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EDITORIAL:

THE RESEARCH ATTACK ON CANCER

The Age

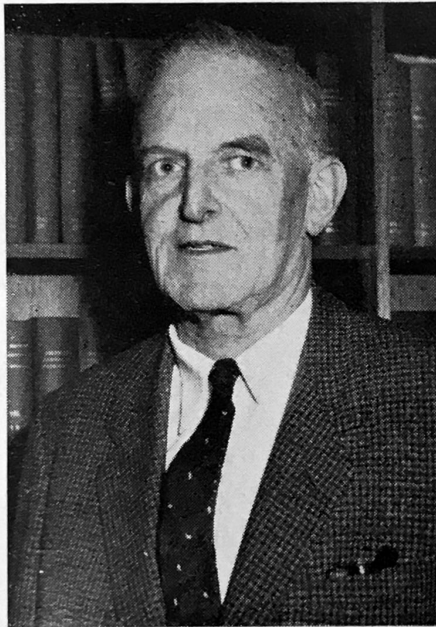
by

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The problem of cancer is world-wide, and tremendous efforts are being made in all highly developed countries to combat this menace to health and longevity.

The scientific attack is coming from all directions. It is, in fact, one of the greatest research attacks ever made on a particular disease.

As would be expected, those countries with large populations and advanced technologies such as Britain and the United States of America contribute a large proportion of new information. At the same time, smaller nations such as France, Canada and Sweden add their share.

It is sometimes suggested that Australia, faced with many problems of development, should wait for the discoveries which are to be, and will be, made in the large laboratories of the great powers.

There are two important reasons why this argument should not be accepted:—

- (a) Brilliant research workers and first class research are not confined to any one country, however large; and
- (b) It is reasonable to argue that our own people should not be deprived of the best knowledge even for a short time (perhaps two or three, but possibly many more, years).

In Australia, and particularly in Victoria, as a result of the research facilities provided by the Anti-Cancer Council, we have been able to take our place in the forefront of scientists who are exploring the unknown. This applies to studies carried out in Melbourne on leukaemia, on the mode of action of some of the cancer-producing chemicals, and on developing methods of cancer treatment, amongst others.

Our work here has been recognized by scientists in other parts of the world and our research workers have been invited to address many conferences overseas. An important facet is that Australian doctors and scientists are given the opportunity of contact with those in other countries, and thus are conversant with the most recent advances.

It is the community's generous support of the Anti-Cancer Council of Victoria that makes possible our position in the front rank of cancer research.

APPEAL CHAIRMAN OPENS 1965 CANCER CAMPAIGN

More than 100 leading citizens representing all sections of the community attended the inaugural meeting of the 1965 Cancer Campaign, held in the Melbourne Town Hall under the patronage of His Excellency Major General Sir Rohan Delacombe, K.C.M.G., the Governor of Victoria.

"With such co-operation and enthusiastic assistance", said the Appeal Chairman, Lieutenant General Sir Ragnar Garrett, in his address of welcome, "I have very little doubt that the target will be attained".

Promises Kept to the Letter

"In the 1958 Appeal", said Sir Ragnar, "the Council promised that the money donated would be spent over the next 5-10 years on cancer research (75%) and cancer education (12½%). These promises have been kept to the letter, and Victoria has now a vigorous, effective anti-cancer campaign with a record of real achievement. The remaining 12½% is employed on assistance to cancer sufferers and administrative expenses of the Council".

To enable this vitally important work to continue, however, adequate financial support must be assured now.

