



EXPERT COMMITTEE ON EARLY DETECTION OF CANCER

Geneva, 11-16 November 1968

INDEXED

THE EARLY DETECTION PROGRAMME

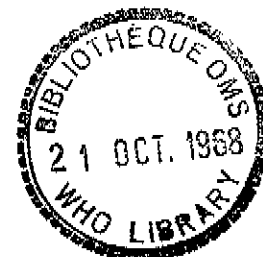
Basic working paper

prepared by

Dr William L. Ross
Chief, Cancer Control Program
National Center for Chronic Diseases Control
USPHS, Arlington, Virginia
United States of America

and

Dr R. Eker
Director, Det Norske Radiumhospital
Oslo, Norway



INTRODUCTION AND GENERAL CONSIDERATIONS

"Preservation of health is without doubt
the chief blessing and the fountain
of all other blessings in this life."

Descartes

"The superior physician helps before the early
budding of disease . . . the inferior physician
begins to help when the disease has already
developed; he helps when destruction has
already set in."

Huang Ti Nei Ching Su Wen, 2800 B.C.

The philosophy of preventive medicine - as embodied in the above quotation from ancient China - is old and acceptable. However, we have yet to fully recognize the validity of this concept in any significant manner.

Historically, medicine seemingly passed through the "preventive medicine" stage with milestones marked by the work of Pasteur, Lester, Koch and Salk. Recently, this progress has been overshadowed by advances in antibiotics and surgical techniques. In practical terms, the concept remains the most promising area for future medical advances. Although no cure for most forms of systemic cancer has been discovered, it has nevertheless been possible to make significant advances in saving the lives of patients in whom cancer is detected. One hundred years ago, a patient with cancer had little chance of survival. Ten or twenty years ago, a cancer patient had perhaps one chance in four of recovery. Today, fairly accurate statistics

The issue of this document does not constitute formal publication. It should not be reviewed, abstracted or quoted without the agreement of the World Health Organization. Authors alone are responsible for views expressed in signed articles.

Ce document ne constitue pas une publication. Il ne doit faire l'objet d'aucun compte rendu ou résumé ni d'aucune citation sans l'autorisation de l'Organisation Mondiale de la Santé. Les opinions exprimées dans les articles signés n'engagent que leurs auteurs.

suggest that a patient with frank cancer has one chance in three of getting well. Much of this progress has been due to technical improvements in the treatment of cancers by surgical procedures and by radiation therapy. However, certainly some of this gain is due to improvements in examination procedures that enable the early detection of cancer or precancerous lesions at a time when the cancers are sufficiently localized to be amenable to standard therapy.

It has been authoritatively estimated that today more than 50 per cent. of all cancer patients could be cured if their lesions were detected as early as is now possible, with regular examinations and the best examining techniques, and if they were treated with all of the best resources of modern medicine and surgery. Advances on several fronts will need to be made to close this gap between the one-third of cancer patients cured today and the potential cure rate of over 50 per cent., but it is manifest that one important step towards improving the cancer cure rate is wide application of cancer detection procedures to asymptomatic patients plus application of the best diagnostic procedures, combined with skill and insight in interpretation of the findings. Also needed is constant attention to improvement of cancer detection procedures as well as possible development of new ones.

Control of cancer has in recent years been assuming increasing importance in the health work of most developed countries. Cancer control embraces a series of measures based on modern knowledge of prevention, diagnosis, treatment, after-care and rehabilitation. Its aim is to reduce the incidence of the disease, improve its prognosis and prevent morbidity (invalidism).

The World Health Organization Expert Committee on Prevention of Cancer stated in its report^a that in light of present knowledge, the majority of human cancer seems to be potentially preventable. The control of carcinogens plays an essential role in primary prevention. At the present stage, however, secondary prevention by means of early detection and prompt and adequate treatment of precancerous and cancerous conditions is of major public health importance.

It is now recognized all over the world that fundamental changes have occurred and are still occurring in the relative role of different groups of diseases as causes of morbidity and mortality. One of the most striking features in mortality statistics at present, apart from the increased number of deaths due to accidents, is that certain chronic, non-contagious diseases, amongst them cancer and diseases of the cardiovascular system, have replaced communicable diseases as the leading causes of death. This trend is most pronounced in countries with a relatively high standard of living and well-developed health services, but may now also be observed in developing countries.

It is, however, not only the increasing role of cancer as a cause of death and invalidism that has stimulated the interest of health authorities as well as the public in the cancer problem. Encouraging progress in knowledge of the etiology of malignant tumours has opened the road to the prevention of certain types of cancer and the results of surgical, radiological and chemical treatment of the disease have furnished a number of new approaches.

The time when the management of patients with malignant tumours could be left to individual clinicians has long passed. Control of cancer, in the wider sense of the term "control", has in recent years become an integral and important part of the health services of a number of countries. Cancer control consists of a series of measures based on present medical knowledge in the fields of prevention, detection, diagnosis, treatment, after-care and rehabilitation, aimed at reducing significantly the number of new cases, increasing the number of cures, and reducing the invalidism due to cancer.

^a Wld Hlth Org. techn. Rep. Ser., 1964, 276.

In some countries philanthropic organizations have been able to raise funds for the control of cancer which have been utilized with great effect by farsighted health administrations to increase knowledge of the disease and to improve facilities for the protection of the public. Greatly improved cancer control systems have been developed or are being developed in most parts of the world. Both the public and the health authorities of most countries now expect a plan and an organization for cancer control.

The scientific approach to cancer control has its origin in observations on occupational cancers made some two hundred years ago. The identification and elimination of carcinogens from industry was the first step in effective control and has resulted in legislation in many countries prohibiting or restricting the use of a large number of carcinogenic substances, and leading thereby to the eradication of certain types of cancer. The control of carcinogens continues to play an essential role in primary prevention, but in the cancer problems that are of greatest public health interest today improved methods of secondary prevention play an important part. This latter development has largely been due to improved methods of detection, diagnosis and treatment of cancer and precancerous conditions. Personal habits and customs are now known to be major etiological factors in some cases.

The first steps in a control policy have been developed by legislation introducing cancer services and cancer education. These services extend from control measures in the hands of the specialist of large-scale methods involving the active co-operation of the public.

The time has now arrived for a consideration of the present situation of early detection of cancer from an international point of view.

DEFINITIONS

Inasmuch as the terminology used in early detection such as screening, case-finding, surveillance, etc., has different meanings in different countries and even, in many instances, different meanings in the same country, it was felt that a section providing common definitions of the terms that will be most widely used in this report would be needed. That is the purpose of this section, and it is hoped that all Committee members will utilize these definitions unless there is a consensus that any of the definitions should be rewritten. It should be clearly recognised that a common definition for each of the terms outlined below is necessary if the report is to be understood by those concerned.

(1) Early detection

In this report, detection covers all measures aimed at isolating suspect cases within a given population. Persons so detected are given detailed complementary examinations to enable a diagnosis to be made. It should be stressed that the techniques envisaged as belonging to detection will not of themselves enable a firm diagnosis to be made. It is sometimes useful, we think, to use a term that refers to all forms of early detection, whether by screening, physical examination or other means.

(2) Screening

The United States Commission of Chronic Illness (CCI)^a defined screening as "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 apparently well persons who probably have a disease from those who probably do 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". This definition was adopted in principle by the WHO Expert Committee on Cancer Control in 1963^b and

^a United States Commission of Chronic Illness - Conference on preventive aspects of chronic disease held in 1951.

^b Wld Hlth Org. techn. Rep. Ser., 251.

the WHO Regional Committee for Europe in 1964. It should be noted that, by definition, unrecognized symptomatic as well as pre-symptomatic disease is included; also, physical examination is considered as part of the procedure so long as it can be classed as rapid. The term "other procedures" may also embrace the use of questionnaires, which are assuming an increasingly important place in screening. Finally, tests may be "diagnostic", though not necessarily so intended; for example, a gynaecological examination could be covered by this definition provided it were rapidly carried out. In general, we have taken the definition to imply a relatively simple (though not necessarily unsophisticated) method of case-finding.

(3) Mass screening

This is a term used to indicate the large-scale screening of whole population groups. We have used it to refer to screening where no selection of population groups is made.

(4) Selective screening

We use this term for the screening of selected high-risk groups in the population. It may still be large scale, and can be considered as one form of population screening.

(5) Multiple (or multiphasic) screening

This procedure has evolved by combining single screening tests, and is the logical corollary of mass screening. Where much time and effort has been spent by a population in attending for a single test (e.g. mass radiography) it is natural to consider the economy of offering other tests at the same time. Multiple (or multiphasic) screening has been defined as "the application of two or more screening tests in combination to large groups of people".^a

(6) Surveillance

This term is often used as a synonym for screening and essentially, in the sense the term is used, it does have the same meaning. However, a useful and important distinction can perhaps be made between the two terms. Webster's Third New International Dictionary (1966) defines "surveillance" as "close and continuous observation", while the definition of "to screen" is "to examine . . . methodically in order to make a separation into different groups". "Screening" tends to be thought of as (and in practice often is) a cross-sectional, short-term operation on a population at risk (e.g. "health weeks", "health fairs"); while "surveillance" conveys rather the sense of a long-term vigil over the health of an individual or of a population.

In this report "surveillance" has been used to convey the idea of a long-term process where screening examinations are repeated at intervals of time.

(7) Case-finding

Throughout this report this term is applied to that form of screening of which the main object is to detect disease and bring patients to treatment, in contrast to epidemiological surveys (see below).

(8) Population or epidemiological surveys

While screening tests may well be used in population surveys (e.g. sphygmomanometry for blood-pressure or tonometry for intra-ocular tension), the principle aim of surveys is not to bring patients to treatment but to elucidate the prevalence, incidence and natural history of the variable or variables under study, though case-finding is a natural by-product of surveys. A good example of an epidemiological survey is the Framingham study of ischaemic heart disease.^b

^a Commission on Chronic Illness (1957) Chronic illness in the United States: Prevention of chronic illness, Cambridge, Mass., Harvard University Press, vol. I, p. 45.

^b Dawber, T. R., Moore, F. E. & Mann, G. V. (1957) Coronary heart diseases in the Framingham study, Amer. J. publ. Hlth, 47, Suppl., 4.

4.1 MASS SCREENING

GENERAL CONSIDERATIONS

The aim of early disease detection (sometimes called secondary prevention) is simple. Primary prevention seeks to abolish disease by protecting the individual and the population from attack before the challenge has been made. Early detection (case-finding) aims at discovering and curing conditions which have already produced pathological change but which have not so far reached a stage at which medical aid is sought spontaneously. Therefore, cancer detection can be defined as the search for an identification of cancer or its precursors in the asymptomatic, presumably healthy individual by means of a standardized routine examination.

Detection versus diagnosis. Cancer detection is to be contrasted with cancer diagnosis which usually refers to the identification of the disease in an individual as a result of physical, laboratory, or other examinations prompted by specific symptoms or complaints. If not found first by a cancer detection examination, presumably all such malignant lesions will declare themselves eventually and yield to efforts at cancer diagnosis.

It is felt that such a distinction between detection and diagnosis is not a mere academic exercise in precise semantics. The belief that there is biologic justification for such a distinction in clinical cancer is a tacit reflection of principles which provide the rationale, direction and scope of present-day efforts at cancer control.

Rationale of cancer detection. Efforts to promote the more widespread adoption of cancer detection examinations throughout the world makes certain assumptions:

- (1) In many instances cancer is preceded for a period of months or years by a microscopically benign lesion which ultimately becomes or gives rise to microscopically and clinically malignant disease. Removal of such lesions prevents the subsequent development of cancer. This is true cancer prevention.
- (2) Most cancer at its inception goes through a phase in which it is quite localized either at the cellular or organ level. If cancer is found at this stage, a high rate of cure is obtainable.
- (3) Over 75 per cent. of cancer occurs in areas which are readily accessible to periodic survey by reliable cancer detection procedures.
- (4) Although far from ideal, present-day methods of treatment are often very effective when applied early enough.
- (5) In most sites and in most cases there is a clearly demonstrable relationship between early diagnosis and good prognosis.

It is, however, considered to be rightly stated that "none of these assumptions has received complete clinical, statistical or experimental confirmation although they are being studied in various countries. As far as in situ carcinoma is concerned, these so-called pre-invasive lesions are not truly malignant in the usual definition of the word; they are peculiar lesions which develop into cancer at an unknown rate of frequency. It is necessary, therefore, to record separately these precancerous changes and in situ lesions in the statistics of cancer detection".

No claim is made that this search for and treatment of the early case is the ideal approach to the problem or that it is always successful. Perhaps before long it will be supplanted by a new method oriented to a quite different concept of the disease, more reliable, less expensive and time-consuming, and, most important of all, more effective.

However, it can be safely said that in the light of our current understanding of the disease and considering the clinical, laboratory and treatment methods now available, programmes of cancer control which emphasize the detection and early diagnosis of cancer and its precursors afford the best protection possible for the individual and the community at present.

4.1.1 TECHNIQUES AND METHODS FOR SCREENING AND THEIR APPLICABILITY TO VARIOUS CANCER SITES

Cancer detection tests. Cancer detection tests can be divided rather simply into two groups: (1) those which purport to indicate the presence of the disease anywhere in the individual's body and (2) those which point to the presence of cancer in a specific single organ or site.

The purpose of a cancer detection test is to single out from a large group surveyed those relatively few individuals in whom a diagnosis or suspicion of cancer is suggested by this screening process. These patients can then be subjected to more intensive evaluation by conventional diagnostic measures.

Criteria for cancer detection tests. The ideal cancer detection test, whether general or site-specific, should possess the following characteristics:

- (1) Simplicity. The procedure should be uncomplicated, easily and quickly carried out, with a minimum of discomfort to the patient. It should be adaptable for screening large numbers of patients.
- (2) Low cost. The procedure should be inexpensive in terms of equipment required and professional and technical time consumed.
- (3) Reliability. The percentage of false positives must be kept to a minimum.
- (4) Sensitivity. The percentage of false negatives must also be low. Furthermore, the procedure must be capable of detecting disease in its early, localized stages.
- (5) Productivity. Assuming a test is sensitive and reliable, the yield of cancer is a reflection of the incidence of the disease rather than the procedure itself.

