

A Multiple Screening Clinic

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Acheson *et al.* (1963) have suggested criteria for selection of diseases suitable for presymptomatic diagnosis. The tests used must be simple, quick, reliable, and readily acceptable, and the condition subsequently discovered should prove amenable to treatment. In many areas screening tests for single diseases or groups of diseases are now widely applied: such techniques as mass radiography in adults, tests for phenylketonuria in infants, and pure-tone audiometry in schoolchildren have gained general acceptance. A few authorities have successfully conducted examinations of large populations for other conditions, such as diabetes. When two screening tests were offered together (Donaldson and Connolly, 1963) the public response was greater than could have been expected for either test alone.

It was therefore decided to offer a battery of five tests, to detect chest diseases, diabetes, anaemia, deafness, and cervical carcinoma. Rotherham is a compact town with a population of 86,510, the main industry being steel production. A suite of rooms in the centrally situated town hall was used. Publicity, mainly directed at young and middle-aged adults, was confined to the two weeks immediately preceding the clinic, which was open for six consecutive days in the afternoon and evening.

Only the age groups considered to be mainly at risk were encouraged to take the individual tests. These were listed as follows: anaemia, all ages; diabetes, all ages; chest x-ray, over 15; hearing, 15 to 60; cervical cancer, parous women aged 30-60. Quite clearly, it would be a waste of effort if conditions discovered were already known to the family doctor.

Anaemia

The anaemia test was the simple gravimetric method whereby a drop of blood is allowed to fall into a solution of copper sulphate of known specific gravity (Ministry of Labour, 1964). A drop which fails to sink represents a haemoglobin level below 85% for females and below 90% for males (Haldane). Except for an hour or two on the busiest day, the section was staffed only by one technician, kindly loaned by the Sheffield Regional Blood Transfusion Centre, and a clerk.

Approximately three tests every two minutes could be done without undue fatigue; the maximum completed in 4½ hours by one technician was 425. The persons whose tests were positive numbered 178, all except 19 of them female; this total represents 6.49% of the 2,743 persons examined.

Diabetes

The diabetes test was conducted on similar lines to a previous campaign. Clinistix test strips were prepared in envelopes printed with instructions for self-testing. Persons attending were invited to take packets home for other members of the family over 10 years old: 5,673 packets were issued and 116 were returned, the test strips having changed colour (Table I). Of these persons 112 attended for further tests and 29 were confirmed as having glycosuria. As a result of glucose tolerance tests at the hospital laboratory, 7 new diabetics were discovered.

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The eighth case, a severe diabetic, turned out to have already been correctly diagnosed at the previous campaign and brought under appropriate treatment.

TABLE I.—Results of Diabetic Test

No. of test packets issued	5,673
Reported positive by patient	116
Attending for further check	112
Referred for glucose tolerance test	29
Reported normal	4
Low renal threshold for glucose	13
"Lag" curve	2
Diabetes (severe 1, moderate 4, mild 3)	8
"Intermediate"—to be repeated later	2

Chest Radiography

A total of 2,824 persons were x-rayed (837 men, 1,987 women). The recall rate was low, owing chiefly to the preponderance of women in the 30-60 age group, who are not especially prone to chest diseases. Table II gives the abnormalities discovered.

TABLE II.—Abnormalities Discovered on X-ray

Tuberculosis, active	3
" inactive	7
Bronchial neoplasm	2
Secondary deposits	1
Acute inflammatory disease	10
Bronchiectasis	3
Pleural effusion, possibly malignant	1
Post-inflammatory and honeycomb lung	1
Pleural thickening	2
Pneumoconiosis	8
Bronchitis and emphysema	21
Heart disease	34
Entravention of diaphragm	3
Thyroid enlargement	1

Hearing

The hearing test was conducted in a soundproof box, a Madsen transistor pure-tone audiometer being used. It was fairly easy to pick out those with a hearing loss greater than 25 decibels at any frequency; these persons were briefly examined by a doctor, and wax was removed if necessary. Of the 1,184 persons who took the test 251 (21.2%) failed. Thirty (2.5%) were referred to their general practitioner, and a preliminary classification of these is given in Tables III and IV.

