

Papers and Originals

Multiple Screening in General Practice

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In the past the medical practitioner has usually been ready (perhaps in some instances too ready) to accept that early diagnosis yields a better prognosis and enhances the likelihood of cure. He has, however, paid little more than lip-service to the notion that prevention is better than cure. The routine examination of healthy or allegedly healthy citizens was of no immediate concern to him and was at best a laudable activity for someone else to pursue. The preventive approach to medicine was an academic rather than a practical issue. This is no longer so. The pattern is changing. Two practical considerations likely to lead to a more active involvement on the part of the clinician in presymptomatic diagnosis are the current trends in morbidity which point to an increasing involvement of our curative services with chronic progressive and degenerative disease, and the limits imposed by our available medical manpower which force us to reconsider the role of paramedical and supporting personnel in the provision of medical care. These factors are relevant to all sectors of the health services but pose particularly urgent problems for the general practitioner.

This first report describes the organization and gives some results of a multiple-screening programme carried out by the Department of General Practice of the University of Edinburgh. We seek here to raise a number of practical issues which arise, and to illustrate some of the advantages and disadvantages of introducing screening as an integral part of a curative service.

Definition

Early diagnosis is a feature of the daily work of the general practitioner. At many routine consultations in his surgery, and certainly at all consultations for new episodes of illness, he is concerned not only with the establishment of a diagnosis but also with the routine exclusion of pathology by the use, in varying degree, of history-taking, observation, physical examination, and laboratory tests. This routine exclusion of disease is also a feature of his work in connexion with the surveillance and follow-up of certain patients in his practice in whom the primary diagnosis has already been established—for example, in the management of the diabetic, the hypertensive, the child with coeliac disease, or his grandmother suffering from pernicious anaemia. Routine antenatal care, postnatal examinations (including cervical cytology), immunization, and the supervision of the growth and development of children in his practice offer further examples.

While the term "screening" may be loosely applied to much of what is in fact routine in many general practices, we are

here using the term quite deliberately and strictly in accordance with the definition enunciated by Wilson and Jungner (1967).

Screening is "the presumptive identification of unrecognized disease or defect by the application of tests, examinations, or other procedures which can be applied rapidly. Screening tests sort out the apparently well persons who probably have a disease from those who probably may not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment." Multiple screening consists in using two or more tests in combination, and these are frequently offered to large groups of the population.

Organization

The functions of this university department include the day-to-day provision of medical care in the setting of general practice for a defined population of registered patients. The practice has two sets of premises and is operated by two staffing units. Each unit comprises two doctors (general practitioners), a medical social worker, a nurse, a secretary, and a receptionist. Patients register with one of the doctors in either of the two units. So far as the daily work of medical care is concerned each of the two units is autonomous. In terms of administration, records, and clinical routine, however, the practice is in fact a single entity providing care for about 5,500 patients.

At the time of this study the number of patients registered in the practice was 5,511. Our age-sex register yielded the names and addresses of the 2,158 females aged 15 years or over. It was decided to write a personal letter to each one offering her a multiple-screening examination. The patient's own doctor signed the letter of invitation; he also retained the right to decide whether or not a particular patient should be excluded from the survey and gave his reasons for this exclusion. A total of 358 women were in this way excluded. The commonest reasons for not sending letters were major severe incapacity, patients who were bed-fast or confined to their home, and pregnancy. We were thus left with a list of 1,800 women to whom letters were sent.

Only one letter offering an examination was sent. Each patient who replied in acceptance was given an appointment to attend, but if this appointment was not kept a second appointment was offered. No further action was taken (at this stage) to increase the acceptance rate.

The examinations were carried out between March 1966 and March 1967 in the practice premises at special sessions held two or three times a week. Two and sometimes three intercommunicating examination-rooms were used. The examinations were carried out by a doctor (P.D.R.) who was not responsible for the medical care of the patients, together with one of the practice nurses. They were assisted by a secretary, who was afterwards responsible for collecting and recording the results of the various tests on special survey forms, for

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extracting a summary of these results to be recorded in the patient's own notes, and for making an appointment for each patient to see her own doctor, who would give her, or discuss with her, the results of the examination. After two or three sessions it was found that the routine could be speeded up, and thereafter the time spent by each patient in the examination-room was approximately 15 minutes, six of which were occupied in clerical work and the use of a questionnaire.

Method

The following procedures were carried out.