It is immediately apparent that these criteria are not absolute but are relative. Not only that, they are interdependent. For example, proctosigmoidoscopy is not exactly a "simple" procedure. However, what it lacks in simplicity it more than makes up in reliability and productivity. On the other hand, whatever virtues screening or detection methods for bone tumours, pheochromocytomas, etc., might have in terms of simplicity, reliability, sensitivity, etc., are cancelled out by the very low yield to be expected. The final assessment of the value of a cancer detection method lies in a critical evaluation of the number of these criteria it satisfies and to what degree.

General screening tests for cancer. The desire for a general cancer detection test which would screen large population groups is an obvious and natural one, but it seems no closer to fulfilment today than when the search began in earnest over a quarter of a century ago. The advantages of a relatively simple, reliable, and universally applicable test for cancer similar to the laboratory serologic test for syphilis, require little amplification.

Despite continual failures, many investigators are searching for a general test for cancer which will shorten the time from the development of malignant cells somewhere in the body to definitive treatment of the primary site. Numerous tests have been proposed to

exploit and measure some alleged characteristics of the cancer patient's blood, urine, body secretions, or immunologic or enzyme systems. Thus far, all the tests have been found wanting for a number of reasons.

Site-specific or single organ screening tests for cancer. While there is currently no available general cancer screening test, a number of different methods and techniques for diagnosing precancerous conditions and early invasive cancer have been extensively studied in recent years. While many of these techniques are still in the experimental stage and their value can only be definitely assessed after further development and testing, there are many screening techniques which have proven of value for the detection of cancer in various sites throughout the body.

Listed below are a number of techniques and methods which, in the main, have proven themselves to be of value, under appropriate conditions, when utilized for mass screening purposes. However, the techniques and methods for detection will often not, in themselves, enable a firm diagnosis to be made. Suspected cases identified through screening programmes must be given detailed complementary examinations before definitive diagnoses can be established.

Techniques and methods for screening

- (1) Clinical examination. One of the most important methods is still the judgement which follows a good clinical examination of the patient, which in a screening procedure should be classed as rapid and may usually include one or more body sites without necessarily being a complete physical examination.
- (2) Exfoliative cytology. The rapidly developing field of cytodiagnosis has introduced new possibilities for the detection of cancer in many parts of the body. Exfoliative cytology, in this context, refers to the study of cells shed from a surface such as that from the bronchial, gastric, or uterine mucosa, into the secretions of these organs. The presence of malignant disease may then be detected by examination of secretions from these areas. It should be noted that this technique is one of the most important of the techniques available for early cancer detection. This method has been extensively used with great success in mass screening for precancer and cancer of the cervix uterine. It is considered of value, too, in screening for cancer of some other sites. Cytologic specimens can be prepared from exfoliated material as well as from material obtained directly from the mucus surface by scraping or from more deeply located tissues by aspiration.
- (3) X-ray techniques. There are a number of techniques utilizing various types of X-ray examination. Because of the number of these and the fact that several of them are site-specific, they will be discussed at the time the specific body site is discussed in terms of cancer screening.
- (4) Thermography. Fever, as registered by the clinical thermometer, has long been known to signify illness but localized skin temperature elevations have received scant attention. Being homiothermic, maintaining a uniform core temperature of approximately 37°C, and living in an electro-magnetic environment, man radiates energy in the infra-red portion of this spectrum according to the second law of thermodynamics. The recent development of highly sensitive infra-red detection devices for use by the military in their space programmes has eventuated in the adoption of such devices for biological and medical use. One of the most significant capabilities of these devices or thermographs is the detection of minute amounts of heat generated in and around multiplying cancer cells.
- (5) Endoscopy. A number of potential cancer sites can be examined by this technique, e.g. by broncoscopy, colposcopy, and proctosigmoidoscopy.

(6) Enzyme tests. Although some promising results from experimental screening with various enzyme tests for precancer and early cancer have been reported, much research is still needed before the value of this technique can be adequately assessed.

(7) Other techniques. Colposcopic examination of the cervix has been included as a complementary technique in experimental mass screening programmes. As a screening tool it must, however, be regarded as less efficient than accurate cytological examinations in pointing to cervical pathology. Its application as a routine technique in mass screening has many disadvantages. Colposcopic examinations are, however, considered of great value for the complementary examination of suspected cases.

Screening for carcinoma of the stomach by intragastric photography (gastro-camera) must still be regarded as in the experimental stage. It seems doubtful whether this technique will be of practical importance in mass examinations, except in special high-risk groups.

In some instances the use of self-examination by the population being screened may be useful. In the use of self-examination, probably the two most important techniques are self-inspection and self-palpation. The applicability of self-examination to the various body sites will be discussed in the succeeding section on the application of screening techniques and methods to cancer sites.

Applicability of techniques and methods for screening to various cancer sites

This section will identify the most common body cancer sites that lend themselves to one or more screening technique or method. A brief listing of each technique or method will be given for each body site, following which, where indicated, additional descriptive information will be given.

As noted in the previous section, one of the most important methods for detecting cancer is a good examination. Since this examination in some form or another might be given for most of the body sites being considered, in the interest of not being repetitious they will not be listed.

(1) Lung

- (a) Chest X-ray.
- (b) Exfoliative cytology.

We do not possess accurate morbidity data on lung cancer that would indicate the size of the problem. Nevertheless, an idea can be obtained from the general practice survey carried out by the College of General Practitioners and the General Register Office in England and Wales in 1955-1956,¹ since it is likely that all patients with lung cancer consulted their family doctor at least once during the observation year. The rate for "patients consulting" for neoplasm of the lung, bronchus and trachea is 0.5 per 1000 persons (1.0 per 1000 for males and 0.1 per 1000 for females); for men between the ages of 45 and 64 the rate is 2.1 per 1000. In this high-risk group lung cancer is found, therefore, at a rather lower prevalence rate than is carcinoma in situ of the uterine cervix in all adult women (3.0 per 1000). However, lung cancer is so lethal that deaths from this condition are more than five times as frequent as those from cancer of the cervix. Moreover, mortality has been increasing annually at an alarming rate in the highly-developed countries, in step with earlier cigarette smoking; in England and Wales the number of deaths due to malignant neoplasms of the trachea, bronchus and lung has increased in males by nearly two-thirds between 1954 and 1964, having

risen from 14 000 to 24 500.² Such is the nature of lung cancer, therefore, that if early detection could be made effective, mass screening of the adult population in highly-developed countries would be indicated.

Unlike the accessible cancers (cervix, lip and skin) lung cancer is customarily at an advanced stage when diagnosed with the help of X-rays and the prognosis is nearly always bad. The corrected survival rate at five years for males in England and Wales registered during 1945-1947 was only 14 per cent. for early cases submitted to radical treatment.³ For all early cases, whether treated or not, the five-year survival rate was only two per cent. Seven out of eight cases were in men and of these only 13 per cent. were classified as early at diagnosis, while nearly one-quarter had metastases. The median duration of symptoms was about six months for the early cases but only four-and-a-half months for those already with metastases. The five-year survival rate of both early and late cases treated radically was unaffected by the duration of the symptomatic history, being 12 per cent. for persons with symptoms of from 0 to 2 months' duration and 10 per cent. for those who had had symptoms for 12 months and over.

This is a gloomy picture, but it is necessary to remember that it is based on persons developing the disease 20 years ago. Since then mass radiography (MR) has been practised widely and it is necessary to study its effect in combination with advances in thoracic surgery. MR was, of course, developed for case-finding in the epidemiological control of pulmonary tuberculosis. With the decline of tuberculosis in many countries, attention has turned towards the possibility of using MR mainly for diagnosing other lung conditions, of which cancer is the most important, rather than just for seeking out tuberculosis. We therefore need to see as clearly as possible what is the evidence for benefit so that a sensible policy can be evolved.

Four surveys will be considered: that of Posner, McDowell & Cross in Birmingham;⁴ Cuthbert's review of the Glasgow X-ray campaign;⁵ Waddington's comparison of the Liverpool survey with his own and Gifford's routine hospital admissions;⁶ and Boucot, Cooper & Weiss's experience with the Philadelphia Pulmonary Neoplasm Research Project.⁷

Birmingham. Posner and his colleagues analysed all cases of lung cancer diagnosed by mass miniature radiography (MMR) units in the Birmingham Hospital Region during one year (1955-1956), 238 in all being investigated. As with the Glasgow series, patients diagnosed by "conventional" MMR ("routine MMR cases") were compared with patients referred to the units by general practitioners ("referred cases"). There were rather more older patients in the group referred by general practitioners. At one year the survival of the routine MMR group was better than that of the referred group - 50 per cent. compared with 36 per cent. - though this difference is not significant. More of the routine MMR cases proved to be resectable than the referred cases - 44 per cent. compared with 30 per cent.; also there was a higher proportion of lobectomy as opposed to pneumonectomy in the routine MMR group, which is usually considered to equate with a better prognosis. As with the Glasgow series, 85 per cent. of the routine MMR group had had symptoms at the time of presenting for examination. Posner et al. concluded that the smallest cancers were very easily missed and recommended the selective screening, by static 100-mm camera units, of men over 35 referred by their own doctors, irrespective of symptoms. They considered it would be a major mistake if the relatively high cost of a programme of this kind were to be allowed to deflect attention from the importance of primary prevention.

Glasgow. Forty-eight patients with proved bronchogenic carcinoma were found through the operations of one of the city chest clinics, and these patients were compared with 48 consecutive patients referred to the same clinic by general practitioners. The average age of the two series was about the same with a similar range, most of the patients being between 50 and 65. Of the 48 MMR cases, 36 were found to have had one or more of the cardinal symptoms of chest illness; but on several counts the disease in the patients referred by

general practitioners was more advanced. As might be expected, the patients in both series who were considered suitable for surgery had the better survival at 18 months; but the MMR group did better than the referred group, 13 of the MMR group surviving at 18 months compared with only eight of the referred group.

Liverpool. Of more than 450 000 persons over the age of 15 years X-rayed in the Liverpool campaign of February-March 1959, 235 were admitted to surgical wards for investigation. Of these, 163 were suspected of suffering from bronchial neoplasm - a rate of 0.36 per 1000 persons (0.5 per 1000 males), which is somewhat lower than the general practice survey rate quoted above. Of the 163 suspects, 118 were proved to have a primary bronchogenic carcinoma, and Waddington compared these with his earlier series of patients admitted to the Liverpool Thoracic Unit. Of the 118 from the Liverpool campaign, 80 (68 per cent.) were resected, which amounted to 90 per cent. of all those surgically explored. This is a rather higher rate than was found in the hospital series, where only 70 per cent. of those explored could be resected. Moreover, a higher proportion of the Liverpool campaign patients could be treated by lobectomy (as opposed to pneumonectomy) than in the hospital series. However, at the time of compiling the report, while only 61 per cent. of all the operated patients from the MMR campaign (who had survived the first two months) had survived one year, 67 per cent. of the hospital series had so survived. There therefore seems to have been no advantage, at the time of writing, for those presumptively diagnosed earlier by MMR.

Philadelphia. In this well-known project 6137 men of 45 years of age or more were enrolled in an experimental prospective survey with the aim of following them up by means of six-monthly 70-mm chest X-rays and a short medical history. A previous MR campaign in Philadelphia has shown a prevalence rate for lung cancer of 2.7 per 1000 men over 45, which is rather more than was found in the survey carried out by College of General Practitioners in a similar age-group.

During the course of the study, 26 men, in whom no radiological evidence of neoplasia had been discovered on entry to the project, developed lung cancer. Only five were without symptoms up to the time of the first positive X-ray and only two were asymptomatic actually at the time of the examination. The other finding of direct interest is the period of survival: only two of the 26 had survived to the time of writing the paper, which could have given a maximum survival time of seven-and-a-half years, though there is no statement as to actual survival times.

From these surveys it is clear that the prognosis of lung cancer is little influenced by detection by routine radiography and that, in fact, most of those who are detected in this way are symptomatic at the time of their X-ray. It seems probable that, as at present carried out, routine chest X-ray at any interval greater than six months would be of little use. More frequent X-ray examination not only would be uneconomic but would also pose problems of persuading subjects to attend and of causing possible harm from radiation exposure. The best use of routine radiology at present is likely to be for the selective screening of middle-aged persons, particularly males, who are heavy smokers and/or have a persistent cough.

In considering the results of these (and other) early detection surveys it is important to remember that like is not being compared with like; and that the slightly better prognosis in the screened, as compared with the routinely diagnosed, series of patients is probably accounted for by the fact that the disease in the screened group was discovered earlier in its course. It is therefore unwise to attribute, without better evidence, the improved prognosis to the effects of treatment. Truly to compare two series in this way, it is necessary to follow the treated patients over a much longer period, in order to observe the long-term effect of earlier diagnosis on the cure rate.

Another point of importance in comparing series in this way is the need for random allocation of the population into screened and control sections. Without this precaution there is the real danger that the patients diagnosed early by X-rays may differ in important respects (which might affect the prognosis) from the routinely diagnosed group.

The examination of sputum by exfoliative cytology has also been employed as a means of detecting early cancer of the lung. Compared with the use of exfoliative cytology for cervical cancer there are drawbacks. The bronchus is not as accessible as the cervix; and examining the sputum is considerably more time-consuming than examining cervical smears if the results are to be at all reliable. At the Johns Hopkins Hospital, Baltimore, the positive sputum rate in patients with bronchial carcinoma rose from only 20 per cent. when one sputum specimen was examined to 56 per cent. when five specimens (three smears of each - i.e. 15 slides) were examined (or from 42 per cent. to 95 per cent. when suspicious as well as definitely positive reports were included). In another series of 144 patients with suspected lung cancer at St Bartholomew's Hospital, London,⁸ 10 per cent. of the results obtained from examining three smears from one specimen of sputum were false-negative. The time needed to achieve this degree of accuracy was unacceptably long. A rapid sputum cell concentration technique is needed to shorten examination time, and work on these lines is proceeding.

Lilienfeld has reported on a comparison between sputum cytology and radiology in the early detection of lung cancer in persons living in United States Veterans' Administration homes. Up to 1960 over 12 000 persons, aged 45 and over, had been submitted to a six-monthly X-ray and sputum cytological examination at least once, and some 4000 had been screened three or four times. Of 43 cases of lung cancer diagnosed by follow-up, cytological screening contributed to the diagnosis in 15, and this diagnosis would have been missed if X-ray screening alone had been used. On the other hand, if cytology alone had been used, 21 of the 43 would have been missed. Unfortunately survival at six months was no better than that observed on previous occasions, where repeated screening was not carried out.