TABLE III.—Age Distribution of Those Referred to General Practitioner

Age (years):	15-	30-	45-	60-	Total
Male	—	2	8	1	11
Female	4	3	10	2	19
Total	4	5	18	3	30

TABLE IV.—Preliminary Classification of 30 Patients Referred to General Practitioner

Chronic otitis media	4
Conductive deafness (? cause)	10
Eustachian obstruction	1
High-tone loss with no demonstrable pathology	8
Ménière's disease	1
Minimal loss with marked tinnitus	1
Aetiology doubtful	5

In 22 further cases (1.9%) the general practitioner already had the patient under treatment or knew about the condition: a copy of the audiogram was forwarded. A total of 199 cases were neither referred nor notified to the general practitioner.

This was because treatment was not required or was unlikely to be effective. Provisional diagnoses are given in Table V.

TABLE V.—Classification of 199 Patients Not Notified or Referred to General Practitioner

Minimal loss	28
Long-standing disease of middle ear (including operations 5, perforations 22)	60
Chronic catarrh of nose and sinuses	9
Family history of deafness	5
High-tone loss in older persons	30
Long-standing and congenital deafness	14
Occupational deafness	15
Ménière's disease	2
Other causes of perceptive loss	5
Already supplied with hearing-aid	4
Chronic otitis externa	3
Recent U.R.T.I.	9
Other and unclassified abnormalities	15

Cervical Cytology

The original arrangements for taking cervical smears involved two health visitors, three midwives, and a lady general practitioner. Demand was so overwhelming that more staff had to be brought in, and by the end of the week four health visitors, five midwives, and four doctors (two male, two female) were working almost full-time. Queues were extremely lengthy; even a three-hour wait did not discourage some of the stalwarts who arrived at the busiest times. The preponderance of social classes I and II was not so great as we had anticipated. Many women travelled long distances to take the test. Two elderly ladies came from Morecambe, 100 miles away; one of them had previously undergone a total hysterectomy.

The number of women attending was 1,375, and 1,369 smears were taken. Eight of the smears (0.58%) proved positive, and the patients concerned have all undergone operative treatment. Thirty unsatisfactory or doubtful smears were repeated, and 21 of these have so far been reported negative. Three cases are to be kept under observation. It was expected that a number of other conditions would be discovered incidentally, and 85 patients were referred directly to general practitioners for investigation or treatment. Their diagnoses are given in Table VI.

TABLE VI.—Patients (85) Attending for Cervical Smear Who Were Referred to General Practitioners

Lesions of body of uterus	
Retroversion	4
Fibroids	4
? Neoplasm	3
Enlargement (? cause)	3
Dysmenorrhoea	1
? Retained products	1
Post-menstrual bleeding	1
Lesions of cervix	
Cervical polyp	14
Cervical erosion	13
Suspected neoplasm	8
Unspecified abnormality	3
Lesions in vagina	
Vaginitis and vaginal discharge	11
Prolapse	6
Caruncle	3
Pessary removed (two years in vagina)	1
Other conditions	
Low back pain	1
Senile diabetic vulvitis	1
Dyspareunia	6
Not stated	1

Discussion

The object of a screening programme is the pre-symptomatic detection of disease. For such a programme to become established as an efficient tool in preventive medicine and in order to give a maximum return for the effort and expenditure involved, the aim must be to examine, with due accuracy, a large number of persons in a short time, using as many tests as possible grouped together in a multiple screening clinic. Besides the technical considerations, this demands competent administrative machinery and, above all, courteous and gentle handling of the public who attend.

Such a clinic is not intended for patients with clearly defined symptoms who should be consulting their family doctor: a positive policy is needed to prevent it becoming a succession of tedious consultations. It was explained to those attending that the tests were specific for certain diseases and that a detailed account of their symptoms was not necessary. This was particularly stressed to the women attending for cervical smears, because many had a tendency to discuss their troubles at length; the problem also arose to a lesser extent with the hearing test. Persons attending with clearly defined symptoms were advised to consult their own doctor.