Outstanding Research

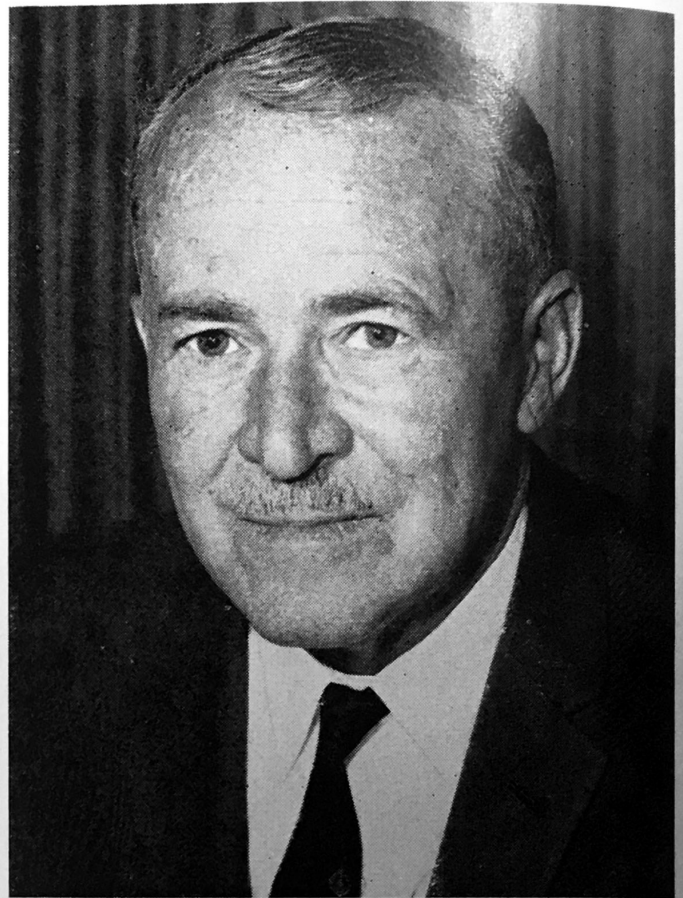
Over three quarters of a million pounds has been spent on cancer research to date, reported Sir Ragnar. No less than £120,000 is needed each year to support some 40 research projects involving 100 scientists and assistant staff.

"Much important new knowledge about cancer has been obtained, improvements in diagnosis and treatment have resulted, and several Victorian cancer research workers have gained world renown. The Council's Carden Fellow, Dr. Donald Metcalf, to quote one example, recently shared the Syme Research Prize for the most outstanding research carried out in Australia during the past 2 years. Dr. Metcalf has been invited to accept an appointment as Visiting Research Professor in 1965 at one of the leading Cancer Research Institutes in the United States."

Education and Welfare

Referring to the public education and patient welfare programmes Sir Ragnar said:

- The Council's public education campaign has reached almost every Victorian by means of television, radio, films, lectures, exhibitions, posters and distribution of pamphlets. Surveys indicate a greatly increased knowledge of cancer and its warning signs and symptoms.
- Patients, because they are better informed, now seek medical advice sooner, when the prospects of successful treatment are better.



Lt. Gen. Sir Ragnar Garrett, K.B.E., C.B.

- There has been much favourable comment in Australia and abroad about the Victorian educational campaign. Last year the Council's television short was awarded the Public Service Trophy of the Hollywood Advertising Club, U.S.A. It was the only non-American film to win a prize from over 1,500 entries.
- Assistance to cancer sufferers remains a major responsibility. Over the past 7 years about £150,000 has been needed to help upwards of 4,000 patients.

Continuity of Effort

Sir Ragnar pointed out that the target of £500,000 amounted to only 3/4d. per head of the population of Victoria, or **no more than the price of one bottle of beer to help save future generations from this dreaded disease.**

At least this amount is needed to ensure continuity of effort for the next 4-5 years, he said.

"By May approximately £350,000 will still be available from the Appeal conducted 7 years ago. At the present rate of expenditure this will last until the end of 1966. If the work is to be continued beyond that time additional funds must be sought NOW".

WOMEN WANT TO KNOW ABOUT THE 'CELL TEST'

Women throughout Victoria are showing a keen interest in the 'cell test' for cancer of the uterus, report the two nursing sisters now touring the State with information about the new facilities for the cytological diagnosis of cancer.