It appears, therefore, that while sputum cytology is complementary to chest X-ray, its use does not improve the prognosis by earlier diagnosis in lung cancer; and that the technique is too time-consuming for it to be economically justifiable as a mass screening measure.

Clearly the prevention of lung cancer would be far better than early detection, and it is interesting that the American Cancer Society and Veterans' Administration study just referred to showed that one per cent. of present smokers had positive or suspect sputum cytology as compared with 0.35 per cent. of those who had never smoked and 0.47 per cent. of past smokers.

(2) Female genital organs

- (a) Exfoliative cytology.
- (b) Colposcopy.
- (c) Schiller's iodine test.

The evidence of the value of detecting cervical cancer early is relatively strong. The earlier the stage at diagnosis the better is the survival rate. It is also reasonable to suppose that diagnosis and treatment at the pre-invasive, carcinoma in situ stage would very greatly improve the existing survival rate, though it is as yet too soon for the relevant statistical data to have accumulated; nor is there evidence of a reduction in the death-rate directly attributable to diagnosis and treatment of the pre-invasive lesion (though mortality from cervical cancer is in general decreasing at a slow but steady rate in advanced countries). It is, indeed, probably too soon to expect to see this effect, since intensive community screening for cancer of the cervix has only been practised for a few years, and then only in relatively few centres. A considerable fall in the incidence of invasive cervical cancer has, however, been observed in British Columbia and other centres since the introduction of widespread screening by exfoliative cytology, which may or may not be attributable to such screening.

Unfortunately, the relationship between so-called intra-epithelial carcinoma of the cervix, or carcinoma in situ, and invasive cervical cancer has not so far been clearly elucidated beyond the shadow of a doubt. Now, because the evidence is highly suggestive that the one is a precursor of the other - if not always, at least frequently - it can no

longer be considered ethical to carry out a definitive trial. Were it feasible, the ideal trial would randomize between two groups of women in a large population. One group would be screened and re-screened at intervals for carcinoma in situ (as well as for preclinical, micro-invasive cancer) and those women found with lesions would be treated by surgery; while the other, control, group would not be screened, but clinical cancer of the cervix would be diagnosed and treated in the conventional way. Such a trial should demonstrate whether incidence and mortality were lowered and survival lengthened in the screened group, as compared with the controls. It might still be ethical for a trial of this kind to be carried out where facilities for screening, diagnosing and treating uterine cancer are as yet strictly limited by the degree to which medical care is advanced. The nature of the evidence required for a rigorous appraisal of the relationship between carcinoma in situ and invasive cervical cancer has recently been reviewed by Knox.⁹

Short of such a definitive randomized trial, the natural history of pre-invasive cervical cancer has been reasonably closely studied. Firstly, there is relatively good evidence that the in situ lesion of the cervix may become invasive cancer of the cervix. The direct evidence for this is both retrospective¹⁰ and prospective.^{11,12,13,14} There is also indirect evidence based on the age-specific distribution of in situ and invasive cancers.^{15,16} Secondly, estimates are available of the proportion of in situ lesions that become invasive,^{11,12,13,16,17,18} though these estimates vary widely (from one-quarter to two-thirds).

Another important feature of the pre-symptomatic lesion about which there is incomplete information is its duration. Dunn¹⁸ has done useful work on this point, based on his study of the United States Public Health Service survey in Memphis, Tennessee. He and his colleagues¹⁹ now estimate an average duration of about 10 years (calculated from the age-specific prevalence and incidence rates). This accords reasonably well with the estimate of Boyes, Fidler & Lock¹⁶ of 12 to 13 years, based on mean age of onset of both in situ and clinical invasive carcinoma.

Some of the picture presented by pre-invasive cancer of the cervix has therefore been filled in, but there are still important gaps in our knowledge. We need to know about the effect on mortality as quickly as possible since it is possible that incidence could fall without a reduction in the death-rate. To obtain this information, mortality data related to numbers of examinations in populations screened are needed. It is also important, for practical purposes, to discover how frequently cytological examinations need to be carried out. To learn this it is necessary to note the time elapsing between the last negative examination and the first positive one in as large a number of reported screenings as possible, the screening interval being varied in different groups of women. In this way it should be possible to construct a frequency distribution of the rate of progression from cytology negative to invasive cancer in the small number of women in the population who develop cancer of the cervix. Depending on the shape of this distribution curve, it may be possible to select an optimum screening interval at a point where there is a steep increase in the number of invasive cancer cases. Registration of cytological examination and linkage with invasive cancer registration are one way in which this can be done.

There are other practical problems associated with population screening, the solution of which depends on epidemiological knowledge. One of the problems is that of ensuring that examination is offered to women at greatest risk. The evidence shows that the incidence of cervical cancer increases with age; that it affects married rather than unmarried women; that early coitus is an etiological factor rather than parity; that there is a sharp social-class gradient, with the higher incidence in the lower social classes; and that there are marked cultural and geographical differences.^{20,21,22}

It is therefore important, in organizing population screening, to take steps to ensure as far as possible that married women, particularly those who married young, and women in the lower socio-economic groups are not only offered, but accept, examination. This means a "free" service and organized health education along lines planned according to prior attitude

studies. Without this approach it is doubtful whether merely providing facilities will in practice achieve results. It is also necessary to plan health education, based on a knowledge of the fundamental attitudes of the public, both women and men, to cancer of the cervix and cervical cytology, so as to reach that part of the population most in need. The surveys with this aim in view, in Alameda County, California,²³ on a national sample of the population of the United States of America,²⁴ and on a sample of the population of Manchester, England,²⁵ are good examples of this.

A recent development, at present still in the evaluation stage, shows signs of overcoming the difficulty of persuading women at high risk to undergo cytological examination. This is the irrigation pipette,²⁶ a plastic pipette that can be inserted by the woman herself into the posterior fornix of the vagina. The pipette contains fixative, which is expelled into the vaginal pool and sucked back together with exfoliated material. The pipette is then placed in a container and mailed to the laboratory, where smear preparations of the material are made. Davis²⁷ has reported a nearly 80 per cent. rate of acceptance of this technique among "semi-indigent" women in Washington County, Maryland; and a similar acceptance rate has been found both by F. Koch²⁸ in Copenhagen and by Elizabeth MacGregor and her colleagues²⁹ in general practices in Aberdeen - to give only three examples. This method has the possible advantage of making it much easier to obtain cytological specimens. It may also make it possible to obtain specimens from women who, for various reasons, are not reached by the conventional screening programmes. Examination of a moderately efficient self-aspiration may be better than no examination at all, though if this technique, with widespread application, proves less accurate than the conventional methods, it will increase the problem of how to avoid imparting a sense of false security. This technique is being evaluated on a wide scale by the Cancer Control Program of the United States Public Health Service and other groups in the United States of America, and a report on the definitive evaluation of this technique will be issued in the near future.

With the general acceptance of the value of cytological screening for uterine cancer, attention has naturally turned to the possibility of developing automated techniques.

A number of workers are examining the value of estimating the 6-phosphogluconate dehydrogenase (6-PDG) level in vaginal aspirate as an index of the presence of malignant cells. So far this technique has proved too unreliable for case-finding. Though apparently reliable as regards sensitivity as a test for invasive cancer of the cervix, it has a false-negative rate in the region of 50 per cent. for carcinoma in situ.³⁰ The false-positive rate is also high - between 20 per cent. and 40 per cent. The value of varying the technique is now being examined.

The development of an automatic electronic scanner of preparations of vaginal cells has been in progress since the 1950s. A practicable instrument has not so far been developed, but work employing the principle of scanning with a flying spot microscope is advancing. There are numerous possible uses for an instrument of this type and more than medical interests are involved. The cost of developing a prototype instrument is considerable and there might well be a case for co-operative effort in this field. More recently, the possibility of detecting cervical cancer cells in vaginal aspirate, using the Coulter Counter, has been reported.³¹ In addition, several other automated versions using a modification of the Coulter Counter with or without computer techniques added are being investigated. The principle in the latter instance is based on either cell size, nuclear size, or DNA content of the nucleus. It should be noted again that all of these techniques are still being critically investigated.

As noted earlier, colposcopic examination of the cervix has been included as a complementary technique in experimental mass screening programmes. Its application as a routine technique in mass screening has many disadvantages and certainly must be regarded as less efficient than accurate cytological examinations in pointing to cervical pathology.

Schiller's iodine test is based on the lack of glycogenic content of the abnormal epithelial cells and is not considered specific enough for cancer to be useful in mass screening programmes. It has been found to be useful by some investigators in determining abnormal areas and to select the place where a specimen for biopsy is to be taken.

(3) Breast

- (a) Self-examination.
- (b) X-ray techniques:
 - (i) mammography;
 - (ii) xeroradiography.
- (c) Thermography (infra-red photography).
- (d) Ultrasonic scanning.

According to Segi et al. the age-adjusted death-rate from cancer of the breast among women in 1960-1961 ranged from 3.8 (Japan) to 24.2 (Netherlands) per 100 000 per year in the 24 countries covered by their survey. However, only five of these countries had death-rates lower than 15 per 100 000 and 11 had death-rates higher than 20.

In a large number of countries today breast cancer is the most frequent form of cancer among women. It is estimated that in the United States of America one in every 20 women will develop this form of cancer. In many urban areas the annual number of new cases exceeds 70 per 100 000 women and in high-risk groups such as unmarried women over the age of 75, annual incidence rates as high as 400 per 100 000 have been reported.

For a highly prevalent and lethal condition that tends to run its course whatever the treatment, the question of early diagnosis, with a view to more complete eradication of the tumour and consequent improvement in the prognosis, assumes high importance. We should inquire whether, if breast cancers can be brought to treatment at an earlier stage than at present, by health education, frequent self-examination of the breast, or screening by soft X-rays (or possibly by infra-red or ultrasonic scanning), the prognosis is likely to be improved. Delay among women at risk may occur for two main reasons: firstly, fear, and secondly, failure to be aware of a small lump in the breast. Another cause of delay is a lack of awareness by the medical profession of the importance of early diagnosis.

The first of these reasons for delay is gradually diminishing pari passu with a rising level of general education. Better general education enables people to reason more clearly and to plan rational steps to meet a situation. More specifically, ignorance and fear go hand in hand, and health education, in seeking to overcome ignorance, at the same time aims to dispel the fear that may prevent a woman from consulting her doctor as soon as she notices something wrong.

The second reason for delay - the fact that the lesion is small enough to escape attention at all unless looked for in a special way - can be overcome by organized mass screening. Screening may take the form of physical examination, examination by the woman herself, or an externally applied technique, such as mammography or thermography.

Physical examination and self-examination of the breast. While physical examination by a physician is to be encouraged whenever a woman at risk presents as a patient for whatever cause, we must realize that this may be risky. The danger is that women may be falsely reassured and that, during the probably long intervals between examinations, breast cancer may develop with symptoms, and perhaps signs, that are ignored. For this reason it is advisable always to teach self-examination of the breast at the time of the first physical

examination, so that early danger signals are not disregarded through ignorance or fear. Naturally, teaching breast self-examination is only a part (though an important part) of health education. It is likely that physical examination of the breast will keep its importance in early cancer detection, since mammography and examination by a physician appear to be complementary, and not mutually exclusive.

X-ray mammography. Mammography was first developed as a clinical diagnostic technique to assist the clinician when diagnosis was difficult. For example, Gershon-Cohen & Borden³² discovered 28 cancers in 1100 women over the age of 35 examined every six months for eight years. Again, in a hospital series of 2500 women with unrelated breast pathology Egan detected 58 malignant growths.³³

For the reasons we have already considered it has been suggested that earlier diagnosis of breast carcinoma at a preclinical and perhaps impalpable stage by population screening using mammography should improve the prognosis. This is a reasonable hypothesis but one that is difficult to test.

In order to determine the value of X-ray mammography in population screening a controlled trial on a defined population is needed, with a comparison of the results of standardized treatment in a randomized group of women diagnosed by X-ray mammography with those of a second group in whom the diagnosis of breast cancer has been made in the usual way. A very large population is needed in order to provide adequately sized treatment groups. The annual incidence of carcinoma of the breast in England and Wales is of the order of 64 per 100 000 women aged between 35 and 74, so that a population of 100 000 women between these ages, representing a total population of some quarter-of-a-million persons, would only yield annually individual treatment groups of 30 patients each, regardless of age, clinical stage and histological type. Further difficulties in a therapeutic trial of this kind are its very long-term nature (follow-up for a comparison of mortality between the two groups is essential, with consequent loss to the trial from migration and deaths from causes other than cancer), and the large amount of apparatus and of skilled radiologists' and radiographers' time that need to be available. However, a survey of this kind is being undertaken in the State of New York, in association with the Hospital Insurance Plan of Greater New York.³⁴ Preliminary findings show, as we have just noted, that mammography and physical examination appear to be complementary.

Screening programmes utilizing mammography are not yet commonplace. There are a number of reasons for this, including insufficient numbers of trained radiologists and radiological technicians who can utilize this technique, the relative high cost of providing training and facilities are prohibitive in many instances, plus the fact that several new screening techniques are emerging which might come closer to fulfilling the criteria for a screening technique which was discussed earlier in this document. At this point in time, it would seem that the conventional X-ray mammography should be limited to its use as an adjunct to diagnosis.

Another radiographic procedure called xeroradiography may also be used to portray breast architecture and may have certain advantages over conventional mammography, including the possibility that it may fulfil the criteria for a screening technique. With xeroradiography, an X-ray image is obtained on a selenium-coated plate instead of on photographic film. The plate is subjected to an electric charge before making the X-ray exposure; the charge leaks off on the selenium in direct relationship to the X-ray exposure. The plate is developed under a cloud of oppositely-charged powder in a light-proof box. These several steps have posed drawbacks in the past, but new equipment to overcome these factors is currently being developed.

Among the advantages of xerography over conventional mammography are (1) better definition of detail on the xerogram than on the X-ray film; (2) the exposure time is shorter; (3) all the breast structures are delineated on a single xerogram, which is not possible on a

single mammogram; and (4) the amount of radiation exposure is approximately one half. In addition, further refinement may well result in this technique becoming a screening tool in the near future.