Questionary.—A series of questions were put in a standard manner. These were mainly, but not entirely, related to our interest in urinary infection and its symptomatology.

Urine Examination.—A midstream specimen was obtained after cleansing of the vulva with a 1% aqueous chlorhexidine solution. The urine specimens were refrigerated in paper containers and then taken to the laboratory for examination. Tests done on the urine comprised a quantitative bacterial count, culture and sensitivity testing, protein (Albustix), glucose (Clinistix), a nitrite test, and a white cell count.

Haematology.—Hb, P.C.V., M.C.H.C., E.S.R., W.C.C.

Biochemistry.—Urea, cholesterol protein-bound iodine (P.B.I.), and glucose estimation by the Dextrostix method.

Blood Pressure.—This was estimated with the patient in a semi-recumbent position. Only one reading was taken.

Height and Weight Measurement.—The weight was measured with the patient in indoor clothes. The height was measured without shoes.

Breast Examination.—This comprised inspection and palpation of the breasts.

Cervical Smear.—This was carried out in all patients except those who had been examined in the previous year, single women, those menstruating at the time of the examination, and those who refused examination.

Chest Radiography.—This was arranged for each patient who had not had a chest x-ray examination in the previous year. The films were read by a consultant radiologist.

A summary of these results was given to the doctor in advance of his interview with the patient two weeks after her examination. The results were entered on a standard form affixed to the patient's notes (see Form). The normal criterion for each test or examination procedure, usually that of the appropriate laboratory, was defined at the beginning of the survey, and these criteria are detailed in the appropriate sections later in this paper; values which were outside the normal range were entered in red ink on the summary form. In the case of the chest radiograph the radiologist's report was marked in red ink only if the report fell into the "abnormal—action required" category. In all instances it remained the responsibility of the patient's general practitioner to interpret the examination results and to take what action he thought necessary.

SCREENING RESULTS		DATE.....	
NAME.....		PRACTICE NO.....	
HEIGHT (cm.)	URINE Prot. Glucose W.B.C. Org..... Sens.	BLOOD Hb % P.C.V. M.C.H.C. W.C.C./cm. E.S.R. Dextrostix	
WEIGHT (kg.)			
IDEAL WEIGHT			
B.P.			
CERV. SMEAR (Pos. or Neg.)			
BREASTS (Normal or Abnormal)			
CHEST X RAY (Normal or Abnormal)		Urea mg./100 ml. Chol. mg./100 ml. P.B.I. µg./100 ml.	

Form for filing results in patient's notes.

Results

Of the 836 patients who replied accepting the offer of an examination (46% of those receiving a letter), 767 actually attended and were examined (43% of those invited). In commenting below on the results obtained we are aware that there were many selective factors at work in determining which women attended for screening. To begin with, the doctors themselves selected out a number of patients who were not even invited to attend, mainly the aged and infirm, but also a high proportion of the youngest age groups. Table I gives the total practice population of females aged 15 years or over, the percentage in each age group who were given the offer to be screened, the proportion in each age group who were screened, and finally the proportion of each age group screened expressed as a percentage of those who received the initial offer.

TABLE I.—Proportion of Patients Screened by Age Group

Age Group	Total Population	No. of Patients Sent a Letter		No. of Patients Screened (Percentage of Total Population)		Patients Screened as a Percentage of Those Sent a Letter
		No.	%	No.	%	
15	46	4	8.7	3	6.5	75.0
16-25	514	429	83.5	146	28.4	34.0
26-35	471	417	88.5	203	43.1	48.7
36-45	408	344	84.3	169	41.4	49.1
46-55	269	255	94.8	120	44.6	47.1
56-65	222	194	87.4	84	37.8	43.3
> 65	228	157	68.9	42	18.4	26.8
Total	2,158	1,800	83.4	767	35.5	42.6

The limitations imposed on these data are being studied as well as the factors influencing the success or otherwise of the screening offer. At this point we merely draw attention to the fact that of those women who were invited to be screened the highest acceptance rate was in the age group 26-55 years.

The most common conditions found at examination were anaemia, bacteriuria, raised blood pressure, obesity, and hypercholesterolaemia. Table II lists these conditions and indicates their prevalence in each age group expressed as a percentage of those screened.

