4 Screening for Disease

"Health should mean a lot more than escape from death or, for that matter, escape from disease."

Iceberg phenomenon of disease

Epidemiologist and others who study disease find that the pattern of disease in hospitals is quite different from that in a community. That is, a far larger proportion of disease (e.g., diabetes, hypertension) is hidden from view in the community than is evident to physicians or to the general public. The analogy of an **iceberg**, only the tip of which is seen, is widely used to describe disease in the community.

The concept of the "iceberg phenomenon of disease" (Page 39) gives a better idea of the progress of a disease from its sub-clinical stages to overt or apparent disease than the familiar **spectrum of disease**. The submerged portion of the iceberg represents the hidden mass of disease (e.g., sub-clinical cases, carriers, undiagnosed cases). The floating tip represents what the physician sees in his practice. The hidden part of the iceberg thus constitutes the mass of unrecognized disease in the community, and its detection and control is a challenge to modern techniques in preventive medicine.

Concept of screening

The active search for disease among apparently healthy people is a fundamental aspect of prevention. This is embodied in screening, which has been defined as "the search for unrecognized disease or defect by means of rapidly applied tests, examinations or other procedures in apparently healthy individuals."

Historically, the annual health examinations were meant for the early detection of "hidden" disease. To bring such examinations within the reach of large masses of people with minimal expenditures of time and money, a number of alternative approaches have come into use. They are based primarily on conserving the physician–time for diagnosis and treatment and having technicians to administer simple, inexpensive laboratory tests and operate other measuring devices. This is the genesis of screening programmes. The original screening programmes were for individual diseases such as tuberculosis, syphilis or selected groups such as antenatal mothers, school children and occupational groups. Over the years, the screening tests have steadily grown in number (Table 8). Screening is considered a preventive care function, and some consider it a logical extension of health care.

Screening differs from **periodic health examinations** in the following respects *(1)*:

1) capable of wide application
2) relatively inexpensive, and
3) requires little physician–time. In fact the physician is not required to administer the test, but only to interpret it.

Screening and diagnostic tests

A screening test is not intended to be a diagnostic test. It is only an initial examination. Those who are found to have positive test results are referred to a physician for further diagnostic work-up and treatment. Screening and diagnostic tests may be contrasted as in Table 1.

TABLE 1
Screening and diagnostic tests contrasted

	Screening test	Diagnostic test
1	Done on apparently healthy	Done on those with indications or sick.
2	Applied to groups	Applied to single patients, all diseases are considered.
3	Test results are arbitrary and final	Diagnosis is not final but modified in light of new evidence, diagnosis is the sum of all evidence.
4	Based on one criterion or cut-off point	Based on evaluation of a number of symptoms, signs (e.g., diabetes) and laboratory findings.
5	Less accurate	More accurate.
6	Less expensive	More expensive.
7	Not a basis for treatment	Used as a basis for treatment.
8	The initiative comes from the investigator or agency providing care.	The initiative comes from a patient with a complaint.

Source : *(2)*

However, the criteria in Table 1 are not hard and fast. There are some tests which are used both for screening and diagnosis, e.g., test for anaemia and glucose tolerance test. Screening and diagnosis are not competing, and different criteria apply to each.

Concept of "lead time"

Fig. 1 shows the possible outcomes for a given disease process. There is nothing to be gained in screening for diseases whose onset is quite obvious. Detection programmes should be restricted to those conditions in which there is considerable **time lag** between disease onset and the usual time of diagnosis. In this period, there are

usually a number of critical points which determine both the severity of the disease and the success of any treatment in reversing the disease process. There is clearly little value in detecting disease in advance of the usual time of diagnosis unless such detection precedes the final critical point beyond which treatment would be unsuccessful and/or permanent damage would be done. Detection programmes should, therefore, concentrate on those conditions where the time lag between the disease's onset and its final critical point is sufficiently long to be suitable for population screening *(3)*.