The nurses are Sister Elizabeth Warr, whose nursing career began with the A.I.F. in New Guinea during the last war, and Sister Patricia McLaughlin, whose experience in midwifery and gynaecology has brought her into contact with many cases of uterine cancer.

Appointed as education officers by the Anti-Cancer Council to help in the 1965 Cytology Education Campaign, they have the support of the Country Women's Association, the Federation of State School Mothers' Clubs and many other women's organisations, as well as the Health Department and the Hospitals and Charities Commission.

Woman to Woman

"Women will approach another woman rather than a man about this form of cancer", says Sister Warr. "At our meetings many come to ask us questions that they would hesitate to ask even a male doctor. And each question asked is vital to that particular person."

Her audiences are surprised to learn, she reports, that altered cells discovered through cytological examination may reveal the presence of pre-cancerous conditions years before symptoms would appear.

"We tell women that with prompt treatment at the first appearance of a warning sign the cure rate for cancer of the cervix (neck of the womb) is now high, about 75%, but with the 'cell test' which we urge them to have as part of a routine health examination, changes in cells may be picked up so early that the likelihood of cure is practically 100%".

Bringing Cancer into Open

Like her colleague a native of Melbourne, Sister McLaughlin trained at St. Vincent's Hospital, and later did midwifery at the Royal Women's. She has seen many patients with gynaecological cancer in women's wards and before taking up her present appointment spent two months as a relieving sister at the Peter MacCallum Clinic.

"Our job now", she explains with determination, "is to bring this form of cancer into the open. We aim to encourage women to accept the test as a regular health habit rather like a routine chest X-ray. If the result is negative, as it will be in nearly all cases, they gain the peace of mind that comes from knowing no signs of cancer are present".

"If the smear should be positive, which will happen in only about 5 in every 1,000 examinations, we believe we will have helped these patients to undergo treatment with confidence and hope".

Both sisters agree that the meetings held so far could not have been better. Country and city audiences alike have been very interested in the lectures and films, and the sisters have no doubt that women appreciate the chance to learn how to protect themselves against the risk of uterine cancer.

"We believe that this campaign will prove to be a major step forward in bringing this form of cancer under control in Victoria," they conclude with enthusiasm.



Dr. Michael Drake discusses the cytology education programme with Sister Patricia McLaughlin and Sister Elizabeth Warr (seated).

'CELL TEST' HAS PROVED ITS VALUE

The greatly increased facilities now available in Victoria for cytological diagnosis — the modern cancer detection test which reveals the presence of cancer cells in secretions from the uterus or womb — offer protection against the risk of uterine cancer to thousands of women.

The Director of the newly-established State Cytology Service, Dr. Michael Drake, points out that the value of the test has been proved in the Canadian province of British Columbia, where after 10 years of 'smear testing' the incidence of invasive cancer of the uterus has fallen

by 50%. "Today in Canada", he says, "they can count on whole-hearted co-operation from women".

Even more impressive is the example of Southern Norway, where more than 80% of the adult female population turned up for the first screening.

Dr. Drake believes that if the same level of participation can be achieved in Victoria, cancer of the uterus may be virtually eradicated as a cause of death.

"The figures from British Columbia show that this is a real possibility", he says.

CANCER OF THE SKIN



by **Dr. F. URBACH**

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(Reprinted from the bulletin of the International Union against Cancer)

THE COMMONEST CANCER, IT IS ALSO THE MOST CURABLE

The beneficial effects of sunlight have been known since antiquity. Many early civilisations worshipped the sun, and even the term "radiation" is by some thought to be derived originally from the name of the Egyptian sun-god Ra.

Since the discovery of ultra-violet radiation by Ritter in 1801, a great number of studies have shown that this very small band of sunlight, comprising less than 0.1% of the total energy output of the sun, is indeed biologically and chemically most active.