TABLE II.—Main Pathological Findings by Age Group of Patients Examined

Age Group	Patients Screened	Anaemia (%)	Bacteriuria (%)	Diastolic B.P. > 90 mm. Hg (%)	Obesity (%)	Cholesterol 260 mg./100 ml. (%)
15	3	66.6				33.3
16-25	146	6.8	6.8	2.7	27.4	8.9
26-35	203	6.4	3.9	4.9	30.0	9.3
36-45	169	6.5	2.4	10.1	28.4	18.3
46-55	120	5.0	7.5	27.5	25.8	24.2
56-65	84	4.8	5.9	45.2	39.3	34.5
> 65	42	2.4	2.4	47.6	38.1	40.5
All ages	767	6.1	4.8	15.9	29.9	19.4

Anaemia

A haemoglobin of 11.5 g./100 ml. was chosen as the lower level of normal for this study. There were 47 women (6%) with estimations below this figure, and they were diagnosed as anaemic. The anaemia found was usually of the hypochromic type; no macrocytic anaemias were discovered.

The blood examination included an estimation of the erythrocyte sedimentation rate. A one-hour Westergren E.S.R. of 15 mm. was chosen as the upper level of normal in this study. In the case of 113 women (15%) the estimation exceeded this level. An opportunity was taken to match them with a control group in order to study the use of the E.S.R. as a screening test. The results of this study will be the subject of a separate report.

Bacteriuria

Quantitative bacterial counts were done by the method of Miles and Misra (1938); a count of urinary pathogens exceeding 100,000/ml. was regarded as indicative of infection (Kass, 1956). The incidence of bacteriuria was 4.8%, which is comparable with the overall prevalence of 4.4% found in females aged over 15 years in Jamaica and in Wales by Kass *et al.* (1961).

It seems advisable to include a test for bacteriuria in a multiple-screening examination of women in view of the probable association between asymptomatic bacteriuria and chronic pyelonephritis; there is certainly a strong case for including such a test in pregnancy, as untreated asymptomatic bacteriuria has been shown to be accompanied by a higher foetal loss and lower birth weight than in treated asymptomatic bacteriuria (Kincaid-Smith and Bullen, 1965).

Raised Blood Pressure

A diastolic blood pressure reading exceeding 90 mm. Hg was, in this study, regarded as an indication for further measurement or possibly investigation, but the decision was left for the general practitioner to make in the light of other circumstances. Not unexpectedly, many blood-pressure readings which were raised at the screening examination were found to be considerably lower on repeat examination by the general practitioner.

There were 122 women (16%) with diastolic pressures exceeding 90 mm. Hg; of these, 74 had a reading in the range 90–100 mm. Hg, 32 in the range 100–110 mm. Hg, 13 in the range 110–120 mm. Hg, and 3 exceeding 120 mm. Hg. The percentage of patients with diastolic pressures exceeding 90 mm. Hg rose, as might be expected, with the age group examined.

Overweight

Ideal weights were calculated from the tables of Kemsley (1951–2). A woman was regarded as being overweight if the observed weight exceeded the ideal weight by more than 10%. Of the women examined, 229 (30%) were classified as being overweight by this criterion. There was a rise in the incidence of overweight in those examined over the age of 56 years.

In view of the association of obesity with decreased life expectancy and increased morbidity, it seems advisable to record the patient's weight in screening examinations. Attempted weight reduction is likely to be more successful at an early stage of weight gain than at the stage of long-standing obesity. Regular screening examinations are likely to demonstrate early weight gain.

Hypercholesterolaemia

A serum cholesterol of 260 mg./100 ml. was chosen as the upper level of normal for this study. Of the 149 patients (19%) with a serum cholesterol level exceeding 260 mg., 32 lay in the range 300–400 mg. and 10 had levels exceeding 400 mg. One of the latter 10 patients was later found to have hypothyroidism. The percentage of patients found to have a serum cholesterol level exceeding 260 mg. rose with the age group screened.

The serum cholesterol was estimated, not only for the purpose of detecting hypothyroidism when a high cholesterol was associated with a low P.B.I. estimation, but also for the future surveillance of patients with hypercholesterolaemia for such conditions as ischaemic heart disease (Thomas *et al.*, 1966) and possible hypothyroidism (Fowler and Swale, 1967).

P.B.I.

In this study the normal range of the serum P.B.I. was regarded as 4–7.5 $\mu\text{g.}/100\text{ ml.}$ There were 10 patients with

a level of less than 4 $\mu\text{g.}$, and when a repeat estimation was done in five of these patients the reading was in the normal range. In only one of the 10 patients was the P.B.I. below 3 $\mu\text{g.}$ —namely, 2.4 $\mu\text{g.}$ —and this was confirmed by a repeat estimation of 1.8 $\mu\text{g.}$ This patient's serum cholesterol was 422 mg./100 ml.; she was later diagnosed as suffering from hypothyroidism after full clinical and laboratory investigation.