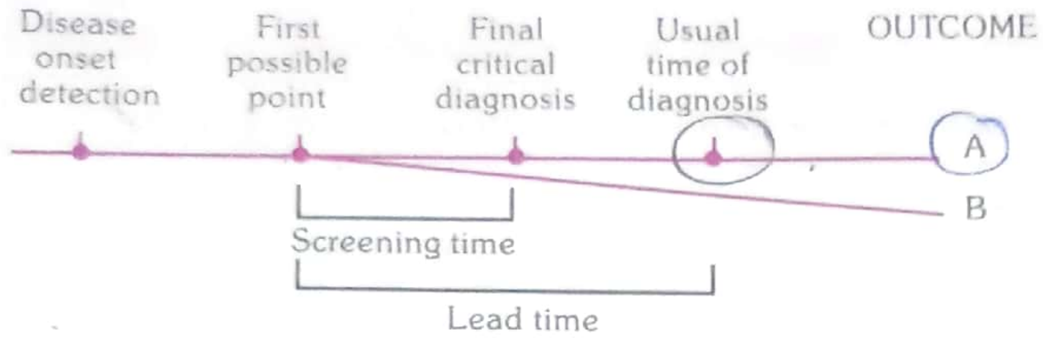

FIG.1
Model for early detection programmes

"Lead time" is the advantage gained by screening, i.e., the period between diagnosis by early detection and diagnosis by other means. In Fig.1, **A** is the usual outcome of the disease, and **B** is the outcome to be expected when the disease is detected at the earliest possible moment. The benefits of the programme are therefore **B–A**. The benefits of the programme must be seen in terms of its outcomes. It is also necessary for the complexities and costs of any detection programme to be viewed against the benefits accruing therefrom *(3)*.

Aims and objectives

The basic purpose of screening is to sort out from a large group of apparently healthy persons those likely to have the disease or at increased risk of the disease under study, to bring those who are "apparently abnormal" under medical supervision and treatment (Fig.2). Screening is carried out in the hope that earlier diagnosis and subsequent treatment favourably alters the natural history of the disease in a significant proportion of those who are identified as "positive" *(4)*.

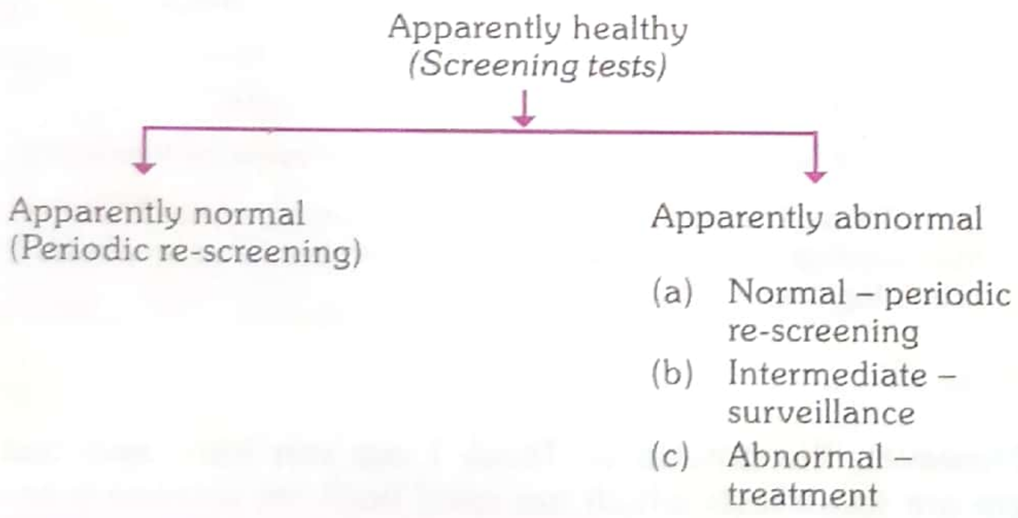

FIG.2
Possible outcomes of screening

Explanation of terms

a. Screening

Strictly speaking, screening is testing for infection or disease in populations or in individuals *who are not seeking health* care; for example, serological testing for AIDS virus in blood donors, neonatal screening, premarital screening for syphilis.