Other techniques are being explored besides that of radiology. Infra-red photography (thermography) is one possible method at present being evaluated, and it has been shown that outlines of tumours can be produced from their increased blood-flow compared with the surrounding tissue by means of an infra-red scanning device (thermovision). Thermography can be employed to detect localized temperature elevations over cancers in the breast with up to 94 per cent. accuracy. Dysplastic conditions display dubious patterns in about 25 per cent. For these reasons, thermography might be used as a preliminary screening procedure to eliminate those women whose breasts are not problematic, reserving mammography for those whose thermographic patterns are suspicious.

Another possibility is the use of ultrasonics, and this field, too, is being explored though the technique has not as yet reached a practicable stage.

(4) Other cancer sites

(a) Bladder. Screening for other cancers has been shown to be of value in certain groups of the population who are at special risk. Of these, perhaps the foremost are workers in certain industries, of which the rubber and electric-cable industries are the most important. In the past, benzidine and beta-naphthylamine or allied substances were used in the manufacture of rubber articles and electric-cable insulating material. These substances are now known to be highly carcinogenic, especially for the bladder. Precancerous polyps and early cancers of the bladder can be accurately detected by means of exfoliative cytology. For those at risk routine cytological examination of the urine at six-monthly intervals is recommended.

(b) Oral. Exfoliative cytology has also been shown to be valuable as a diagnostic aid in the early detection of cancers of the oropharynx. Dental inspection often shows small lesions of the tongue or cheek that would not normally be suspected of malignancy. However, by routine scraping of these lesions and cytological examination of the material, a proportion can be shown to be carcinomatous and radically exterminated. This is probably the best present use for oral exfoliative cytology as a screening technique for the oral cavity.

(c) Stomach. There are some 14 000 deaths annually in England and Wales from gastric cancer, mainly in persons over the age of 55. This is second only to carcinoma of the bronchus and lung as a cause of death from cancer. Methods for its early detection can be employed, though they are difficult to apply. Unfortunately, the prognosis for stomach cancer is appallingly bad when diagnosed by normal clinical means, at whatever stage. Indeed, it is a paradox that the shorter the history of symptoms the worse is the prognosis in terms of survival. The best hope of improving the results of surgery is by diagnosis at a precancerous stage and this may be done either by gastric cytology or by gastric photography, or both. However, the stomach is inaccessible and any kind of mass screening is hardly practicable. The exfoliative cytological technique for examining the stomach requires particular skill and needs to be carried out under hospital conditions; its use is therefore virtually limited to aiding clinical diagnosis in patients with suspected lesions. Both exfoliative cytology and gastric photography are used for screening high-risk populations, particularly elderly men - for example, in Japan, where there is a high incidence of carcinoma of the stomach. Perhaps these techniques will be found to be of particular use in special high-risk groups of persons who have already given positive results in a preliminary screening test. Haemoglobin estimation could be used in this way, applied selectively to the elderly members of the population, since persons with gastric atrophy tend to develop macrocytic anaemia. Another possibility is tubeless gastric analysis for the presence of free hydrochloric

acid, using an electrolyte-combining resin. In the future, it may prove possible to develop a simple test for gastric parietal cell antibodies.

(d) Colon-rectum. Techniques available:

- (i) Endoscopy;
- (ii) Cytological examination;
- (iii) Chemical tests.

The colon-rectum is one of the cancer sites accessible to direct examination and therefore presents an excellent opportunity for early diagnosis and control. With the possible exception of carcinoma of the uterine cervix, the skin, and the oral cavity, the colon-rectum offers the best opportunity for detection, early diagnosis and even actual cancer prevention.

Not only is this area one of the most common sites of cancer, but it is also readily accessible to detection techniques available to a physician in his office and has great potential for mass screening. In addition, cancer of the colon-rectum is thought to be preceded in many instances by a readily identifiable benign pre-malignant lesion that is susceptible to removal months or years before it undergoes malignant changes. Thus, true cancer prevention may be possible. In colon-rectum cancer, early diagnosis is not only life-saving, but can eliminate the need for extensive surgery and unpleasant prosthesis. Yet, even though several detection methods for early diagnosis of this disease are available, the yearly colon-rectum cancer deaths total approximately 45 000 in the United States of America alone.

Several methods of early detection have been investigated and evaluated, and it is felt that the best detection procedure is routine proctosigmoidoscopy as part of a clinical examination. While there is no question as to the fact that routine proctosigmoidoscopy can be utilized as a most effective cancer detection technique, at the same time it is quite obvious that those countries where the incidence rate is very low should not consider this as a screening device.

Since routine sigmoidoscopy using the conventional rigid sigmoidoscope is a well-known procedure, no attempt will be made to describe it. It should be noted, however, that several new instruments are either available or are in the final testing stage which will improve even further the ability of the proctosigmoidoscopic examination to detect colon-rectum cancer early. One new instrument that was developed and is currently being evaluated by the Cancer Control Program of the United States Public Health Service is a flexible fiberoptic scope which will enable the examiner to almost double his ability to pass the sigmoidoscope from the 26 sonometers to approximately 45 sonometers with the flexible scope. This scope has flexible glass fibres providing the light source and also has channels for air and water. Flexible plastic fibres, which are much more durable, are being developed to replace the glass fibres. It should also be noted that the rigid scope can currently visualize approximately 45 per cent. of existing lesions, whereas the new fibre-scope can reach approximately 80 per cent. of the colon-rectum lesions.

Several other tests should be mentioned as possible screening devices. One of these is the Guaiac test which is used to detect occult blood in the stools specimen. The routine test, because of its non-specificity and because a patient generally should be on a meat-free diet prior to its use, may not be a very effective screening device. A new version of this test, with a lesser degree of sensitivity, is being studied in the United States of America. The new version, which shows promise, allows patients to be tested without a meat-free diet and has been so devised that a positive test generally means that further examination is necessary or, in other words, the new version has a higher degree of specificity for colon-rectum cancer than the earlier Guaiac tests.

Another technique is the use of exfoliative cytology. Since there are several methods of collecting cells, and the technique of exfoliative cytology has been described earlier, no attempt to describe this technique in detail will be made here. It should be noted that some of the results present an encouraging picture and can be highly accurate in the hands of a highly skilled, interested and enthusiastic team. However, the technique has presented problems to others who are less experienced and who then find it difficult to duplicate the results.

According to Fidler et al.,³⁵ despite the advantages of cytological investigation to a symptomatic patient, the application of the method to general population screening does not seem justified. It would, however, be worth considering its systematic application in high-risk groups such as patients with long-standing ulcerative colitis or polyposis.

4.1.2 EVALUATION OF EFFECTIVENESS OF MASS SCREENING PROGRAMMES FOR DIAGNOSIS AND FOR SUCCESSFUL FOLLOW-UP

The ultimate aim of periodic mass examinations for the detection of cancer is to reduce cancer morbidity and mortality. It is questionable whether any of the mass examinations carried out to date have produced unequivocal evidence that this objective has ever been attained. The major reason why this objective is difficult to assess is based on the fact that the reliability of mortality statistics is affected by numerous factors. In the absence of unequivocal evidence of direct results of mass screening, indirect indices have been studied. Examples of such indirect indices are attendance rates, yield, cost per case detected, the stage distribution of cases, and so on. Such indirect indices are necessary in evaluating mass examination programmes, as they show whether certain prerequisites of achieving the main purposes of the programme have been fulfilled and revealed difficulties that called for revision. However, they are not, in themselves, sufficient for final evaluation of a programme unless the correspondence between them and the ultimate objective has been firmly established. In the cancer field this is not always the case.

While it is felt that the evaluation of various types of mass examination programmes under different conditions is difficult, it is felt that more effort should be made to more properly assess the ultimate objective, namely reduction of cancer morbidity and mortality.

The remainder of this section will be devoted to some of the factors on which success or failure of a mass detection programme depends. As previously indicated, these factors directly influence the results of mass screening programmes and thereby become quite important in the over-all evaluation process.

(1) The diagnostic test

Sensitivity and specificity are standard measures in the evaluation of diagnostic tests. Cytological examination as a screening device for cervical cancer is one example of a test which has been extensively evaluated in terms of these two characteristics. Often, however, in mass examinations, the efficiency of the test used is not well known beforehand. It is important to realize that the results obtained under one set of conditions, for example, when a test is used in a clinic on a limited number of patients, may not apply in widely different circumstances, such as obtain during a mass examination carried out under pressure by different types of personnel in a general population with a relatively low prevalence of disease. The efficiency of the tests to be used must therefore be estimated for each programme. Strictly speaking, this requires that the diagnosis for the disease under study should be established or ruled out for every person tested by the screening procedure, regardless of whether the screening result is negative or positive. In practice, a compromise is necessary. As a minimum, arrangements should be made to ensure that cases of disease diagnosed among persons formerly found negative on screening or among former suspected

cases that failed to attend for further examination are reported to those responsible for the programme. This will enable some estimate of the proportion of false negatives. Where an efficient cancer registry is in operation this solution presents no real problem.

In some mass examinations the yield, i.e. the number of cases detected, has been used to indicate the efficiency of the test procedure. It should be realized, however, that yield depends not only on the test, but also on the prevalence of the disease in the population studied and on the normal level of case-finding in that population.

A very important property of the diagnostic test is its ability to give a positive result early in the development of the disease, i.e. in pre-invasive, preclinical or asymptomatic cases. Two criteria by which this property of the test is commonly judged are the clinical-stage distribution of the cases detected and the presence or absence of subjective symptoms in these cases. It should be noted that in considering the result of a first screening of a population the clinical-stage distribution can be misleading. It has its limitations also when used for this purpose in material obtained by re-screening of the same population at suitable intervals. Moreover, where the material has been derived from first screening of a population, information about the presence or absence of subjective symptoms can be seriously misleading when used for assessing the ability of a certain test to detect cases early.

(2) Public acceptance of the mass examination

One of the important items that need to be considered is the evaluation of public acceptance of the examination programmes offered. The number of persons attending a programme is not in itself a valuable index of public attitude. A much more informative figure is the proportion of the eligible population attending, though this index can only be used if the programme is offered to a defined population. When this is the case, it becomes possible to study the characteristics of those attending and those not attending: e.g. age, sex, marital status, parentage, socio-economic status and educational level. Such information reflects the pattern of motivation in public participation and is of great importance, not only for the evaluation of the programme itself, but for planning future programmes and preparatory health education. For example, several studies on screening for cervical carcinoma have shown that the lowest participation is found among groups of women with the highest morbidity and mortality from that cause, i.e. in the lower income groups. Conversely, the groups of women with the highest attendance rates include those least likely to benefit from the examination, not only because incidence of the disease is low among them, but also because they are the ones most likely to see the doctor if early symptoms develop. Such negative selection for examination may be expected for various reasons in several types of mass examination for cancer. It is not likely, for example, that most heavy cigarette smokers will be very receptive to the idea of periodic screening for lung cancer.

One observation commonly made in mass examination is that the attendance rate tends to drop quite markedly when examinations are repeated. This is particularly disturbing where the drop is accompanied by increased negative selection. One consequence of such a trend from the point of view of evaluation is that it becomes difficult to compare the results of successive examinations. If, for example, a first screening with a high attendance rate and a high yield is followed by a second screening with a low attendance rate and a low yield, attributing the difference in yield exclusively to the preventive effect of the first screening may not be justified.

Another important item to be considered is the concept that a rather limited number of individuals have that much of the educational propaganda used during mass screening programmes may possibly create cancerophobia. Some studies along these lines have been made, and based on these studies and a feeling of most people knowledgeable in this area, it is felt that the danger of creating cancerophobia has been vastly over-estimated in the past, and that, on the contrary, the introduction of well-organized mass detection programmes has helped to reduce

fear of cancer in large sections of the population. It is also desirable to evaluate the potential danger of creating a feeling of false security in the population screened.

(3) Follow-up

Another aspect of mass examination which requires constant appraisal is the organization and efficiency with which those in whom cancer has been demonstrated or suspected at the initial screening are followed up. The following data are indispensable for the evaluation of follow-up measures taken in the period between initial screening and final diagnosis and treatment:

- (a) the proportion of those referred for follow-up who actually comply;
- (b) the final diagnosis for all those referred, whether they have complied or not;
- (c) the time required for establishing the final diagnosis and for starting treatment.

From the administrative standpoint it is of great importance to identify the reasons for any delay between initial examination and final diagnosis. In this context, it has been found in some countries that an important cause of such delay is the overloading of special institutions for the complementary examinations which may accompany mass screening.

(4) Treatment

Treatment as such has been used in trying to evaluate the efficiency of mass examination programmes. One way of doing this has been to compare the proportion of screened cases that could be given radical treatment with the proportion that could be similarly treated among cases diagnosed in the conventional way. Such comparisons have their obvious limitations. It has, for example, been found that the resectability rate is much higher among lung cancer patients incidentally detected by mass X-ray survey, than among other lung cancer patients of similar age. If the prognosis is better for resectable than for non-resectable cases, the conclusion is near at hand that improved control of lung cancer can be achieved by periodic mass X-ray surveys. This may be true and probably is, but the conclusion is not warranted by the kind of data referred to. It has been shown that mass examinations tend to pick up a disproportionate number of the relatively benign tumours. Some tumours are detected by periodic mass X-ray surveys because they are sufficiently slow-growing to permit the patient to wait for the next examination.

Few attempts have been made to assess this selection effect on mass examinations. It could be done with relative ease for those forms of cancer where histological malignancy grading is feasible, e.g. for breast cancer. In such evaluation blind reading would be essential. Studies of this kind are now being attempted, for example, in Norway.

Comparison of the extent of the treatment needed to control the disease in cases detected by mass screening and in those conventionally detected is another possible method of evaluating the efficiency of mass examination programmes.

This type of evaluation is of special interest in connexion with cytological screening for cervical carcinoma. As is well known, the "in situ carcinomas" detected by such surveys can be effectively eliminated by limited surgery. If left untreated, some of these lesions may progress and become invasive. In the early invasive phase, the majority would still be curable, but to achieve this result would then require much more drastic treatment.