The observation that sunlight might cause cutaneous cancer can be traced back to the German dermatologist, Paul Unna, who suggested that long outdoor exposure caused a precancerous skin change on the back of the neck of men which he called "Seemannshaut" (seaman's skin). The first detailed evidence of the relationship of sunlight exposure to skin cancer was reported by William Dubreuilh of Bordeaux. Since then, a number of clinical investigations have greatly added to the weight of the evidence for the causal relationship of ultra-violet radiation to human skin cancer.

The basis for the assumption that sunlight (and the ultra-violet wave band in particular) causes human skin cancer may be summarised as follows:

1. Cancer of the skin occurs more frequently on those parts of the body exposed to sunlight.

2. Cancer of the skin is more common in regions of the earth receiving more ultra-violet radiation.
3. Cancer of the skin occurs much more frequently in light-skinned than in dark-skinned people, and
4. Cancer of the skin occurs more often in people engaged in outdoor occupations.

Incidence of Skin Cancer

Cancer of the skin presents formidable obstacles to epidemiological study. Unlike cancer of most other sites, fatalities are uncommon, many cancers are treated in physicians' offices, information is recorded in many different ways or not at all, and often biopsy and microscopic examination are not performed. Thus, calculations of incidence, age specific rates, or other demographic analyses are difficult and hazardous. There appears to be a great variation in morbidity, as shown in the few carefully designed studies on record.

For Caucasians, morbidity varies from approximately 30 per 100,000 in the Northern U.S., to 140 per 100,000 in the Southern U.S.A. and Hawaii, and to 1,300 per 100,000 in Victoria, Australia. In sharp contrast to this high incidence among light-skinned people is the low morbidity of those with genetically pigmented skin: 4 per 100,000 among Hawaiian, Chinese and Japanese, 2 per 100,000 among the Johannesburg Bantu.

Since it is very likely that even these high figures of skin cancer morbidity in Caucasians seriously underestimate the real magnitude of the problem, cutaneous malignancies must be considered among the most common tumours of man (e.g., in Australia they comprise more than 50% of all cancers and account for one third of all skin conditions seen clinically).

Skin Colour and Cancer

From the accumulated evidence and the above-mentioned estimates of morbidity it appears quite clear that light-skinned people are much more susceptible to skin cancer than genetically more pigmented races. The exact reason for this phenomenon is not clear. Most probably it is not only a matter of melanin present in the skin: its location in the epidermis, and the thickness of the stratum corneum are important factors.

Whether there are other hereditarily controlled differences of response to ultra-violet injury has not yet been determined. Such differences are suggested by the observation that there is only a general correlation between skin colour and cancer in light-skinned individuals.

Here, it appears that degree of reaction to ultra-violet injury (i.e., sunburn) and ability to "tan" and maintain a "tan" are of great importance. Thus, the Irish and Scots are much more likely to develop skin cancers than the Mediterranean races. For example, in our Tumour Clinic in Philadelphia (an urban area at latitude 40° North), over

80% of all patients with skin cancer are either 1st or 2nd generation Irish — presumably those most likely to develop cancer with the least amount of ultra-violet exposure are thus selected out.

The problem, however, is not so simple: squamous cell cancer among Bantu and Indians is much more frequent than basal cell cancer, but it clearly is often due to causes other than ultra-violet light—chronic leg ulcers in the Bantu, chemicals, pressure and heat (Kangri, Dhoti, Khaini cancer) in Indians.

While there appears to be no question that dark-skinned races are quite resistant to the carcinogenic effects of sunlight, careful studies of the genetic history of patients with skin cancer need to be made before any rules can be formulated.

Latitude and Outdoor Exposure

The incidence of skin cancer seems to be distributed geographically in the way that would be expected if sunlight were a causal factor. Exact comparisons of morbidity with ultra-violet intensity are, however, very difficult, because of the uncertainties inherent in estimates of the amounts of potentially carcinogenic radiation reaching various geographic areas annually.

