation could be remedied only by acquiring a wider experience of short-term prognosis in hypertension, and this was the object of the present study.

The observations were begun in 1946 at a clinic for hypertensive patients. In addition to the selection of cases for sympathectomy it was proposed to follow the progress of every patient by full examination at regular

intervals; the hope being that when eventually each individual course or fate came to be related to the original clinical findings these would establish the guiding principles by which even at the first examination a hypertensive patient's future might be predicted.

Patients were not accepted for this study unless their diastolic pressure was 100 mm. Hg. or above (the systolic pressure has been largely ignored), or if their age exceeded 60; later, with interest becoming centred on the younger group, the age limit was lowered to 50. The period of observation ranged between two-and-a-half and five years and the patients were examined at intervals of twelve months, six months, and in a few cases three months; according to the severity of their disease. The clinical examination and investigation were strictly standardized, and a progress sheet incorporating the main features in graph form was maintained for each patient.

Since blood pressures were often found to differ considerably in the two arms, the average of a number of readings in both arms was recorded, the final figures being taken after 20 minutes' undisturbed rest. The blood pressure was also taken with the patient standing, and in the leg as well at the first examination, lest coarctation of the aorta be missed. Retinal changes were classified in the conventional five grades as initiated by Wagener and Keith (1939): grade 0, normal; grade I, spastic retinal arteries with or without variations in calibre; grade II, compression of veins at arteriovenous crossings; grade III, the presence of exudate or haemorrhages; and grade IV, papilloedema. The investigations included intravenous pyelography; 6 ft. (1.8 m.) chest x-ray film for record of heart size in terms of cardio-thoracic ratio; 12-lead electrocardiography; chemical, microscopical, and culture examination of urine; urea-clearance test; modified urine-concentration test; and standard blood biochemistry.

The review is based on the study of 151 hypertensive patients (93 women, 58 men) who fulfilled the necessary criteria. These were first examined during the period October, 1946, to June, 1949; they were treated conservatively, and their fate or condition was known at the end of 1951.

Mortality

During the period of observation 51 patients (34%) died as a consequence of hypertension. The death rate for men alone was 44%: the male mortality was higher in each of the main causes of death, with the exception of cerebral vascular accidents, in which proportionately the sexes were equally represented. Even this slight difference may not be fortuitous, since Frant and Groen (1950) showed an actual preponderance of women dying from strokes.

The age at which the 51 patients died and the individual causes of death are shown in Fig. 1. As would be expected, most of the deaths occurring before the age of 45 were due to uraemia, whilst most deaths from other causes occurred in the sixth decade. The height of the diastolic pressure has obviously an important bearing upon mortality, particularly in the case of hypertensive men (see Table).

Percentage Mortality in Relation to Diastolic Blood Pressure at First Examination

		Diastolic Pressure					
		100-119 mm. Hg		120-129 mm. Hg		130+ mm. Hg	
		No.	Deaths	No.	Deaths	No.	Deaths
Men	18	1	(5.5%)	16	7 (43.8%)	24	19 (79.2%)
Women	39	4	(10.3%)	17	5 (29.4%)	37	15 (40.5%)