b. Case-finding

This is use of clinical and/or laboratory tests to detect disease in individuals seeking health care for other reasons, for example, the use of VDRL test to detect syphilis in pregnant women. Other diseases include pulmonary tuberculosis in chest symptomatics, hypertension, cervical cancer, breast cancer, diabetes mellitus, etc.

c. Diagnostic tests

Use of clinical and/or laboratory procedures to confirm or refute the existence of disease or true abnormality in patients with signs and symptoms presumed to be caused by the disease; for example, VDRL testing of patients with lesions suggestive of secondary syphilis; endocervical culture for *N. gonorrhoea*.

The distinction between screening, case-finding or diagnosis should be clear-cut. Often, however, it is blurred by the multiplicity of tests used and the haphazard nature of diagnostic decision-making. Thus the same test may be used in different contexts for both screening and diagnosis. Each step may involve multiple tests as in the case of syphilis. In evaluating a test, then, one must consider whether it is for screening or diagnosis, alone or in conjunction with other tests *(19)*.

Uses of screening

Four main uses have been described:

a. Case detection

This is also known as "prescriptive screening". It is defined as the presumptive identification of unrecognized disease, which does not arise from a patient's request, e.g., neonatal screening. In other words, people are screened primarily for their own benefit. Specific diseases sought by this method have included bacteriuria in pregnancy, breast cancer, cervical cancer, deafness in children, diabetes mellitus, iron deficiency anaemia, PKU, pulmonary tuberculosis, haemolytic disease of the newborn, etc. *(5)*. Since disease detection is initiated by medical and public health personnel, they are under special obligation to make sure that appropriate treatment is started early.

b. Control of disease

This is also known as "prospective screening". People are examined for the benefit of others, e.g., screening of immigrants from infectious diseases such as tuberculosis and syphilis to protect the home population; and screening for streptococcal infection to prevent rheumatic fever. The screening programme may, by leading to early diagnosis permit more effective treatment and reduce the spread of infectious disease and/or mortality from the disease.

c. Research purposes

Screening may sometimes be performed for research purposes. For example, there are many chronic diseases whose natural history is not fully known (e.g., cancer, hypertension). Screening may aid in obtaining more basic knowledge about the natural history of such diseases, as for example, initial screening provides a prevalence estimate and subsequent screening, an incidence figure. Where screening is done for research purposes, the investigator should inform the study participants that no follow-up therapy will be available.

d. Educational opportunities

Apart from possible benefits to the individual and the acquisition of information of public health relevance, screening programmes (as for example, screening for diabetes) provide opportunities for creating public awareness and for educating health professionals.

Types of screening

Three types of screening have been described:

a. Mass screening
b. High-risk or selective screening
c. Multiphasic screening.

a. Mass screening

Mass screening simply means the screening of a whole population *(6)* or a sub-group, as for example, all adults *(7)*. It is offered to all, irrespective of the particular risk individual may run of contracting the disease in question, (e.g., tuberculosis).

Mass screening for disease received enthusiastic support in the past. However, when a number of mass screening procedures were subjected to critical review, there appeared to be little justification for their use in many instances *(8)*. Indiscriminate mass screening, therefore, is not a useful preventive measure unless it is backed up by suitable treatment that will reduce the duration of illness or alter its final outcome.

b. High-risk or selective screening

Screening will be most productive if applied selectively to high-risk groups, the groups defined on the basis of epidemiological research *(7)*. For example, since cancer cervix tends to occur relatively less often in the upper social groups, screening for cancer cervix in the lower social groups could increase the yield of new cases. One population sub-group where certain diseases (e.g., diabetes, hypertension, breast cancer) tend to be aggregated in the family. By screening the other members of the family (and close relatives), the physician can detect additional cases.