In applying this method of evaluation it should be realized, however, that the prognostic significance of dysplasias and in situ lesions when found incidentally by mass examinations is not well known. Possibly the proportion that would have progressed and become invasive if left untreated may be lower than has been found by observation on clinical patients.

Furthermore, it may be asked whether those detected in the pre-invasive stage by mass examination are not likely to be the more benign cases and whether this would not still have been the situation had they been allowed to become invasive. Answers to these questions can only come from population studies. To this end repeated screenings of large, well-defined and carefully controlled population groups would be required.

(5) Survival after treatment

An important step in the evaluation of mass examination is the study of survival after treatment among those detected by the survey as compared with cases diagnosed in the usual way. Although, in many mass surveys, the number of cases available for study has been small, most comparisons of this kind have shown or suggested that the length of survival after treatment is increased for those detected by the survey. This is often taken as evidence of the greater effect of treatment when applied early in the evolution of the disease. It should be realized that comparisons of this kind are likely to be seriously misleading. Firstly, when treatment is started earlier, the length of survival afterwards is likely to be increased even though life may not be prolonged. The only increase may be in the "length of life with recognized disease". Secondly, it is likely that the material from the mass examination may contain disproportionately many relatively benign cases.

(6) Other areas of evaluation

We believe that the evaluation of a mass screening programme would be incomplete if confined only to the technical and organizational components outlined above. In order to ensure that mass screening programmes have the maximum efficiency, carefully planned and executed operational research into the financial and administrative aspects of cancer detection programmes is also needed.

Evaluation of the various components of mass detection programmes does not obviate the need for direct assessment of the effect of mass examination on cancer mortality in the population. The various difficulties in evaluation which have been briefly outlined are not equally disturbing in all situations. They are least disturbing and can best be studied when evaluation is based on programmes involving periodic examination of well-defined populations. Under this condition, assessment of the effect of the programmes on mortality becomes a relatively simple method, especially where the population is that of an administrative subdivision which has for years prior to the study had an adequate vital and health statistical system. If the population has also been covered for some time by an efficient cancer registry the possibility of sound evaluation is greatly enhanced. Evaluation of various types of mass examination carried out under such conditions is now being undertaken in several countries.

To facilitate an adequate evaluation of any specific programme and increase the possibility of comparing the results of programmes conducted by different workers and in different countries, there is an urgent need for the standardization of terminology in cytology and histology. It is not enough to agree on definitions in, say, histology, if the pathologists are interpreting their findings in a different way. After reaching agreement on terms and criteria, it is essential to test comparability between various laboratories, and even between workers in the same laboratory, in carefully planned studies with blind readings. It is felt that the problems of terms and criteria should be considered at an international level by or through WHO.

Further progress in this field would also be greatly enhanced by standardizing methods of presenting the data from mass screening programmes. Reports on mass examinations giving sufficient details of the objectives, organization and results should be published without delay and thus made available to others. WHO might usefully act as a clearing house for the information of all countries on current and projected studies and the hope is expressed that WHO will continue to give attention to mass screening and assist with expert advice when requested.

4.1.3 REVIEW OF MAJOR LARGE-SCALE SCREENING PROGRAMMES

The review of major large-scale screening programmes is well described in UICC Monograph Series, 1967, Cancer Detection, N.Y., vol. 4, pp. 60-74. It should be recognized that this listing does not include a complete coverage of all programmes but merely represents selected examples which would reflect rather diverse activities both in terms of single or multiple site cancer screening.

4.2 ORGANIZATION OF EARLY DETECTION PROGRAMMES

In the last few decades programmes for screening the whole population or large segments of it for cancer and precancerous lesions have been organized in countries all over the world. The first aim of such programmes is to discover malignant and premalignant conditions at the earliest possible stage of their development so that prompt and adequate treatment can be given.

The organization, as well as the coverage of cancer detection programmes, varies considerably between and within countries. This seems to be due, not so much to differences in opinion about the desirability of such programmes, but to a number of other factors: the importance of cancer and priority given to it in relation to other health problems in the community; the relative frequency of cancer of different sites; the organization of the health services; the economic resources of the countries; and the availability of qualified personnel, laboratory facilities, and institutions for treatment.

In some of the socialist countries of Eastern Europe, special services for the early detection of cancer are an integral part of the community-wide preventive and curative work carried out by the public health services. The governments take full financial and technical responsibility for planning and carrying out the programmes. Although there are some slight differences in the organization and scope of the programme between these countries, there is a common general pattern.

From the standpoint of organization and coverage, the broad types of programmes are multiple. Among these are:

- (1) early detection services integrated with public health services;
- (2) special detection programmes covering fairly large selected populations;
- (3) detection programmes limited to the screening of certain hospital or other patients;
- (4) examinations for precancerous lesions and cancer forming part of a multiphasic medical screening programme, which may be restricted to certain population groups such as factories or industries or part of a large generalized multiphasic screening programme;
- (5) detection programmes consisting of special-purpose screening of selected groups of the population covering, for example, women for gynaecological cancer, and high-risk groups in various industries for cancer of the lung or bladder, etc.;
- (6) individual generalized preventive examinations of all body sites for cancer and precancer patients of appropriate age who attend a "cancer detection centre".

It should be noted again that the listing of these types of detection programmes is not all-inclusive and it should further be understood that many countries may utilize only one type of programme while others may utilize multiple or all types of these programmes.

In many polyclinics and hospitals the individual preventive examinations are carried out by specialists, whereas in many screening centres examinations may be performed by an experienced, specially trained midwife or paramedical person, who refers suspected cases to a specialist. Such individual preventive examinations are regarded as of great importance because they also cover the non-employed part of the population, including elderly people, a category with particularly high cancer incidence.

Experience in some eastern European countries where the early detection of cancer in this manner has been integrated with the public health network has shown that detection by examination of patients attending cancer dispensaries and other centres was much better (as assessed by the yield) than in mass screening carried out among the general population.

In a second group of countries, programmes are operating in which relatively large selected population groups are screened through specially organized programmes aimed at diagnosing cancer of specific sites. Most of these programmes are organized and financed outside the public health services by voluntary health organizations or cancer institutes, but often with some financial support from public funds.

In another group of countries early detection work is still limited to the examination of hospitalized patients or out-patients at a few special hospitals, and to examinations carried out by practising physicians as part of their ordinary work. In some of these countries, however, plans are at present being worked out for increasing cancer detection activities.

In most of the countries the screening of high-risk groups in industry is carried out routinely as a part of ordinary public health work.

Only in a few countries do the detection programmes aim at covering all cancer sites. In most, screening for gynaecological cancer and, more specifically, cancer of the cervix uteri by means of cytological smear examinations, is the only detection activity undertaken on a relatively large scale. Special screening programmes for precancer and cancer of other sites (e.g. skin and breast) have been carried out on an experimental basis among segments of the population in some countries. In many, mass screening for lung cancer has been achieved as a by-product of mass miniature X-ray screening for tuberculosis.

In some of the mass screening programmes the examinations have been made in special detection centres. In others, mobile teams of doctors and auxiliary personnel have visited the various communities being covered as, for example, in the breast cancer surveys and screening programmes for cervical carcinoma carried out in Norway.

Although the special-purpose mass screening of selected population groups may, at present, be the most efficient method for early cancer detection in most countries, careful consideration should be given to the possibility of organizing multiphasic screening programmes and of including cancer tests as a routine in other medical programmes. An example would be the inclusion of cervical cytology in antenatal care programmes.

It is of prime importance to have efficient documentation and cancer registration in connexion with cancer detection programmes. Cancer registries will be of assistance in defining high-risk groups and furnishing the data necessary for evaluating programmes. In this context epidemiologists and medical statisticians have an important role to play in planning, supervising, and evaluating mass examinations.

Here, consideration must not only be given to the technical and administrative aspects. Willingness of the public to participate is also essential for the success of such programmes. Health education must therefore be an integral part of any form of cancer detection activities and take into account people's motivations and other psychological factors affecting their attitudes. It should also be mentioned that a successful mass screening programme in itself is of educational value both for the public at large and for the medical community.

In planning mass screening programmes adequate provision should be made for following up individuals in whom cancer is demonstrated or suspected at the initial screening. Facilities must be available for carrying out the detailed complementary examinations necessary to enable a firm diagnosis to be made, and it must be possible within a short time to provide adequate treatment for the cases detected.

In some countries, cancer detection programmes are regarded as transitional in the sense that, after establishment of their efficiency and their acceptance by the public and the profession, these techniques should be incorporated in the daily routine of all physicians and/or health services of that country. This results in what may be called surveillance as an integral part of the comprehensive medical service.

It is also important to consider the relationship between cancer detection generally and what, in most countries, is regarded as conventional public health work. We need to be continually aware of the pioneering work done in this field by voluntary health organizations and other non-official bodies in many countries.

As a final comment on this general section concerned with organization of early detection programmes, it should be noted that the old distinction made in many countries between financing preventive and curative medicine is obsolete and should be abolished. The various health schemes, in those countries where they are available, should give full financial coverage to programmes for the early detection and prevention of cancer. Cancer control is an important and essential part of medical care and should, consequently, be placed on the same financial basis as curative medicine.

The points considered above will be dealt with in greater detail below.

4.2.1 ROLE OF HEALTH SERVICE AND CENTRAL PLANNING BODY

Early cancer detection is part of the general problem of cancer control. The role of the health services and a central planning body in cancer control has been carefully studied by an expert committee. We concur entirely with the points of view expressed here.

It is felt that every cancer control programme should have a central planning body. The function of this body should be to establish policy, set standards, implement operations, co-ordinate efforts in all fields of cancer control, and integrate cancer control measures with the work of other health services and voluntary agencies. This central body will usually be established in a national, district, or local administrative area.

It is also felt that all nations should have a national cancer control programme of suitable size which is planned and carried out within the structure of the official health agency. Control measures, however modest, can then be planned for all parts of the nation and executed under central supervision. The measures employed will vary according to: (a) the system of government, (b) the distribution of population, (c) geographical factors, (d) the density of population, (e) the availability of medical personnel and equipment and (f) the availability of funds.

The central planning body for cancer control should be composed of individuals as far as possible expert in the several aspects of the programme. It might therefore include surgeons, radiologists, pathologists, health administrators, social workers, lawyers, psychologists and general practitioners of medicine. Depending upon the nature and content of the programme being developed, the addition of other individuals with different skills and competences may be advisable. Planning should cover all control measures, with appropriate attention to balance as the problem or problems demand, the actual organization of the programme should be entrusted to a competent staff; and the programme should be reviewed by the central planning body at intervals, to ensure that the policy laid down is being followed and is successful. It is essential that a planning body be aware of and quick to take advantage of advances in the field of cancer control, and be able to adjust its operating principles as may be necessary.

4.2.2 COLLABORATION BETWEEN BASIC HEALTH SERVICES AND SPECIALIZED CANCER SERVICES

The question concerning collaboration between general health services and specialized services has been covered for communicable diseases in various publications of WHO.^{36,37} Much of the general philosophy and the principal points of view set forth here, are in our opinion also valid for the relationship between basic health services and special services for cancer detection. For the purpose of this section, the following adapted definitions will be utilized:³⁸

- (a) General health services. A country-wide system of established institutions with multipurpose objectives having a definite organizational structure at all levels - local, intermediate, and central - which would provide services for the promotion of health as well as for the prevention and cure of disease and disability.
- (b) Integration. A series of operations concerned, in essence, with the bringing together of otherwise independent administrative structures, functions and mental attitudes in such a way as to combine these into a whole.

General health services are almost invariably nation-wide in their operation and are organized in a system in which at least three distinct levels, i.e. local, intermediate and central, are clearly identifiable. Their types of organization and grade of development, especially at the local and intermediate levels present many variations from country to country. The ultimate aim should be that general health services should incorporate preventive, social and curative health activities. This is generally accepted, and as a consequence general health service institutions will take a positive attitude towards all cancer detection programmes whether they are experimental or routine. General health services are established and organized as permanent institutions covering the total health field.

In certain countries early detection of cancer is already part of the programme of the general health services. These services have the responsibility for planning, implementation and evaluation of the programme. The cancer detection programmes are permanent and aim at examining the whole population.

In many other countries, however, early cancer detection campaigns will, like mass campaigns against communicable diseases, have a definite beginning, and an anticipated end-point. For many reasons such programmes should be integrated to the fullest possible extent with the general health programme.

Cancer detection programmes, apart from their primary purpose of detecting cancer, have a number of features which are highly desirable from the point of view of the general health services. The campaigns are associated with intense health education among lay people and also in the medical profession. They arouse interest in health problems and have in many countries contributed to improved registration of cancer and a better follow-up. Mass cancer campaigns open the possibility for operational research with respect to the most effective organization and lowest possible costs. In general they attempt to carry out their work with a minimum of doctors and using to the greatest possible extent allied and auxiliary personnel.

The general health services depend on appropriations from official sources. Cancer screening programmes will increase the understanding of the significance of prophylactic work also against cancer. A widespread understanding of the significance of the preventive cancer work is necessary to insure adequate appropriations from official sources for this purpose. In many countries the government agencies contribute relatively little to this work which is largely organized and financed by voluntary organizations.

The execution of cancer detection programmes will, on the other hand, be greatly facilitated by a close contact and co-operation, at all levels, with the general health service. Contact at the central level should be established by including in the central planning body

representatives of the health services. This will ensure that the programme is integrated in the general health programmes of the country and will open the possibility that cancer detection programmes will be established on a more permanent basis.

The necessity for co-operation at the top level with the health services may be illustrated with reference to screening programmes based on cytological examinations. The value of the cytological diagnostic method is now well established. In most countries the main factors limiting a more widespread use of this method are the scarcity of cytological laboratories and the lack of trained personnel. This problem can only be solved by the general health services.

Co-operation with the health service at the intermediate level (district, county) will facilitate the implementation of a cancer detection programme. The medical officer of health will have at his disposal the organization of the health service. He has knowledge of the medical facilities available for diagnosis and treatment. Frequently he will know personally the medical personnel in the area and have information about numerous factors of importance such as the local voluntary organizations, living conditions of the population, transport possibilities and so forth. Also the endorsement of a cancer detection programme by the official health services is likely to ensure a better acceptability of the programme by the population.

Screening programmes organized at the local level without support of the general health service will frequently be of little value as they are often carried out as a single screening without adequate follow-up and possibilities for evaluation.

