content, sand, feathers, etc. in the raw material. This is not enough. We must know what the quality of the extract is, i.e. its suspending power, and how this property is affected by region, season, and other factors. We must develop means for measuring quality and for determining if there are other valuable materials in the residues from the extractions. This is a most useful field of research, aimed at maintaining an existing industry and expanding it in a more profitable form to an even greater number.

Alginate-bearing weeds. Regarding the industrial or alginate-bearing seaweeds, we know all too little. To what extent does this class of seaweed exist along the shores of the Maritime Provinces? Before an industry could be established it would be necessary to conduct adequate and competent surveys. Work of this type cannot be the sole responsibility of the new laboratory, but in co-operation with the Nova Scotia Research Foundation and other Provincial organizations, it can assist by determining the quality and composition of the material. Little has been done in this field in Canada, but recent work throughout the world, Britain in particular, has shown that alginates are exceedingly useful industrial products.

Sodium alginate forms insoluble films or threads when it is treated with calcium salts. The materials produced are non-inflammable and have many uses. Some of the more promising are in the textile industry. By the incorporation of a calcium alginate thread, which can subsequently be removed, less spinning is necessary on the wool fibres before weaving than is done at present. In this way, woollen goods have been produced that have the fineness of silk.

With the object of intensifying Canadian scientific effort on the study and utilization of seaweeds, the National Research Council is convening a scientific conference in Halifax in September, 1948.

Apart from the scientific and technological possibilities, the project is valuable because it will bring about cooperation between all the scientific and industrial institutions in the Maritimes which are interested in the problem. It is such team-work that makes for the best scientific results.

Cancer Research

By J. LLEW. LITTLE

THE death toll from cancer is not declining. Surgery has made technical advances; X-ray and radium therapy has been improved; organized education of the lay public to seek early diagnosis has been extended; expert care in new, modern cancer clinics is becoming increasingly available and the medical schools are devoting special attention to the teaching in this subject. Nevertheless, it is still a fact that no cancer centre in Canada has yet been able to arrest the disease in more than one-third of the total cases applying for treatment.

True it is that cancers of the skin, lip, tongue and other sites where the disease is noticeable or accessible can be almost invariably cured with surgery, radium or X-rays. On the other hand, cancers of bone, lung, uterus, brain and gastro-intestinal tract are difficult to diagnose in the early stages and these account for the high death rate. Early cancer in the deeper recesses of the ody is often slow to manifest itself. Even doctors die of cancer. Few people

EDITOR'S NOTE: J. Llew. Little, M.D., a graduate of the University of Toronto, practised medicine in Japan, Hong Kong and Guelph. He was during the war Director of the Medical Intelligence Division of the Canadian Armed Forces. He holds now the position of Executive Director of the National Cancer Institute of Canada realize that the cancer mortality rate in the medical profession is only slightly less than in the population at large.

Some better method of early cancer diagnosis will have to be uncovered if the difficult and hidden cases are to reach treatment centres at a stage where cure is possible by modern methods. Treatment methods will also have to be improved to cope with the sites of internal cancer. In plain words, the public cannot expect much progress until research workers provide the answers.

Scientists have set themselves three urgent objectives. In the first place there must be a correlation of the presently known facts and an extension of enquiry into the causative process of cancer. Secondly, the search must be accelerated for a simple, inexpensive and universally applicable diagnostic test, (if any such test can actually be found for a disease of such complexity). Thirdly, a renewed effort must be undertaken to prevent and arrest the disease not only in the individual patient but also in the population at large and throughout the entire realm of biology.

Out of the Past

Cancer is an old disease. It is doubtful if it has much to do with our so-called changing civilization. It may even date back to the dawn of time. In the British Museum, a dinosaur fossil of approximately sixty million years, exhibits what has been considered to be a periosteal sarcoma. Such a tumour is recognized to-day as of undoubted malignancy.