Epidemiologists have extended the concept of screening for disease to screening for "risk factors", as these factors apparently antedate the development of actual disease. For example, elevated serum cholesterol is associated with a high risk of developing coronary heart disease. Risk factors, particularly those of a patho-physiological nature such as serum cholesterol and blood pressure are amenable to effective interventions. In this way, preventive measures can be applied before the disease occurs. Besides effectiveness, economical use of resources will also occur if the screening tests are selectively applied to individuals in high-risk group.

c. Multiphasic screening

It has been defined as the application of two or more screening tests in combination to a large number of people at one time than to carry out separate screening tests for single diseases. The procedure may also include a health questionnaire, clinical examination and a range of measurements and investigations (e.g., chemical and haematological tests on blood and urine specimens, lung function assessment, audiometry and measurement of visual acuity) – all of which can be performed rapidly with the appropriate staffing organization and equipment *(7)*.

Multiphasic screening has enjoyed considerable popularity, and evidence from randomized controlled studies in UK and USA suggested that multiphasic screening has not shown any benefit accruing to the population in terms of mortality and morbidity reduction *(9)*. On the other hand, it has increased the cost of health services without any observable benefit. Furthermore, in multiphasic screening, as currently practised, most of the tests have not been validated. These observations have cast doubts on the utility of multiphasic screening *(10, 11)*.

CRITERIA FOR SCREENING

Before a screening programme is initiated, a decision must be made whether it is worthwhile, which requires ethical, scientific, and, if possible financial justification *(4)*. The criteria for screening are based on two considerations: the DISEASE to be screened, and the TEST to be applied *(12,13,14,15)*.

Disease

The disease to be screened should fulfil the following criteria before it is considered suitable for screening:

1. the condition sought should be an important health problem (in general, prevalence should be high);
2. there should be a recognizable latent or early asymptomatic stage;
3. the natural history of the condition, including development from latent to declared disease, should be adequately understood (so that we can know at what stage the process ceases to be reversible);
4. there is a test that can detect the disease prior to the onset of signs and symptoms;
5. facilities should be available for confirmation of the diagnosis;
6. there is an effective treatment;
7. there should be an agreed–on policy concerning whom to treat as patients (e.g., lower ranges of blood pressure; border-line diabetes);
8. there is good evidence that early detection and treatment reduces morbidity and mortality;
9. the expected benefits (e.g., the number of lives saved) of early detection exceed the risks and costs.

When the above criteria are satisfied, then only, it would be appropriate to consider a suitable screening test.

Screening test

The test must satisfy the criteria of acceptability, repeatability and validity, besides others such as yield, simplicity, safety, rapidity, ease of administration and cost. Tests most likely to fulfil one condition may however, be least likely to fulfil another – for example, tests with greater accuracy may be more expensive and time consuming. The choice of the test must therefore often be based on compromise.

1. Acceptability

Since a high rate of cooperation is necessary, it is important that the test should be acceptable to the people at whom it is aimed. In general, tests that are painful, discomforting or embarrassing (e.g., rectal or vaginal examinations) are not likely to be acceptable to the population in mass campaigns.

persons having the disease, and to a reference group not having the disease (Table 3). Sensitivity and specificity, together with "predictive accuracy" are inherent properties of a screening test. These are discussed below.

TABLE 3–A

Screening test result by diagnosis

Screening test results	Diagnosis		Total
	Diseased	Not diseased	
Positive	a (True-positive)	b (False-positive)	a+b
Negative	c (False-negative)	d (True-negative)	c + d
Total	a + c	b + d	a + b + c + d

The letter "a" (Table 3–A) denotes those individuals found positive on the test who have the condition or disorder being studied (i.e., true-positives). The group labelled "b" includes those who have a positive test result but who do not have the disease (i.e., false-positives). Group "c" includes those with negative test results but who have the disease (i.e., false-negatives). Finally, those with negative results who do not have the disease are included in group "d" (i.e., true-negatives).