As there is probably a lengthy period of hypometabolism before thyroid failure is detected clinically, hypothyroidism seems an ideal condition for screening examinations; however, hypothyroid patients by nature of their metabolic disturbance may be less inclined to volunteer for screening examinations than euthyroid patients. There is no definitive information on the prevalence of hypothyroidism in the general population.

What is surprising is that 130 patients (17%) had a P.B.I. exceeding 7.5 $\mu\text{g.}/100\text{ ml.}$, but in respect of 103 patients (79%) the estimations lay in the range of 7.5–10 $\mu\text{g.}$ At the screening examination the patient was asked if she was taking thyroid hormone or any antithyroid drug. We did not, however, at this stage question the patient or extract from her notes information about the use of drugs which raise the P.B.I.—for example, the contraceptive pill. This is a salutary reminder of the importance of including questions concerning the contraceptive pill in any survey of healthy women which includes P.B.I. determinations.

Diabetes

Blood glucose estimations were done with the Dextrostix glucose oxidase paper strip on blood samples taken at the time of examination. If the Dextrostix reading was 130 mg./100 ml. or higher, the patient was invited to have an oral glucose tolerance test. The glucose tolerance tests were done with a 75-g. glucose load and after the patient had been three days on a high carbohydrate diet; these were interpreted by means of the criteria suggested by the World Health Organization (1965). As the glucose tolerance test blood sugar estimations in the present study were done by the ferricyanide method with the use of the Autoanalyser, the figures suggested by the W.H.O. Committee were adjusted; a two-hour blood glucose level of less than 120 mg. (W.H.O. 110 mg.) was taken to exclude diabetes, and a reading of 140 mg. or higher (W.H.O. 130 mg.) as indicative of diabetes. Values between these levels were classified as equivocal.

Of the 36 patients with a Dextrostix reading of 130 mg. or higher, 5 were known diabetics and the remaining 31 were offered an oral glucose tolerance test. This test was done on 26 of the 31 patients; two had abnormal results suggesting diabetes, and a further four had equivocal results. This study will be the subject of a separate report.

Breast Tumour

Of the 754 patients in whom the findings of the breast examination were recorded, only two were reported as having abnormalities. One woman aged 36 was found to have a malignant tumour and she subsequently had a radical mastectomy; the other, aged 39, had a tumour which at biopsy was found to be benign. It is of interest to note that no woman refused this examination. The records of the examination are incomplete in respect of 13 patients.

Cervical Smear

In the case of 278 women cervical smears were not taken, either because the patient was unmarried (by far the vast majority) or because the patient had previously had the examination done in the past year, or was menstruating at the time of examination. Of those screened, 13 women refused the

examination. Cervical smear records are thus available for 475 women (62%). The record was incomplete in respect of one patient.

No cases of cervical carcinoma were found, but two patients had abnormal smears which necessitated a second test. In both instances the results were negative.

Chest Radiograph

The consultant radiologist who read the films was asked to give a report in detail but also to put the radiograph in one of three categories: "normal," "abnormal—no action," or "abnormal—action required." The decision to put the chest radiograph into one of these categories was made solely by the radiologist, and it must be noted that he possessed no clinical knowledge concerning the patient. If the radiograph was put in the "abnormal—no action" category this implied that the radiographer thought there was no need for further investigation by him, or possibly even by the patient's general practitioner. If the report was put in the "abnormal—action required" category this implied that the radiologist thought that further investigation was necessary, either entailing further referral to him or some other steps by the patient's general practitioner. The final decision on whether further investigation of an abnormal report was required was left to the patient's general practitioner.

Of the 279 patients who were not radiographed 245 (88%) were excluded because they had had such an examination in the previous year. The results of radiography in respect of the 488 women examined were classified as follows: "normal" in 368, "abnormal—no action required" in 101, and "abnormal—action required" in 19.

"Abnormal—no action required" in the main consisted of bronchitic changes, minor degrees of cardiac enlargement, and healed tuberculosis. Conditions which featured in the 19 cases reported "abnormal—action required" were lung opacities requiring repeat radiographic examination, tuberculosis of doubtful activity, and cardiac enlargement. Three patients in this group had non-tuberculous pulmonary infections requiring immediate treatment.