The local authority incurred expenses of about £400 in providing administrative and clinical facilities, and, in addition, £100 for sessional work from general practitioners. The estimated cost of the mobile x-ray unit was £200, of the cervical cytology service £300, and of the testing for anaemia £30. The cost to the hospital service was therefore about £530. On the basis of the pathological conditions discovered the total approximate expenditure of £1,030 represented more than a reasonable return.

The total attendance at the multiscreening clinic was 3,753. This was far higher than we had anticipated, because previous visits by the Mass Radiography Unit alone had attracted about 800 persons in a week. There seem to be two reasons for this large attendance: a multiplicity of tests was available and the clinic was based on the "open door" principle, no appointments being necessary. Members of the public seemed to be attracted to the idea that they could walk in and have a variety of "health checks" with little loss of time or inconvenience. It is clear that the demand for such a service exists and may easily prove overwhelming.

Though it might be possible to set up such a clinic on a permanent basis, we are convinced that our arrangements suited the available facilities. We therefore do not agree with the Seminar Group of the Society of Medical Officers of Health (Burns and Warren, 1965) that the "blitzkrieg" approach is necessarily to be deprecated. The "centrepiece" of a multi-screening clinic should be the Mass Radiography Unit. This is available locally for only a limited period each year. The public attitude is already favourably disposed towards the unit, and the other tests are readily established around it. Though the strain on staff is considerable this is offset by their enthusiasm for new techniques, and they are encouraged by a brisk public response.

This clinic was a combined venture by all three branches of the Health Service. The local authority provided premises, administration, and staffing. The Regional Hospital Board supplied technical facilities and undertook further investigation, treatment, and follow-up. All positive findings were referred to general practitioners, who were therefore called upon to interpret and counsel, to refer or treat, as appropriate. The success of the clinic hinged entirely on co-operation and close communication between the three bodies concerned, and this was at no time lacking.

As far as can be ascertained the conditions discovered were unknown to the family doctor except where specifically mentioned in this paper. This certainly applies to the cases of carcinoma-in situ, to the minor gynaecological conditions, and to the seven new diabetics; it is also true for most of the cases of deafness referred. The cases of tuberculosis and bronchial neoplasm discovered on chest x-ray examination were not known to the family doctor, but, on the other hand, about half of the chronic pulmonary and cardiac conditions were already under treatment. A few of the patients with anaemia admitted that they were already attending their own doctor for that condition.

By detecting disease at an early stage, when it is more easily treated, some of the work is being relieved which, sooner or later, would almost inevitably have fallen on the hospital services. This mitigates to some extent the additional pressure

imposed at the time of the clinic and in the subsequent few weeks.

The sharpest criticism of multiphasic screening is that the patient, having successfully completed the tests, emerges with what he imagines is a clean bill of health. Though we tried hard to dispel this attitude, it is difficult to impress on each individual that a negative result does not necessarily imply the absence of other disease, either at the time of the test or in the future.

The next clinic is being planned on broadly similar lines but with the inclusion of tests for visual acuity and glaucoma. The clinic will be held for two weeks, mainly to deal with unsatisfied demand but also to enable women who may be menstruating to be examined for cervical carcinoma. Instruction will be given in self-examination of the female breast. In the case of the anaemia test, venous blood will be obtained from those failing the initial drop-test, and this will be submitted for full haematological examination. Pre-loading with glucose should raise the number of diabetics detected to a more acceptable level. The administrative arrangements will also be improved.

Summary

At a multiple screening clinic held in Rotherham for one week the attendance was 3,753. Eight positive cervical smears

were reported, and seven new diabetics were diagnosed. We discovered 178 cases of anaemia, 99 of chest diseases, 30 of significant deafness, and many minor gynaecological conditions. Most of these cases were unknown to the family doctor.

The organization and aims of such clinics are discussed, and it is emphasized that close co-operation between the three branches of the Service is required.