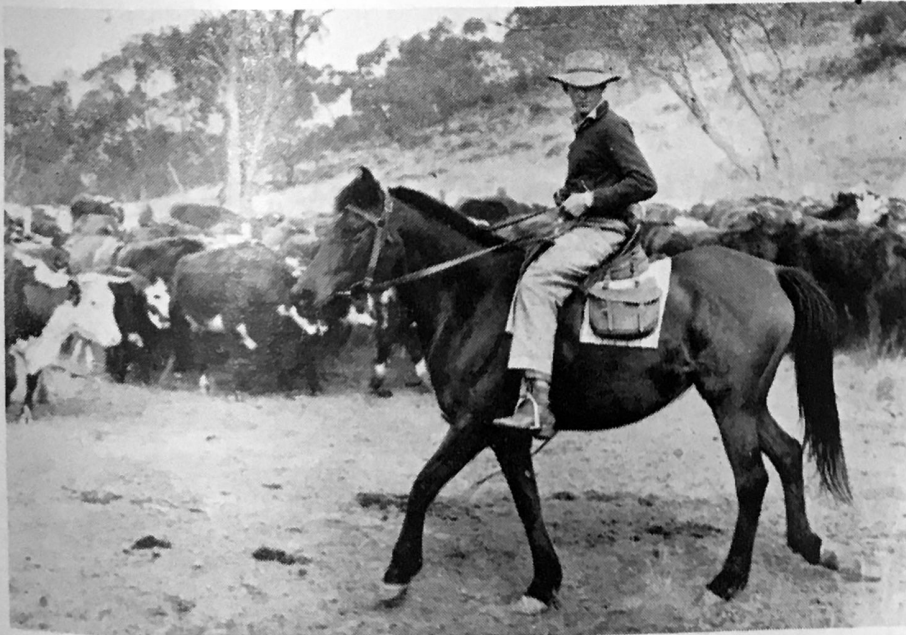
The sum of the biologically effective radiation reaching a population at risk depends on latitude, time of day, thickness of ozone layer, season, cloud cover, and nature of the reflecting ground surface — to

mention just some of the more important factors. Thus, "sunlight hour" measurements are meaningless, and exact calculations of ultra-violet dose very difficult.

The recent development of simple ultra-violet indicator systems for field use by Robertson of Australia, Schulze of Hamburg, and ourselves promises to result in direct quantitative measurements of ultra-violet radiation which can be correlated with incidence of skin cancer. The data of Dorn for the U.S. show a 50% increase in skin cancer between latitudes 41° North and 32° North, which fits reasonably well with calculated ultra-violet dose figures. The great difference in morbidity between Victoria, Australia, and the Northern U.S. probably is due to a combination of differences in ultra-violet intensity, degree of outdoor exposure, and genetic make-up of the population.

The complexity of the problem is best exemplified by a recent excellent study by Silverstone in Queensland, Australia. In two communities at the same latitude, with almost identical (measured) ultra-violet radiation quantities reaching the population, there were significantly more cancers in people working "mainly indoors" in the area with high humidity than in the area with a dry climate. Most likely this is due to differences in area of body usually clothed, and in type of recreational activities (outdoor recreational activity fostered by moist climate).

WALKABOUT Magazine



Droving in the Australian outback. The long hours of sunlight and the hot dry climate are important factors in Australia's high rate of skin cancer.

Further studies taking into account actual ultra-violet exposure, work and play habits, type of clothing, etc., are badly needed. Attempts to develop an objective index of cumulative lifetime skin ultra-violet exposure are being made, and, if successful, will help in unravelling this part of the problem.

Topographical Distribution

It has been said that in white races, more than 80% of all skin cancers occur on the head and neck. The unfortunately almost forgotten study of Magnusson (Sweden, 1935) and present work going on in our Institute clearly show very great differences between the distribution and the relation to latitude of basal cell and squamous cell carcinomas.