Discussion and Commentary

This screening programme, in spite of its limited nature, showed a substantial amount of morbidity in the women who were examined and who were patients in a practice in which the doctors had already incorporated a substantial amount of physical and laboratory investigation as part of the practice routine, and in which 70% of the patients at risk see their doctor at least once in the course of a year.

Since 17% of the total practice population of females aged over 15 years were excluded for a variety of medical and social reasons by their doctor, and only 43% of those who were invited were actually screened, we cannot from these results comment on the incidence or prevalence in the total practice population of disease detected by this procedure. Still less can we generalize from our findings to the population as a whole. The practice records, however, can be used and if necessary reinforced to obtain information about certain characteristics of the patients who were excluded in the first instance and also to compare and contrast certain characteristics of those who responded with those who failed to respond to the invitation.

We have offered a brief commentary in the appropriate sections above on some of the results obtained so far. We think it appropriate here to supplement this by a general comment on the reactions of the doctors taking part in the survey, and on some of the practical problems and difficulties which they raised.

In the planning discussions the doctors expressed some concern about the possibility of creating iatrogenic disease, particularly in our more nervous patients. This has not materialized in our experience so far at least. A majority of patients reporting back to their doctor to obtain the final results make spontaneous and favourable comment about their experience. We are aware, however, that since those particular patients may not be representative of the practice as a whole a final commentary on the patient's reaction to screening must await the result of further studies, which are in fact proceeding. From these we hope to be able to describe the patient's reaction after the receipt of the invitation and before the examination was carried out. We hope also to compare these responses with her reaction after the examination. Of even greater importance will be studies of the characteristics of those who were not examined.

The project was so arranged that the organization and conduct of the actual examination would be carried out by supernumerary staff. Even so, the patient's own doctor at the planning stage raised questions about the additional work involved; firstly, in interviewing each patient at the end of the examination, and, secondly, in taking any further action arising out of the results themselves or from the patient's reaction to the examination. In the event our experience has been that once the routine had been established such eventualities did not present major problems. We do, however, intend to obtain objective information on patient consultation patterns following the screening examination.

When a gross pathological condition was uncovered as a result of the screening tests the doctor had little difficulty in taking appropriate action. What was reported back to the doctor, however, was in effect clinical or laboratory findings rather than diagnoses. Not unexpectedly the doctor sometimes had difficulty in deciding on the appropriate further action when presented with laboratory findings which were borderline departures from arbitrarily determined normal values. In discussing this three points emerged. Firstly, the position of advantage occupied in these circumstances by the general practitioner, who already has the full notes and findings from previous records of his patients, in determining the significance of such findings in a particular case. Secondly, the need for more information about the natural history of disease and more studies to obtain such information in the setting of general practice. The third point is that of the problem posed to the doctor regarding the future management of the patient after the chance discovery of abnormality in an apparently healthy person. This is a common experience in general practice, but it is accentuated in this situation where the doctor sponsors and promotes the health examination of individuals who do not happen to be consulting him at that point in time.

Perhaps the most important commentary we can make on the practical experience of this particular survey relates to the use of ancillary personnel. There were two elements in the procedure outlined above; one clerical, the other technical and clinical. As a result of this experience we are satisfied that after the initial planning and the working out of the techniques the actual screening need not require the services of a doctor. The range of examination offered to these patients was certainly within the competence of a qualified nurse provided that she had been given the necessary initial training and supervision, and provided that adequate laboratory services were available for the examination of specimens.

Further Studies

This study has yielded tangible results which are interesting in themselves. In this first communication, however, we have sought to emphasize matters of methodology relevant to the setting in which the study took place. In the course of planning and carrying out the study and discussing the results as

they became available the group have gained experience which we wish to communicate to others who may be concerned with the development of multiple screening in the setting of general practice. Many questions have been raised. Even if these are not particularly new we hope by reporting our experience to encourage others to pursue similar or parallel studies focused on some of the following questions.

What is the effect of multiple screening, carried out in the setting of general practice, on the work-load of the practice? Do patients who have been screened consult more or less often as a result? What kinds of patients consult more or less often after such a screening? What is the subsequent effect on the doctor's routine diagnostic or therapeutic activity in respect of those patients in whose notes are recorded the results of a multiple-screening examination? What is the short-term or long-term effect on the health of the patient as distinct from the patient's patterns of utilization of medical care? What kinds of patients do not readily accept an offer of screening? What changes would occur in the doctor's professional role in a practice in which such screening examinations were carried out routinely and entirely by the deployment of ancillary staff?