The written records of history abound with references to lesions resembling cancer: In early Egyptian papyri, 1400 B.C.; in the notes of Galen, 50 A.D.; in Avicenna's medical memoirs, ca 1000 A.D.; in the notes of John Hunter, 1780 A.D., and in the writings of many others, endless thought was expended in an attempt to understand the rationale of cancer. Cancer theories throughout the years have been as varied as the types of tumours. It was not until the introduction of the experimental method in the latter part of the nineteenth century that cancer research began to progress. To-day, all the older theories are being re-scrutinized, while at the same time each new, promising lead is being systematically investigated and applied either on animals or man.

Into the Present

Nothing less than a mobilization of men from all the sciences will suffice to penetrate the mysteries of growth and cell-reproduction. Each group will bring their own disciplines and technics. It is a study in the origins of life—in fact it is almost a quest in theology. The life of the cancer cell like the life of any cell is a divine mystery. It craves understanding. To the scientist, cancer is more than a disease—it is a manifestation of abnormal life processes. These cells are more vigorous than the normal and yet in the profligate economy of nature their purpose remains unknown.

The Contribution of Optics

For centuries, cancer theorists were compelled to study tumour masses by watching the growth progress week after week; sectioning the growths to see the internal arrangement and vainly trying to see into the structure aided only by their reasoning and what they could see with the naked eye. In spite of these limitations a great deal of practical knowledge was gleaned. The surgeons at least learned to respect the "non-healing ulcer" and coined for their students the pithy caution "noli me tangere."

With the advent of the compound microscope the cell as the unit of living tissue was universally accepted in scientific circles. Organs and tumours were classified into special cell types and the role of the supporting matrix or stroma with its nutrient circulation was readily understood.

It was noted that the so-called "benign growths" had the capacity of slow enlargement, compressing the cells in the neighboring tissues into a thin capsule through which the tumour cells made no attempt to escape. The cells in these "benign" growths retained a close resemblance in size and shape to those of the organ from which they originated but they were more profuse and performed no useful function.

In contrast, the "malignant growths" were not content with pushing the neighbouring tissues ahead of them; rather, they infiltrated into the adjacent structures, destroying the tissues in their widening advance. These "malignant" cells showed less resemblance to type than the "benign" cells in that they were significantly varied in size, shape and staining qualities. They were vigorous dividers, refusing to conform to accepted patterns—reproductive perverts which throve as parasites on the neighboring cell community.

It was a period of considerable achivement as the histologists identified the cell morphology of organ after organ. The microscope which could magnify a cell by 1000 diameters was wonderful but they soon found that it was not quite wonderful enough. The limitations of their vision into nature tantalized the microscopists. Hope was frequently expressed that, if only greater magnification were possible, the mystery of the cell might be solved.

Further Contributions of Physics

A further spurt in cancer research coincided with the invention of the phase and electron microscopes. With these powerful, precision instruments older mysteries were replaced with new. The phase instrument permitted study of intra-cellular, unstained preparations magnified to 5000 diameters while the electron microscope permitted minute particles to be viewed in 200,000 magnification. Nor have the physicists been content with this triumph. Experiments were begun to devise an instrument, utilizing atomic particles for the energy for illumination and which it was hoped would produce up to 1,000,000 diameters of magnification. Seeing these minute structures, however, will never be quite enough. There will always remain the necessity for man's mind and logic to interpret and correlate the rationale of what he sees.

Expanded vision added new complexity. The structure of the new cell, under the new magnification, revealed a further maze of minute organization. Cell chromosomes which had formerly appeared to be simple rods now stood forth as giant coils or wavy strands. Genes took on a new spore-like reality. Under the phase microscope the cell appeared to be a seething microcosm. The old concept of a membrane-like cell wall containing a cytoplasmic jel was confronted with a new theory of particulate life controlled in a mosaic of monomolecular films. Cell morphology had again reached a plateau demanding a pause while biophysics and biochemistry moved forward to reveal the function of the new particles coming into man's ken.