In summary, a close co-operation between the bodies organizing cancer screening programmes and the general health service is mutually beneficial. The work should be integrated with that of the health services as early as possible. The ultimate aim should be that the cancer prevention work should become a part of the programme of the health services, equally important as their other activities in preventive and curative medicine.

4.2.3 IMPLEMENTATION

In the preparation of the material for this section it was felt that it would be very difficult to determine a plan for organization and implementation of mass examinations which would be applicable to every country. The organization on implementation of such examinations, while based on certain general principles, must differ from country to country. What is an efficient organization and implementation set-up in one type of economic, political and administrative environment may not be equally successful in countries with a different structure. Therefore, this section will deal with principles and concepts that should be considered by any country planning to develop a cancer screening programme. In addition, due to the feeling that the principles and concepts that will be outlined in this section, are applicable in varying degrees at national, regional and community levels, we have not attempted to break these down into separate parts for each of these levels.

(1) General considerations

In developing the organization and implementation of a cancer detection campaign, we should concern ourselves as to how to relate the respective activities of a mass campaign and general health services, aiming to merge at a future date, if possible. It has previously been pointed out³⁶ that before mass screening is undertaken, the following points should be taken into consideration:

- (a) Since the general value of such examinations in reducing the incidence and prevalence of cancer is still under discussion, screening programmes should be so designed that the results can be properly evaluated;

- (b) The discovery during systematic examination of benign lesions capable of being treated may constitute a method of cancer prevention;
- (c) The scale of the methods needed in mass screening is so large as to make it preferable, as often as possible, to extend the search for pathological conditions to a whole range of diseases, thus converting it into a systematic examination for disease in general;
- (d) A number of health education measures must be taken, in order to convince the public, or the groups that are to be examined, of the importance of the examination for the prevention or early diagnosis of malignant tumours. Examinations should be based on persuasion, not compulsion.

(2) Factors influencing the implementation

The implementation of a cancer screening programme will be influenced by a number of factors:

(a) The incidence and prevalence of cancer will obviously be an important factor in determining the choice of programme. It is well known that the geographic distribution of cancer differs considerably from one country to another.³⁸ For instance screening of oral carcinoma would be justified in certain countries, such as India, where this form of cancer occurs frequently, while such screening would not be warranted in western European countries, where this disease is rare. Breast cancer, lung cancer, gastric cancer, colon-rectum cancer and cancer in the prostate gland occur at high rates in many countries, and screening programmes for these cancer sites would therefore be highly desirable.

The choice of screening programme will, however, be strongly influenced by the availability of suitable detection methods. In spite of the fact that cancer of the uterine cervix does not belong to the most frequent forms of cancer in women, numerous screening programmes have been implemented all over the world due to the fact that an excellent cytological diagnostic method is available. Such screening programmes are of proven value and should be extended and preferably become part of the general health service. Periodic clinical examinations are also of definite value and should preferably be carried out where the necessary medical facilities are available. For many other important cancer sites screening programmes are being tested, e.g. the use of mammography in the detection of breast cancer. Further pilot studies and research are necessary to establish the value of such programmes.

(b) An absolute requirement for the successful implementation of a screening programme is that it is acceptable to the population. Suitable education is therefore an important part of all such programmes, and must take into consideration the social, cultural and religious conditions.

The choice of test method may decide whether a screening programme will be accepted or not. Whereas a gynaecological examination involving the taking of smears is acceptable for most women, rather unpleasant methods such as proctosigmoidoscopy and gastroscopy will probably be resented by the population and be unsuitable for mass screenings. Also it should be realized that in many countries gynaecological examinations on a large scale will only be accepted if carried out by female doctors. The experience from many screening programmes, particularly for cervical cancer, show that a certain percentage of women refuse to attend. As will be further discussed below, studies on motivation are therefore greatly needed.

(c) Acceptability by the medical profession is also an absolute requirement for the successful implementation of any screening programme. In many countries the medical profession has limited understanding of the significance of preventive measures. This

attitude is partly a consequence of the nature of their education which has primarily been directed towards curative medicine. Also it is due to the fact that in most countries medical doctors are overworked and their whole working capacity is demanded for the necessary care of sick people. A contributing factor is also that in many countries prophylactic medical work is not covered by the social security system. It is considered important that this situation should be altered. The screening programme must also be acceptable to the health services and included in the general health policy of the government concerned. Particularly in certain developing countries cancer detection programmes must necessarily, however, be given low priority in relation to other pressing medical problems such as the control of communicable diseases.

Obviously economic factors are of decisive importance in the planning and implementation of cancer detection programmes. Many developing countries do not have the necessary economic strength to implement programmes which are highly desirable. Assistance from international bodies will be necessary.

(3) Significance of international co-operation

A disease such as cancer, susceptible to control, may be prevalent in a number of neighbouring countries. Experience has shown that in such cases it may be advantageous to carry out simultaneous co-ordinated mass campaigns in each of the countries concerned, for a number of reasons. In the first place, it may be of great importance to consider undertaking joint international projects for purposes of epidemiological studies to provide a clearer picture of the distribution of malignant tumours. It may be expected that studies carried out across national boundaries would provide greater contrasts in possible etiological factors, thus permitting more detailed analyses to be made and firm conclusions to be drawn. An important aspect of such international studies would also be the creation of closer contacts between investigators in the countries concerned. In addition, such a joint project might prove to be advantageous economically to those countries co-operating.

4.2.4 METHODOLOGY FOR IMPLEMENTATION

Effective implementation of an early cancer detection programme requires careful and detailed planning. As pointed out above it is necessary to have a central planning body responsible for the necessary co-ordination and supervision. A number of factors must be taken into consideration:

(1) Selection of population group to be examined. It is a prerequisite for the necessary evaluation of the results that a stable population group is selected for study. The identification and selection of high-risk groups is an important factor in determining whether or not an examination should be done and the type of programme to be chosen.

The high risks for certain types of cancer such as cancer of the urinary bladder and lung are well known in certain industries.

In recent years epidemiological research has delineated the high-risk groups for various types of cancer. The incidence of many cancer forms is clearly related to age and sex. Thus lung cancer has its highest frequency in age-groups of about 60, and it is known that heavy cigarette smokers represent a special high-risk group. Gastric cancer occurs largely in groups over the age of 50 and mammary cancer is also most frequent in the higher age-groups. Several investigations have indicated that the precancerous changes in the case of cervical cancer are most frequent in the age-group 35-45 years, whereas the incidence of invasive carcinomas are highest between 40 and 64 years of age.

In this connexion it may be mentioned that the country-wide plan for screening of cervical carcinoma in women in Sweden will be limited to women between 35 and 50 years. This implies that by screening 40 per cent. of the women it is expected that 70 per cent. coverage of precancerous lesions and invasive cancers will be achieved.

In addition to age, other factors may be important in the determining of the incidence of certain types of cancer. For example cervical cancer is strongly related to race, social-economic background, and sexual activity. Thus it is well known that Jewish and Moslem women have a very low incidence of cervical cancer. Investigations in the United States of America have shown that certain poor negro populations as well as women from Puerto Rico, Mexico and Latin-American countries represent high-risk groups with respect to cervical cancer, with incidence up to 39 per 1000 examined.

It has been found in many countries^{35,39} that in screening women in the age-group 30 to 60 years for cervical cancer a substantial fraction (about 20 per cent.) failed to participate in spite of intensive propaganda and educational efforts. It is particularly important that this group, which seems to belong largely to the lower social economic classes, demonstrates higher incidence of cervical cancer than the group of women attending the examinations. These women in general are less health conscious, and consequently their carcinomas are usually diagnosed at a late stage, a fact which tends to maintain the mortality rate within the population at a high level. Special efforts should therefore be made to reach this group. One possibility which has been considered is to take routinely smears for cytological examination in adult women submitted to hospitals, as well as in women participating in ante-natal care programmes. Married women have a higher incidence of uterine cancer than unmarried women. This is particularly true for those who married early, and it is generally believed that early sexual activity is an ethological factor.

(2) Detailed plans must be made to ensure a high rate of attendance. The problems will differ widely in different countries. In modern industrial societies, the interest of the population in the programme can be aroused through the press, radio and television. Moreover, the population can be mobilized by personal calls through letters or through voluntary organizations. In well-organized societies, this work is facilitated by the existence of official registries which possess all the necessary information (name, address, age, sex). Special forms should be prepared to record the necessary information, both personal data and the results of the medical examination.

In developing countries the problem may be more complicated. Here collaboration should be sought with already established organizations or mass campaigns, for instance those for malaria eradication. It may be necessary to organize a special staff of home visitors in order to take care of the necessary education, registration and mobilization of the population. Under certain conditions it may be necessary to conduct an educational programme of the screening programme.

(3) Selection of suitable place for examination. It is necessary to utilize the existing facilities such as special detection centres, out-patient clinics, health units, rural hospitals, mobile units, etc. Sometimes it will be necessary to erect new buildings for this special purpose. The layout and the necessary equipment must be planned in detail. A flow sheet should be made to ensure a smooth working operation.

(4) Medical and allied personnel. The size of the necessary staff should be estimated in detail. It may be necessary with pilot studies to establish how many patients a doctor can examine per day.

Suitable time-tables must be made for the examinations.

(5) Training of the participating doctors, one of whom will be the responsible medical officer for the programme.

(6) Training of allied and auxiliary personnel. In certain countries it will be necessary to train special personnel such as cytotechnicians.

(7) The financial basis for the project must be secured and worked out in detail.

(8) Adequate facilities must be available for further examinations and possible treatment of all persons found to be suspect with regard to cancer.

(9) The necessary registration and follow-up must be organized in detail. In order to be able to evaluate the over-all results, it is necessary also to secure data on morbidity and mortality of that part of the population which does not attend the screening programme.

For adequate evaluation of the results a re-screening of the population at a later time is necessary. The interval between the examinations must be decided upon and included in the original planning. The interval will differ with different types and sites of cancer. In the case of cervical carcinomas, the length of the optimal interval between examinations is not known with certainty. In certain high-risk groups, the optimal interval may vary from three months to three years.⁴⁰ In this connexion the results from the Norwegian examination³⁹ are of interest. The results indicate that some cases of cervical carcinoma appeared only a few months after a negative screening. These cases proved to have a very rapid and malignant course.

In actual practice a compromise will have to be reached between what is desirable and what can be done under the circumstances.

(10) Operational research should be an integrated part of the screening programme. The records should permit a continuous evaluation of the cost and the efficiency of the programme. This is necessary not only for the project, but also for future planning.

4.2.5 EVALUATION OF EFFECTIVENESS OF MASS SCREENING PROGRAMMES

The following section is mainly based on documents prepared in connexion with the WHO seminar held in Oslo in November 1965⁴¹ and the article by Fidler et al. (1968).³⁵

The ultimate aim of periodic mass examinations for the detection of cancer is to reduce cancer morbidity and mortality. While several ongoing studies have clearly shown that geological screening programmes can reduce the incidence of cervical cancer substantially, it is questionable whether any of the mass examinations carried out to date have produced unequivocal evidence that the latter objective has ever been attained. One major reason why this objective is difficult to assess is that the reliability of mortality statistics is affected by numerous factors.

For example, in a review of 7146 deaths ascribed to cancer in a province of Canada, over-diagnosis of the disease was found in cancers of the lung, stomach and pancreas, while under-diagnosis was found in cancers of the buccal cavity and breast. This tendency toward over- or under-diagnosis and the extent to which it has affected past mortality makes a retrospective analysis of mortality data unreliable. Added to this is the tendency to be more specific in death certification because of developing interest in cancer detection programmes. This is especially true in cancer of the uterus where greater specificity results in an increase of deaths ascribed to the cervix uteri. In Canada, for example, the proportion of deaths from cancer of the uterus, unspecified as to cervix or corpus, has declined from 30 per cent. to 21 per cent. since 1950. Undoubtedly, many of the cases now being more accurately recorded are in the cervix category, hence it becomes possible for mortality from cancer of the cervix to rise temporarily in the face of a number of organized mass screening programmes. In British Columbia, Canada, however, where a mass screening programme for cervical cancer was organized in 1950, recent statistics show that there has been a drop in the last four years, but this will have to continue for several more years before it can be considered significant.

REFINED MORTALITY RATES FOR SQUAMOUS CARCINOMA
OF THE CERVIX IN THE PROVINCE OF BRITISH COLUMBIA
(CORRECT AS OF JANUARY 1968)

Year	Population in thousands over age 20	No. of deaths	Rate 1/100 000
1958	473.0	54	11.40
1959	478.8	51	10.60
1960	486.4	48	9.90
1961	496.0	51	10.25
1962	503.0	65	12.90
1963	513.0	57	11.00
1964	526.8	56	10.60
1965	543.2	42	7.70
1966	565.4	44	7.80

Perhaps as important as this is the fact that women who come to their doctors with the early symptoms of carcinoma are the same group who report for regular smears. These women have been found in several surveys to be, in general, well educated, interested in their health, in a higher income bracket, and to have good rapport with their physicians. Conversely, the survey has shown that women who ignore symptoms and appear for diagnosis with late disease are those who ignore the screening programme. They are in a lower income bracket, less well educated and, in general, tend to be more apathetic towards medicine and health.

Any voluntary screening project is therefore selective, and tends to eliminate early clinical carcinoma which has a high survival rate after treatment. The advanced cases who often die after treatment tend to persist in a community, and screening must be nearly 100 per cent, before these will be eliminated.

Another assessment of the detection programme can be made by studying incidence of clinical invasive carcinoma in the community. This figure should be established prior to the programme and a falling incidence will reflect its efficiency.

In the screening programmes in British Columbia and in Norway it has been demonstrated that in the screened segment of the population, the incidence of cervical carcinoma is greatly reduced.

In a detection programme for cancer of the cervix it is to be noted that mortality rates will be slow to fall. This is partly because a large proportion of the preclinical lesions that are being removed from the population by early detection would not have become clinical lesions for perhaps five to 10 years or more, thus introducing one reason for a lag period.

In the absence of unequivocal evidence of direct results of mass screening, indirect indices have been studied. Examples of such indirect indices are attendance rates, yield, cost per case detected, the stage distribution of cases, and so on. Such indirect indices are necessary in evaluating mass examination programmes, as they show whether certain prerequisites for achieving the main purposes of the programme have been fulfilled and reveal difficulties that call for revision. However, they are not, in themselves, sufficient for final evaluation of a programme unless the correspondence between them and the ultimate objective has been firmly established. In the cancer field this is not always the case.