Summary

Female patients aged 15 years and over in a general practice were invited to take part in a multiple-screening programme.

The procedures comprised a questionnaire relating to urinary symptomatology, the recording of height, weight, and blood pressure, and the results of a straight x-ray film of the chest. Breasts were palpated and a cervical smear was taken. Total viable bacterial counts were carried out on midstream urine specimens. Biochemical tests included estimation of urea, cholesterol, and P.B.I. Blood glucose was estimated by the Dextrostix method. Haematological tests included estimation of haemoglobin, P.C.V., M.C.H.C., E.S.R., and W.B.C.

Of the 2,158 female patients on the practice list the patients' doctors excluded 358 from this survey. The remaining 1,800 were offered the multiple-screening examination. The acceptance rate was 43%.

The most common conditions found at examination were anaemia, bacteriuria, raised blood pressure, obesity, and hypercholesterolaemia.

Three subsidiary studies which have been undertaken as a result of this experience are an assessment of the Dextrostix method of blood glucose estimation in the setting of general practice, the use of the E.S.R. as a screening procedure, and a study of the factors associated with acceptance or non-acceptance of the offer of a health overhaul offered to patients in a general practice.

In this presentation of the first results emphasis is placed on methodology. The advantages and disadvantages of carrying out this kind of exercise in the setting of general practice are discussed. The role of the nurse in accepting a major personal responsibility for a screening programme is emphasized. Areas in which further studies are required are indicated.

This study would not have been possible without the painstaking and enthusiastic support of our secretarial staff. We also acknowledge our gratitude to those patients who collaborated so effectively, particularly in the early days of setting up the study. We welcome the opportunity to acknowledge our indebtedness for the generous assistance so freely given by individuals in other university departments, and in particular the following laboratory and other services: Dr. S. H. Davies, haematology; Dr. B. I. Davies, bacteriology; Professor R. J. Kellar, cervical cytology; Dr. Eric Samuel, radiology; Professor L. G. Whitby, clinical chemistry; and Dr. G. B. Young and the staff of the Family Doctor (Diagnostic) Centre. Mr. W. Lutz and Miss C. Laidlaw, department of social medicine, gave us advice and considerable material assistance in processing the data. Ames Company generously supplied Uristix and Dextrostix reagents.

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Parietal-cell Antibodies in Patients Undergoing Gastric Surgery

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The present investigation was undertaken in order to determine whether circulating antibodies to gastric parietal cells (P.C.A.) were detectable by immunofluorescence after surgery to the stomach for various conditions. Circulating antibodies to cardiac muscle have been demonstrated after myocardial infarction; similarly, thyroid antibodies have been demonstrated in patients with subacute viral thyroiditis, which disappears when the thyroiditis resolves (Kleinsorge *et al.*, 1957-8; Roitt and Doniach, 1958). Surgical trauma to gastric tissue might be thought to have a similar immunizing potential, as might damage by drugs, particularly aspirin.

Studies have shown that about 60% of patients who have undergone subtotal gastrectomy may develop chronic gastritis or progressive gastric atrophy (Coghill *et al.*, 1958; Lees and Grandjean, 1958). It is said that these patients have an increased chance of developing pernicious anaemia and carcinoma of the gastric remnant (Welbourn *et al.*, 1956;

Krause, 1958). Similarly there is an increased incidence of gastric carcinoma in patients with pernicious anaemia (Jenner, 1939). Antibodies to gastric parietal cells are detectable by immunofluorescence in the serum of 80-90% of patients with pernicious anaemia (Taylor *et al.*, 1962; Doniach *et al.*, 1963; Coghill *et al.*, 1965) and of some with simple chronic atrophic gastritis (Coghill *et al.*, 1965). It has been suggested that the gastric changes in pernicious anaemia are in some way related to an immune response, but there is no direct evidence that humoral antibodies are pathogenetic in the gastritis of pernicious anaemia, though they may reflect an underlying disturbance of cellular immunity. Circulating P.C.A. of the IgG class have been demonstrated in the blood of babies born to mothers with pernicious anaemia. The infants developed normally, their gastric mucosa apparently remained healthy, and P.C.A. could not be detected in their serum four months after birth (Fisher and Taylor, 1967).

If circulating P.C.A. were detected after surgery, this would support the hypothesis of tissue damage causing the alteration

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