The local general practitioners were most helpful and encouraging, and willingly undertook the additional work. We are grateful to the following consultants who freely gave advice and help and to whom many of the patients were referred for further investigation: Mr. D. Ballantine, Miss R. D. Dunsmore, Drs. H. R. Colquitt, A. C. Morrison, H. Richmond, E. Travers, and R. S. Weetch, and especially to Dr. A. MacFarlane, who undertook the examination of cervical smears. We are also indebted to Dr. W. J. Wilson, of the Sheffield Mass Radiography Centre; Dr. C. C. Bowley, of the Sheffield Regional Transfusion Centre; and to Dr. S. Shone, Senior Administrative Medical Officer, Sheffield Regional Hospital Board.

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Plasma Erythropoietin in Chronic Uraemia*

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Haemorrhage and haemolysis may contribute to the anaemia of chronic renal failure, but reduced erythropoiesis seems to be the major factor (Joske *et al.*, 1956; Desforges and Dawson, 1958; Kaye, 1958; Loge *et al.*, 1958; Verel *et al.*, 1959; Ragen *et al.*, 1960; Kurtides *et al.*, 1964). Although the cause of the deficient erythropoiesis is not fully understood there appears to be a disturbance of the mechanism regulating red-cell production. Present theory of the control of erythropoiesis is reviewed by Gordon (1959) and Stohlman (1962). This maintains that under conditions of prolonged tissue anoxia increased amounts of the hormone erythropoietin, which stimulates the bone-marrow, are released into the circulation. Experiments by Jacobson *et al.* (1956), Osnes (1958), and Kuratowska *et al.* (1960) suggest that erythropoietin is produced (or activated) by the kidneys. In accordance with this concept increases in plasma erythropoietin have been demonstrated in patients with most types of anaemia, the single exception being azotaemic anaemia (Gallagher *et al.*, 1959, 1960; Penington, 1961; Naets and Heuse, 1962).

It is tempting to suggest in the light of these findings that the root cause of this anaemia is the inability of the diseased kidneys to produce erythropoietin. Before this can be accepted it would be necessary to show that plasma erythropoietin was lower than normal in patients with renal failure (Penington, 1962a). The evidence on this point is inconclusive. Gurney *et al.* (1957) obtained an erythropoietic response in hypophysectomized rats with normal plasma, but with this technique

pituitary, thyroid, or adrenal hormones may have been responsible. Reichlin and Harrington (1960) also claim to have demonstrated erythropoietin in normal plasma, but their assays did not include an erythropoietin standard, so that "false-positive" results cannot be excluded. Other workers have been unable to detect erythropoietin in normal plasma (Gallagher *et al.*, 1959; Penington, 1961; Naets and Heuse, 1962). On the present evidence, therefore, it is equally possible that the low erythropoietin levels in uraemia reflect failure of the compensatory mechanism to some other cause for the anaemia—for example, toxic inhibition of the marrow (Markson and Rennie, 1956; Saito, 1963). The demonstration of transient improvement in erythropoiesis after haemodialysis (Kurtides *et al.*, 1964) and peritoneal dialysis (Berry *et al.*, 1964) suggests that toxic effects may well be important.

Lack of sensitivity and specificity of the erythropoietin bioassays are responsible for the present difficulties. All the workers mentioned used starved or polycythaemic rats as assay animals, but Jacobson *et al.* (1959) and DeGowin *et al.* (1962) have shown that polycythaemic mice are more sensitive. Greater specificity can be obtained by including a standard erythropoietin in at least two dose levels so that dose-response lines with specific slope can be constructed; test plasma given in similar dose increments will, if erythropoietin is present, produce a dose-response line parallel to that of the standard (Bangham, 1962). Non-specific effects can be recognized by the lack of parallelism.

Such a standard is now available (standard "B" M.R.C.), and a simple reliable method for producing polycythaemia in mice has been devised by Cotes and Bangham (1961) with a decompression chamber (Wright, 1964). With these improve-

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