In brief, the vast majority of all basal cell cancers appear on the face, and approximately 35-40% of these occur in areas normally little exposed to ultra-violet (orbit, upper lip, behind the ear). In contrast, squamous cell cancer occurs most frequently on the surfaces most intensively insolated (rim of ear, lower lip, forehead, zygoma).

Furthermore, squamous cell cancer increases to a much greater extent in frequency with decreasing latitude than basal cell cancer. Also, basal cell carcinoma is extremely rare in pigmented races. It thus appears that there is an excellent relationship between the topographical incidence of squamous cell carcinoma with sunlight exposure, but that in basal cell carcinoma, sunlight is only one of several major factors.

In summary, skin cancer is one of the most common human neoplasms. Its geographical pathology demonstrates **par excellence** the complex factors affecting variation in world-wide distribution of human disease. An attempt has been made to show how the study of such various parameters as heredity, occupation, recreational habits, exposure to the sun, geography, and bioclimatology results in a better understanding of the nature and cause of at least one type of cancer.

Much work must yet be done, obviously, by scientists of different disciplines and in many parts of the world pooling their knowledge and efforts to reach a common goal — the better understanding and perhaps even the conquest of disease.

ENZYMES AND CANCER

Growing knowledge of the inner life of the cell has focussed attention on enzyme activity.

Enzymes — catalytic substances formed by living cells — are now known to play a vital role in the complex metabolic reactions within the cell.

A recent report from the Sloan-Kettering Institute for Cancer Research in New York explains how the study of enzyme activity is pointing the way to better diagnosis and more effective treatment of cancer.

“As more and more came to be known about the internal biochemistry of the cell”, says the Report, “it became clear that nearly all that a cell is and does is a reflection of the enzymes it contains, the various proportions in which they appear, and their intra-cellular organization.”

The basis for the modern science of enzymology was laid by Pasteur during the last century.

Commissioned by French wine makers and German brewers who were anxious to improve the quality of their products, Pasteur provided the first scientific proof that without living yeast cells (“enzyme” means literally “in yeast”) the complex chemical process of fermentation by which sugar is changed into alcohol couldn't take place.

Today considerable data is available not only regarding what various enzymes do, what factors affect their reactions and rate of activity, but also a number of enzyme structures (all of which so far have proved to be proteins) have been identified and named.

Understanding Cancer Mechanisms

Research workers in this field, says the Report, have already done much to help cancer sufferers. The broad purpose of the Institute's Division of Enzymology and Metabolism has been, in fact, the understanding of enzymatic mechanisms involved in cancer growth.

The programme so far has included basic work on the nature and purification of enzymes from human tissues, the devising of methods for investigating enzymes in tissues and in blood, the study of the mechanism of action of such enzymes as phosphatase and phosphoglucomutase, and the establishment of techniques for the large-scale study of enzymes in normal persons and in patients with various types of cancer.

One major area of interest has been the study of changes in the enzyme systems of cancer cells following treatment with drugs.

Another has been the examination of enzymes in the blood, for example, in patients with metastatic cancer of the breast and prostate, in the attempt to discover and evaluate changes that will aid in the detection and treatment of cancer. These particular studies hold out the hope of finding a clue to the long-awaited blood test for cancer.

In the field of chemotherapy, the use of chemical agents against cancer, Institute research workers have already had a number of striking successes.

Progress Against Leukaemia

The Report tells the story of 6-Mercaptopurine, the anti-metabolite developed by the Institute and Wellcome Research Laboratories in 1954. Following such compounds as the anti-bacterial sulfonamides, 6 M P acts by interfering with the metabolic function of one or other of the cell's enzymes.



Louis Pasteur, 1822-1895.

This agent has proved valuable in the treatment of children with acute leukaemia in bringing about temporary remissions. It is used today in rotation with other agents to delay as long as possible the development of resistance to the drugs by the leukaemic cells.