While the evaluation of various types of mass examination programmes under different conditions is difficult, it is felt that more effort should be made to properly assess the ultimate objectives, namely reduction of cancer morbidity and mortality.

The remainder of this section will be devoted to some of the factors on which success or failure of a mass detection programme depends.

(1) The diagnostic test

Sensitivity and specificity are standard measures in the evaluation of diagnostic tests. Cytological examination as a screening device for cervical cancer is one example of a test which has been extensively evaluated in terms of these two characteristics. Often, however, in mass examinations, the efficiency of the test used is not well known beforehand. It is important to realize that the results obtained under one set of conditions, for example, when a test is used in a clinic on a limited number of patients, may not apply in widely different circumstances, such as obtain during a mass examination carried out under pressure, by different types of personnel, in a general population with a relatively low prevalence of disease. The efficiency of the tests to be used must therefore be estimated for each programme. Strictly speaking, this requires that the diagnosis for the disease under study should be established or ruled out for every person tested by that screening procedure, regardless of whether the screening result is negative or positive. In practice, a compromise is necessary.

As a minimum, arrangements should be made to ensure that cases of disease diagnosed among persons formerly found negative on screening or among former suspected cases that failed to attend for further examination are reported to those responsible for the programme. This will enable some estimate of the proportion of false negatives. Where an efficient cancer registry is in operation this solution presents no problem.

In some mass examinations the yield, i.e. the number of cases detected, has been used to indicate the efficiency of the test procedure. It should be realized, however, that yield depends not only on the test, but also on the prevalence of the disease in the population studied and on the normal level of case-finding in that population.

A very important property of the diagnostic test is its ability to give a positive result early in the development of the disease, i.e. in pre-invasive, preclinical or asymptomatic cases. Two criteria by which this property of the test is commonly judged are the clinical-stage distribution of the cases detected and the presence or absence of subjective symptoms in these cases.

It should be emphasized that in considering the result of a first screening of a population the clinical-stage distribution can be misleading. To a lesser extent this will be true also in material obtained by re-screening of the same population at given intervals.

(2) Public acceptance of the mass examination

One of the important items that needs to be considered is the evaluation of public acceptance of the examination programmes offered. The number of persons attending a programme is not in itself a valuable index of public attitude. A much more informative figure is the proportion of the eligible population attending, though this index can only be used if the programme is offered to a defined population. When this is the case, it becomes possible to study the characteristics of those attending and those not attending: e.g. age, sex, marital status, parentage, socio-economic status and educational level. Such information reflects the pattern of motivation in public participation and is of great importance, not only for the evaluation of the programme itself, but for planning future programmes and preparatory health education. For example, several studies on screening for cervical carcinoma have shown that the lowest participation is found among groups of women with the highest morbidity and mortality from that cause, i.e. in the lower income groups. Conversely, the groups of women with the highest attendance rates include those least likely to benefit from the examination, not only because incidence of the disease is low among them, but also because they are the ones most likely to see the doctor if early symptoms develop. Such

negative selection for examination may be expected for various reasons in several types of mass examination for cancer. It is not likely, for example, that most heavy cigarette smokers will be very receptive to the idea of periodic screening for lung cancer.

One observation commonly made in mass examination is that the attendance rate tends to drop quite markedly when examinations are repeated. This is particularly disturbing where the drop is accompanied by increased negative selection. One consequence of such a trend from the point of view of evaluation is that it becomes difficult to compare the results of successive examinations. If, for example, a first screening with a high attendance rate and a high yield is followed by a second screening with a low attendance rate and a low yield, attribution of the difference in yield exclusively to the preventive effect of the first screening may not be justified.

It is often maintained that the educational propaganda used during mass screening programmes may possibly create cancerophobia. Some studies along these lines have been made, and these studies suggest that the danger of creating cancerophobia has been vastly over-estimated in the past, and that, on the contrary, the introduction of well-organized mass detection programmes has helped to reduce fear of cancer in large sections of the population. It is also desirable to evaluate the potential danger of creating a feeling of false security in the population screened.

(3) Follow-up

Another aspect of mass examination which requires constant appraisal is the organization and efficiency with which those in whom cancer has been demonstrated or suspected at the initial screening are followed up. The following data are indispensable for the evaluation of follow-up measures taken in the period between initial screening and final diagnosis and treatment:

- (a) the proportion of those referred for follow-up who actually comply;
- (b) the final diagnosis for all those referred, whether they have complied or not;
- (c) the time required for establishing the final diagnosis and for starting treatment.

From the administrative standpoint it is of great importance to identify the reasons for any delay between initial examination and final diagnosis. In this context, it has been found in some countries that an important cause of such delay is the overloading of special institutions for the complementary examinations which necessarily will accompany mass screening.

(4) Treatment

Treatment as such has been used in trying to evaluate the efficiency of mass examination programmes. One way of doing this has been to compare the proportion of screened cases that could be given radical treatment with the proportion that could be similarly treated among cases diagnosed in the conventional way. Such comparisons have their obvious limitations. It has, for example, been found that the resectability rate is much higher among lung cancer patients incidentally detected by mass X-ray survey, than among other lung cancer patients of similar age. If the prognosis is better for resectable than for non-resectable cases, the conclusion is near at hand, that improved control of lung cancer can be achieved by periodic mass X-ray surveys. This may be true and probably is, but the conclusion is not warranted by the kind of data referred to. It has been shown that mass examinations tend to pick up a disproportionate number of the relatively benign tumours. Some tumours are detected by periodic mass X-ray surveys because they are sufficiently slow-growing to permit the patient to wait for the next examination.

Few attempts have been made to assess this selection effect on mass examinations. It could be done with relative ease for those forms of cancer where histological malignancy grading is feasible, e.g. for breast cancer. In such evaluation blind reading would be essential.

Comparison of the extent of the treatment needed to control the disease in cases detected by mass screening and in those conventionally detected is another possible method of evaluating the efficiency of mass examination programmes.

This type of evaluation is of special interest in connexion with cytological screening for cervical carcinoma. As is well known, the "in situ carcinomas" detected by such surveys can be effectively eliminated by limited surgery. If left untreated, some of these lesions will progress and become invasive. In the early invasive phase, the majority would still be curable, but to achieve this result would then require much more drastic treatment.

In applying this method of evaluation it should be realized, however, that the prognostic significance of dysplasias and in situ lesions when found incidentally by mass examinations is not well known. Possibly the proportion that would have progressed and become invasive if left untreated may be lower than has been found by observation on clinical patients. Furthermore, it may be asked whether those detected in the pre-invasive stage by mass examination are not likely to be the more benign cases and whether this would not still have been the situation had they been allowed to become invasive. Answers to these questions can only come from population studies. To this end repeated screening of large, well-defined and carefully controlled population groups would be required.

(5) Survival after treatment

An important step in the evaluation of mass examination is the study of survival after treatment among those detected by the survey, as compared with cases diagnosed in the usual way. Although, in many mass surveys, the number of cases available for study has been small, most comparisons of this kind have shown or suggested that the length of survival after treatment is increased for those detected by the survey. This is often taken as evidence of greater effect of treatment when applied early in the evolution of the disease. It should be realized that comparisons of this kind are likely to be seriously misleading. Firstly, when treatment is started earlier, the length of survival afterwards is likely to be increased even though life may not be prolonged. The only increase may be in the "length of life with recognized disease". Secondly, it is likely that the material from the mass examination, at least from the first screening, may contain disproportionately many relatively benign cases.

(6) Other areas of evaluation

We believe that the evaluation of a mass screening programme would be incomplete if confined only to the technical and organizational components outlined above. In order to ensure that mass screening programmes have the maximum efficiency, carefully planned and executed operational research into the financial and administrative aspects of cancer detection programmes is also needed.

Evaluation of the various components of mass detection programmes does not obviate the need for direct assessment of the effect of mass examination on cancer mortality in the population. The various difficulties in evaluation which have been briefly outlined are not equally disturbing in all situations. They are least disturbing and can best be studied when evaluation is based on programmes involving periodic examination of well-defined populations. Under this condition, assessment of the effect of the programmes on mortality becomes a relatively simple method, especially where the population is that of an administrative subdivision which has for years prior to the study had an adequate vital and health statistical system. If the population has also been covered for some time by an efficient cancer registry the possibility of sound evaluation is greatly enhanced. Evaluation of various types of mass examination carried out under such conditions is now being undertaken in several countries.

To facilitate an adequate evaluation of any specific programme and increase the possibility of comparing the results of programmes conducted by different workers and in different countries, there is an urgent need for the standardization of terminology in cytology and histology. It is not enough to agree on definitions in, say, histology, if the pathologists are interpreting their findings in a different way. After reaching agreement on terms and criteria, it is essential to test comparability between various laboratories, and even between workers in the same laboratory, in carefully planned studies with blind readings. It is felt that the problems of terms and criteria should be considered at an international level by or through WHO.

Further progress in this field would also be greatly enhanced by standardizing methods of presenting the data from mass screening programmes. Reports on mass examinations giving sufficient details of the objectives, organization and results should be published without delay and thus made available to others. WHO might usefully act as a clearing-house for the information of all countries on current and projected studies and the hope is expressed that WHO will continue to give attention to mass screening and assist with expert advice when requested.

The evaluation of cancer detection would not be complete without the mentioning of some of the ancillary benefits. As a beginning cancer detection offers a unique opportunity to study the natural history of cancer through its early stages and before the host environment has been altered by the disease. This can be accomplished by following all positive cases which, for one reason or another, remain untreated. Undoubtedly, this is the opportune time to investigate all factors in the internal and external environment which have produced positive signs of malignancy.

The value of cancer detection in the study of the natural history of the disease is followed by its contribution to the understanding of "pre-malignant" lesions. Here, information becomes available on the reasons why certain conditions must be considered precursors to cancer and, in addition, data are obtained on the biochemical and morphological differences between lesions with low and high cancer potential.

Since many cancer detection activities are planned to examine the same participants at periodic intervals, it becomes possible to study the growth potential and rapidity of cancer development in an individual at a measured interval of time and after a previous negative report. It is also possible to assess the relative sensitivity of detection techniques particularly in those who appear to have had cancer at the time of a clinically negative examination.

Among so-called "high risk" groups, cancer detection delineates those factors which characterize such groups and so establishes the criteria for selecting segments of the population which require the benefit of periodic cancer detection examinations. The relative values of age, sex, race, family history and environment can be assessed in an attempt to understand those factors which predispose to cancer or develop an immunity to it.

4.3 TRAINING FOR EARLY DETECTION

INTRODUCTION

In this section WHO technical papers have been freely used.³⁶

It has been acknowledged universally that the success of health programmes, particularly cancer detection programmes, depends mostly on the existence of well-trained, adequately maintained, and well-equipped staff. This need is quite apparent today but would be more so in the future as the health workers go through the process of adapting themselves to changes of organizational trends and in the health needs and demands of the population. In this

respect, two basic changes are worthy of mention. In the past, public health administration was characterized by its law enforcement functions. Today its emphasis is on health promotion and disease prevention through an educational approach. People must be contacted and convinced, and this necessitates the existence of an understanding of sociology on the part of all health personnel. Furthermore, there is a definite trend toward a system of comprehensive health care programmes, resulting from the integration of curative and preventive services.

The two aspects cited above indicate the great need everywhere for the proper orientation of existing personnel and the adequate training of the newcomers into the cancer field. For this reason, it is most important that a careful analytical study be made of the training needs of all medical and paramedical personnel that will be involved in any early detection programme. It is also necessary that the present training programmes be appraised continuously to be sure that the quality and quantity of the training programme meets the high standards necessary for the conduct of a successful programme. It is evident that the types of programmes and the personnel who will be trained will vary from country to country depending on the nature of their planned or ongoing cancer detection programmes.

It should be noted that a great effort must be made in order to provide health workers with an outlook broader than that which they have been given in the past. For instance, staff to be assigned to mass campaigns should be trained in such a way as to permit them to assimilate further training at a future date to qualify them to perform multipurpose functions as soon as circumstances so warrant. Similarly, general health service personnel should be given the required basic knowledge to permit them to understand the purposes and procedures of mass campaigns.

The experiences of the various countries which have been concerned with the preparation of health workers cannot be reduced to a uniform pattern. The training for employment in both general and specialized cancer services is neither an easy nor an uncomplicated undertaking. There are differences not only in function but also in the nomenclature applied to apparently identical forms of occupation. In addition, there are differences in the basic educational requirements for training, in its actual content and in its duration.

Some countries are now making great efforts to develop training programmes of varying degrees of intensity, not only for different types of health personnel but also for local government officials, members of voluntary groups and community workers. All this should be given maximum possible support, in order to achieve the desired cross-fertilization, not only between the specialized cancer and general health personnel but also between them and other public servants and voluntary workers.

The content of training programmes should be subject to periodic revision to introduce new knowledge as soon as it becomes available and to exclude material that is no longer of value. Such revision should be correlated with frequent and objective evaluation of the tasks being carried out by health workers at all levels, especially those in the field, in order to avoid the wastage of time and effort on activities which do not produce real benefits for the population but are being carried out merely because of tradition. In addition, the training of auxiliary personnel must always be directed so as to impress on them their limitations: they should appreciate that any departure from what they have been taught would mean a risk to those whom they are entrusted to serve.

As teaching staff constitute a key factor in the success or failure of training programmes, positive steps should be taken to ensure that they are adequately prepared and frequently reoriented in technical and educational developments. International collaboration will be necessary, in some cases, to fulfil this important requirement.

In summary, the satisfactory control of cancer requires the effective organization of prevention, detection, diagnosis, treatment and after-care by comprehensive teams including clinicians, radiologists, pathologists (including cytopathologists), epidemiologists,

statisticians, public-health officers, nurses, health education specialists and other allied medical personnel whose standards of efficiency should be maintained at the highest level. Finally, more attention should be given to the testing of new teaching and training techniques so that they may be applied to the changing needs and trends of health organization.