Evaluation of a screening test

The following measures are used to evaluate a screening test:

(a) Sensitivity = $a/(a + c) \times 100$

(b) Specificity = $d/(b + d) \times 100$

(c) Predictive value of a positive test = $a/(a + b) \times 100$

(d) Predictive value of a negative test = $d/(c + d) \times 100$

(e) Percentage of false-negatives = $c/(a + c) \times 100$

(f) Percentage of false-positive = $b/(b + d) \times 100$

Let us rewrite Table 3–A substituting hypothetical figures (Table 3–B) and calculate the above measures:

TABLE 3–B

Screening test result by diagnosis

Screening test results	Diagnosis		Total
	Diseased	Not diseased	
Positive	40 (a)	20 (b)	60 (a+b)
Negative	100 (c)	9,840 (d)	9,940 (c + d)
	140 (a + c)	9,860 (b + d)	10,000 (a + b + c + d)

(a) Sensitivity (true-positive) = $(40/140) \times 100$ = 28.57%

(b) Specificity (true-negative) = $(9840/9860) \times 100$ = 99.79%

(c) False-negative = $(100/140) \times 100$ = 71.4%

(d) False-positive = $(20/9860) \times 100$ = 0.20%

(e) Predictive value of a positive test = $(40/60) \times 100$ = 66.66%

(f) Predictive value of a negative test = $(9840/9940) \times 100$ = 98.9%

Sensitivity

The term **sensitivity** was introduced by Yerushalmy *(17)* in 1940s as a statistical index of diagnostic accuracy. It has been defined as the ability of a test to identify correctly all those who have the disease, that is "true-positive". A 90 per cent sensitivity means that 90 per cent of the diseased people screened by the test will give a "true-positive" result and the remaining 10 per cent a "false-negative" result.

Specificity

It is defined as the ability of a test to identify correctly those who do not have the disease, that is, "true-negatives". A 90 per cent specificity means that 90 per cent of the non-diseased persons will give "true-negative" result, 10 per cent of non-diseased people screened by the test will be wrongly classified as "diseased" when they are not.

To illustrate, let us compare the sensitivity and specificity of EEG and CAT screening for diagnosis of brain tumours (Tables 4 and 5).

It can be seen from Tables 4 and 5, the CAT screening test is both more sensitive and more specific than EEG in the diagnosis of brain tumours.

In dealing with diagnostic tests that yield a quantitative result (e.g., blood sugar, blood pressure) the situation is different. There will be overlapping of the distributions of an attribute for diseased and non-diseased persons (Fig. 3). False positives and false negatives comprise the area of the overlap. When the distributions overlap, it is not possible to correctly assign individuals with these values to either the normal or the diseased group on the basis of screening alone.

For example, if we decide to use the 2–hour post-prandial blood glucose level of 180 mg/100 ml as an index of the presence of diabetes mellitus, the sensitivity and specificity are 50 and 99.8 per cent respectively (Table 6). In other words, sensitivity is low, but specificity very high. Further it will be seen from Table 6 that sensitivity and specificity are inversely related. That is, sensitivity may be increased only at the expense of specificity and vice versa. An ideal screening test should be 100 per cent sensitive and 100 per cent specific. In practice, this seldom occurs.

TABLE 4

Diagnosis of brain tumours by EEG

EEG results	Brain tumour	
	Present	Absent
Positive	36	54,000
Negative	4	306,000
	40	360,000

Sensitivity = $36/40 \times 100$ = 90 per cent

Specificity = $306,000/360,000 \times 100$ = 85 per cent

TABLE 5

Diagnosis of brain tumours by computer assisted axial tomography

CAT results	Brain tumour	
	Present	Absent
Positive	39	18,000
Negative	1	342,000
	40	360,000

Sensitivity = $39/40 \times 100$ = 97.5 per cent

Specificity = $342,000/360,000 \times 100$ = 95 per cent