Finally, the Report tells of work in progress. The problem of drug resistance, one of the most heart-breaking in chemotherapy, is high on the list of projects.

Research workers at the Institute are currently making studies of the ways in which cancer cells become drug-resistant, searching for compounds that will be effective against cancers that have become resistant to the chemotherapeutic agents now available.

Another major study compares the enzyme activities of normal white blood cells with white blood cells of patients with various types of leukaemia. Preliminary indications are that 6 M P-sensitive leukaemic cells share a common point of metabolic difference, which exposes them to some selective injury by this drug and, perhaps, by others yet to come.

The Ultimate Cause

“It now seems clear”, concludes the Report, “that cancer, regardless of its initiating ‘causes’ — whether viruses, radiation, chemical carcinogens, or other factors yet unknown — is ultimately the result of a change in the genetic material of the cell.

“Any change in the cellular blueprint, it is now known, brings about a change in cellular function, which means simply a change in one or more of the cell's enzymes. Many data have been accumulated that support this concept, and now investigators in the life sciences have set themselves to accumulating the fascinating details of how this is all accomplished within the microcosm of the cell.

“As more and more becomes known of these intimate details, greater attention will be focussed upon the enzymes, for it is these components that are actually in direct charge of the details of cellular life, including the deadly aberration known as cancer”.

"BRILLIANT STEPS FORWARD IN RESEARCH"

World Cancer Expert's View

Although it is unrealistic to hope for a single drug effective against all forms of cancer, research has taken some brilliant steps forward in the treatment of the disease by chemicals and drugs.

This is the view of Dr. David A. Karnofsky of the Sloan-Kettering Institute for Cancer Research in New York, a world authority on the chemical treatment of cancer, who visited Melbourne in March as guest of the Anti-Cancer Council and the Melbourne Medical Post-graduate Committee.

Dr. Karnofsky said that surgery and radiation were still the major forms of treatment for cancer, but that drugs were effective in controlling a few types of the disease and were used quite extensively in treating advanced cancer.

Progress Against Leukaemia

Progress was being made particularly in the treatment of leukaemia, or cancer of the blood.

Until quite recently children with acute leukaemia used to survive on average for only 4-5 months. Now, however, drugs were available which controlled the disease in more than 50% of cases for 13 months or longer, and in 10% of cases the young patients remained alive and well for 2 years or more.



Few would guess that one of these happy youngsters is under treatment for leukaemia at the Royal Children's Hospital in Melbourne. Modern treatment can give children with this blood cancer years of extra life, but more research is urgently needed to fight this tragic disease.



Dr. D. A. Karnofsky talks with Sir MacFarlane Burnet, O.M. (left), and Dr. Ian Mackay, at the Walter and Eliza Hall Institute for Medical Research.

"At present we have 50 children who have survived beyond five years and are apparently free of disease", said Dr. Karnofsky.

While it was too early to say whether total cure was yet in sight, this heartening result suggested that drugs might eventually be developed which could eliminate leukaemia completely.

Definite progress was also being made in controlling the spread of the disease and in alleviating symptoms by the use of drugs in both lung and breast cancers.

The Cell Test

"One of the major areas of interest in cancer research", added Dr. Karnofsky, "is the development of methods to detect the presence of the disease in particular organs of the body. We try to pick up early cancers so that the most effective treatment can be given".

One of the most important steps forward in cancer detection was the cell examination or 'smear test' for cancer of the uterus, or womb. By means of this test it was possible to discover a beginning cancer long before any symptoms would appear.

Found at this earliest stage, the disease was almost 100% curable.

**'I'm cured
of cancer!'**

**TO
CURE MORE
GIVE MORE
TO CANCER
CAMPAIGN
1965**



Leigh Warriner

(Mr. Leigh Warriner is a fully employed
officer in Local Government Administration)