4.3.1 MEDICAL PROFESSION

The approach of the medical profession can greatly affect delay in treatment where pre-cancerous lesions and cancer in its early stages are concerned. There have been repeated instances where patients have sought medical attention owing to symptoms, but a correct diagnosis has not been promptly established because the physician seemed unaware of their importance or did not utilize all the relevant diagnostic tools and techniques, even where readily available. This indicates insufficient knowledge on the part of the physician about the potentialities of various diagnostic techniques.

To improve the situation, it is imperative to secure better education for physicians and other health personnel in the field of cancer diagnosis and control. Such training, taking into consideration all forms of cancer as well as all aspects of cancer control, should start at the undergraduate level and be followed by special post-graduate training programmes. A continuing, lifelong professional education is needed if the public is to benefit from the scientific programme made in early cancer detection and treatment. The aim of all professional education should be to create an alert and competent medical profession oriented towards the early diagnosis of disease including premalignant and malignant conditions.

The detailed organization and content of professional cancer training programmes will have to be adapted to prevailing differences in the organization of the health services and of medical education. Generally, such training can best be provided in special cancer institutes or in other hospitals attended by numbers of cancer patients. As indicated earlier, different methods of training should be tested and evaluated in order to attain the maximum efficiency.

There are many types of training of medical personnel and this will vary within the medical specialty in which the physician has received training. Listed below are some representative examples of types of training depending on area of specialization:

(1) The general practitioner, who has the first contact with the patient, should be trained at both pregraduate and post-graduate levels in methods of detecting malignant disease. This training can best be provided in hospitals treating cancer and in cancer institutions. It is essential that there should be very close contact between the general practitioner and the treatment centre to keep him in touch with the latest developments in detection, diagnosis and treatment. The general practitioner should be familiar with methods of taking smears from the cervix, skin, sputum, and urine for the purpose of cytological examinations. He should also be trained in methods of examining the cervix, the pelvis, the breast and other cancer sites that lend themselves to detection by physical examination. Training in office methods such as Schiller's test and punch biopsies may be included when he practises in remote areas. Since doctors form the principal group concerned in cancer control, methods of health education should form an integral part of their study of cancer.

(2) Special training for medical personnel for out-patient services. In general, the physicians in this group will be considered to have had specialty training beyond the general practitioner level, and where necessary, the latest methods of specific detection in the areas of cytology, biopsy, irradiation, colposcopy, and colpomicroscopy should be made available. Staff for detection, diagnosis and follow-up will generally include a surgeon, a physician and a radiotherapist, and they should be trained to work together as a team, both for the detection as well as the diagnosis of cancer.

(3) Pathologist including cytopathologist. The training of cytopathologists should be carried out wherever possible in cancer hospitals or cancer institutes. The pathologist should have adequate training in cancer diagnosis.

(4) Medical students. The training of medical students in the many facets of oncology and cancer detection and control should be carried out at appropriate cancer hospitals and institutes as well as medical schools. Emphasis should be placed on training in pre-malignant and malignant conditions, cytological examination, and other methods of early detection. These subjects are best taught by participation. For fostering the idea of early disease detection, it is important to introduce the student to a type of medical practice organized in such a way as to make this work feasible - e.g. a well-organized group practice or health centre.

4.3.2 ALLIED PROFESSIONS AND AUXILIARY STAFF

General statement

Due to the general shortage of highly trained medical personnel, whenever possible and feasible, technicians and other auxiliary personnel should be used in conducting mass examinations. For example, specially trained midwives, practical nurses, and/or nurses can obtain samples for cervical cytology, specially trained technicians can screen the cytological smears, and technicians can be trained to utilize the mass application of soft tissue mammography if this technique ever develops sufficiently as a screening device. The provision of training facilities for such auxiliary personnel must therefore be regarded as an important step towards the future extension of mass screening programmes. In the United Kingdom and the United States of America, special training schools for cytotechnicians, as well as the cytopathologists, have been established for some time and plans for similar facilities have been developed for other countries. At present, in some countries such as the United States of America, the initial screening of cytological smears in mass examinations is carried out by specially trained and qualified cytotechnologists. At the same time, in some countries, the initial screening of the same smears have to be carried out by medically qualified cytologists in the absence of trained cytotechnologists. This seriously reduces the capacity of laboratories to handle mass examination material and is one of the main obstacles in the way of introducing cytological screening programmes.

Listed below are some representative examples of types of training depending on area of specialization:

- (1) Public health staff should be trained in the planning of cancer control programmes, and in particular in early detection techniques;
- (2) Dentists should be trained in awareness of early evidence of cancer of the oral cavity and in particular in how to do a good oral examination, as well as being trained in the technique of oral cytology, where indicated;
- (3) The home visitor should be trained in the special needs of the cancer patient as they relate to early detection, e.g. assist in motivation, education and follow-up studies;
- (4) Nurses should be trained in all phases of early detection of cancer and have their role in an early detection programme clearly identified so that they may be adequately trained to assume this role. It should be noted that the role of the nurse and other auxiliary personnel might vary from country to country;

(5) Public health nurses and midwives should also be trained in cancer detection. Such training could include activities that would involve them in motivation, education and assistance with certain technological procedures for which they can assume responsibility;

(6) Health education specialists should be trained in the organization of surveys, projects and programmes concerned with the health education aspects of cancer control and the training of health workers in educational methodology.

A general problem exists as to who should decide on the planning of a programme for training at all levels in the field of cancer. Either a public health planning authority and/or medical specialist trained in oncology might solve the problem of deciding where and when training programmes should take place. In addition to these two groups, the training activities should be co-ordinated by the central planning body for the state or country concerned. There may be a particular need for the training of specialized oncologists in every field of cancer to direct the training campaign at all levels.

Cancer centres developed for diagnosis and treatment should be used for the training of general practitioners, specialists and medical students in cancer control. Medical schools should be encouraged to organize their curriculum in such a way as to keep it constantly abreast of new knowledge in the field of cancer control. It is desirable that national and international bodies give thought to the provision of fellowships in the various fields of cancer to increase post-graduate training at all levels.

4.4 EDUCATION OF THE PUBLIC

For this section we refer to the paper prepared by Dr John Wakefield for this meeting. Further we refer to the chapter on the role of public education in Cancer Detection - UICC.⁴²

4.5 ADAPTATION IN COUNTRIES WITH DIFFERENT ECONOMIC AND SOCIAL BACKGROUNDS

In view of the variety of factors to be considered, it is felt that it is not feasible to propose a detailed plan for a cancer detection programme which would be applicable in all countries. It is further felt that it is impossible to make any comparative analysis of the efficiency of the different ways of organizing cancer detection adopted in the various countries. It is clear, however, that the way in which mass examinations are organized must differ from country to country. What is an efficient organizational set-up in one type of economic, political and administrative environment may not be equally successful in countries with a different structure. From this it follows that it is impossible to work out detailed recommendations for the organization of mass screening programmes directly applicable to all countries. Throughout this working paper some general guide lines have been pointed out and it is felt most appropriate that additional items be considered by each country at the time they reconsider the development and implementation of a mass detection programme. Probably the best way to summarize these concepts would be to present certain questions which would require an answer if a cancer detection programme is to be developed and also be successful. Such a questionnaire will be found in Cancer Detection - UICC, page 52.⁴²

The adaptation of screening programmes to developing countries will cause special difficulties due to the poverty, high percentage of illiteracy, lack of hospitals and medical and allied personnel - not least lack of financial possibilities.

REFERENCES

1. Logan, W. P. D. & Cushion, A. A. (1958) Morbidity statistics from general practice: vol. I (General), London, H.M. Stationery Office (General Register Office, Studies on medical and population subjects, No. 14)
2. Registrar General, England and Wales (1966) The Registrar General's statistical review of England and Wales for the year 1964. Part I. Tables, medical, London, H.M. Stationery Office
3. Registrar General, England and Wales (1957) The Registrar General's statistical review of England and Wales for the year 1952, Supplement on Cancer, London, H.M. Stationery Office, p. 114
4. Posner, E., McDowell, L. A. & Cross, K. W. (1959) Mass radiography and cancer of the lung, Brit. med. J., 1, 1213
5. Cuthbert, J. (1959) Bronchogenic carcinoma: a mass radiography group compared with a practitioners group, Brit. J. tuberc., 53, 217
- 6a. Gifford, J. H. & Waddington, J. K. B. (1957) Review of 464 cases of carcinoma of the lung treated by resection, Brit. med. J., 1, 723
- 6b. Waddington, J. K. B. (1960) Surgical aspects of the mass X-ray campaign, Liverpool, 1959, Med. Offr., 104, 293
7. Boucot, K. R., Cooper, D. A. & Weiss, W. (1961) The Philadelphia pulmonary neoplasm research project: an interim report, Ann. intern. Med., 54, 363
8. Canti, G. (1964) Analysis of 100 cases of bronchial carcinoma, Paper presented at Annual Meeting, British Society for Clinical Cytology, London (Unpublished)
9. Knox, E. G. (1966) Cervical cytology: a scrutiny of the evidence. In: McLachlan, G., ed., Problems and progress in medical care; Essays on current research, London, Oxford University Press, 2nd series, p. 277
10. Jones, H. (1952) In a discussion of a paper by Hertig, A. T., Younge, P. A. & McKelvey, J. L., entitled "A debate: What is cancer in situ of the cervix? Is it the pre-invasive form of true carcinoma?", Amer. J. Obstet. Gynec., 64, 207, 816
11. Petersen, O. (1955) Precancerous changes of the cervical epithelium in relation to manifest cervical carcinoma, Copenhagen, Danish Scientific Press
12. Lange, P. (1960) Clinical and histological studies on cervical carcinoma, precancerosis, early metastases, and tubular structures in the lymph-nodes, Acta path. microbiol. scand., Suppl., No. 143
13. Clemessen, J. (1962) On the prognosis of precancerous conditions of the uterine cervix. In: Proceedings of International Conference: the morphological precursors of cancer, Perugia, University of Perugia, p. 463
14. Koss, L. G. et al. (1961) A long-term cyto-histologic study of untreated carcinoma-in-situ and related abnormalities of the uterine cervix, Paper presented at First International Congress of Exfoliative Cytology, Vienna (Unpublished)

15. Younge, P. A., Hertig, A. T. & Armstrong, D. (1949) A study of 135 cases of carcinoma in situ of the cervix at the Free Hospital for Women, Amer. J. Obstet. Gynec., 58, 867
16. Boyes, D. A., Fidler, H. K. & Lock, D. R. (1962) Significance of in situ carcinoma of the uterine cervix, Brit. med. J., 1, 203
17. Dunn, J. E. (1962) The use of incidence and prevalence in the study of disease development in a population, Amer. J. publ. hlth, 52, 1107
18. Dunn, J. E. (1958) Preliminary findings of the Memphis-Shelby County uterine cancer study and their interpretation, Amer. J. publ. hlth, 48, 861
19. Kashgarian, M. et al. (Unpublished observations)
20. Terris, M. & Oalman, M. C. (1960) Carcinoma of the cervix: an epidemiologic study, J. Amer. med. Ass., 174, 1847
21. Boyd, J. T. & Doll, R. (1964) A study of the aetiology of carcinoma of the cervix uteri, Brit. J. Cancer, 17, 419
22. Aitken-Swan, J. & Baird, D. (1966) Cancer of the uterine cervix in Aberdeenshire: epidemiological aspects, Brit. J. Cancer, 20, 624
23. Breslow, L. & Hochstim, J. R. (1964) Sociocultural aspects of cervical cytology in Alameda County, Calif., Publ. Hlth Rep. (Wash.), 79, 107
24. Kegeles, S. S. et al. (1965) Survey of beliefs about cancer detection and taking Papanicolaou tests, Publ. Hlth Rep. (Wash.), 80, 815
25. Wakefield, J. & Baric, L. (1965) Public and professional attitudes to a screening programme for the prevention of cancer of the uterine cervix, Brit. J. prev. soc. Med., 19, 151
26. Davis, H. J. (1962) The irrigation smear: a cytologic method for mass population screening by mail, Amer. J. Obstet. Gynec., 84, 1017
27. Davis, H. J. & Jones, H. W., jr (1966) Population screening for cancer of the cervix with irrigation smears, Amer. J. Obstet. Gynec., 96, 605
28. Koch, F. (1966) The population screening for cervical carcinoma in the Borough of Frederiksberg 1962-1963; application of the irrigation smear technique in a mass screening, Copenhagen, Munksgaard
29. McGregor, J. E., Fraser, M. E. & Mann, E. M. F. (1966) The cytopipette in the diagnosis of early cervical carcinoma, Lancet, 1, 252
30. Cameron, C. B. & Hussain, O. A. N. (1965) 6-Phosphogluconate dehydrogenase activity in vaginal fluid: limitations as a screening test for genital cancer, Brit. med. J., 1, 1529
31. Ladinsky, J. L., Sarto, G. E. & Peckham, B. M. (1964) Cell size distribution patterns as a means of uterine cancer detection, J. Lab. clin. Med., 64, 970
32. Gershon-Cohen, J. & Borden, A. G. B. (1964) Detection of unsuspected breast cancer by mammography, Ann. N.Y. Acad. Sci., 144, 782

33. Egan, R. L. (1962) Mammography, an aid to diagnosis of breast cancer, J. Amer. med. Ass., 182, 839
34. Shapiro, S., Strax, P. & Venet, L. (1966) Evaluation of periodic breast cancer screening with mammography: methodology and early observation, J. Amer. med. Ass., 195, 111
35. Fidler, H. K., Boyes, D. A. & Worth, A. J. (1968) Screening for malignant diseases by means of exfoliative cytology. In: Presymptomatic detection and early diagnosis (In press)
36. Wld Hlth Org. techn. Rep. Ser., 89, 156, 193, 251, 276, 294
37. Gonzalez, C. L. (1965) Mass campaigns and general health services, Wld Hlth Org. Publ. Hlth Pap., No. 29
38. Segi, M. (1964) Cancer mortality for selected sites in 24 countries, No. 3 (1960/1961) Japan
39. Norwegian Cancer Society (1959-1965) Mass screening for cancer of the uterine cervix in Østfold county, Report No. 1
40. Anderson, W. A. D. & Gunn, S. A. (1967) Cancer of the cervix, C A (N.Y.), pp. 150-156
41. Seminar on the early detection of cancer (1965) Oslo, November
42. UICC Monograph Series, 1967, vol. 4 (Cancer Detection, N.Y.)