The Inner Life of the Cell

Not too much was known about the behaviour of the life process within the cell unit. The time for investigation of the inter-related function of growth, nourishment and reproduction as part of the individual cell unit was a pressing necessity. Biochemistry supplied the Warburg apparatus to trace the oxidative mechanism associated with glucose in vital tissues. Biophysics supplied radioactive isotopes or "tracer elements" to track the course of essential constituents from ingestion to their final resting place in the tissue cells. Photography supplied more sensitive emulsions capable of picking up the emissions of the radioactive tracers without blurring from irresponsible rays. While much of this investigation has been done on normal cell tissues, other workers have been applying their genius directly to the cancer cell.

The Contribution of Genetics

In human genetics cancer inheritance is certainly not a dominant factor. Human mating is entirely uncontrolled.

Inbreeding is not condoned. Where restricted inbreeding occurred in certain aristocracies or among island populations no significant conclusions about cancer inheritance have been drawn.

Mice are different. Their breeding can be controlled. Inbred animals, with twenty or more brother-sister matings, have shown a tendency for tumours of particular types to recur with remarkable constancy. Recurrent tumours in these mice have been largely confined to the breast, lung and blood. The last mentioned, is a cancer-like multiplication of the white blood cells.

It was a long time before investigators realized that these apparently inherited breast tumours in mice were by no means the results of breeding alone. Litters of high-cancer-strain mice all developed tumours if they had been reared in the same cage and suckled hy their mother. This suggested inberitance, contagion or some X factor in the maternal milk. Similarly it was noted that if a high-cancer-strain litter were suckled by a low-cancer-strain mother from birth that few if any tumours developed. This seemed to incriminate a factor in the milk of the high-cancer-strain mother. A reverse experiment was then carried out. Low-cancer-strain mice were suckled by high-cancer-strain mothers and many tumours appeared. A further interesting point was noted, i.e. that tumours did not appear until the mice had matured. In this way it was learned that sex hormones were vital to the causative process. Two further tests were carried out. Male mice, which only rarely develop breast tumour, if similarly nursed by high-cancer-strain mothers and given sex hormones would develop breast tumours almost invariably. Female mice of high-cancer strain nursed by mothers of the same strain would not develop breast tumours if they were castrated before maturity.

It was thus established that mouse mammary cancer was associated with a virus factor transmitted in the milk of the mother and that sex hormones activated the appearance of the tumours in these virus-infected young. In lung tumours and leucemia the genetic concept prevails until an extrinsic factor can be identified.

Chemical Contributions in Cancer Research

For the past thirty years it has been known that tar and its chemically related compounds played an undetermined role in the production of certain types of cancer. An attempt was made to isolate the essential component or carcinogen in tar. A vast number of substances were produced—over three hundred—all with varying degrees of carcinogenicity. Some of these hydrocarbons were found in normal body fluids such as bile acids, steroids and cholesterols. The sex hormones were found to be related and synthetic hormones were developed. These hormones, female and male, had significant growth effects on those tissues regulated by the sex rhythm, such as the breast, uterus and prostate.

The biochemists are paying special attention to the possibility of carcinogenic stimuli arising out of the dietary intake. Degenerations in animal tissues after their functional activity has been completed, are also being investigated for carcinogenic activity. This is an immense field of investigation and much time, effort and money will have to be spent before the search has yielded its ultimate in results.

Botany and Virology

Crown gall in plants is closely related to the cancer process in animals. A bacterium, Phytomonas tumefaciens, has the capacity of setting up a malignant reaction in plants. The reacting plant cells invade and metastasize to other sites in the plant. Although the phytomonad bacterium is necessary to start a gall in the original, curiously, the tissues from secondary galls where no bacteria are present, will produce a further gall if transplanted into healthy plants.

It is as if some further factor arose in the secondary galls which completed and maintained the permanently malignant process. The National Cancer Institute of Canada is planning to support further studies in this field through a project at present under consideration.

Bacteria, in general, have not been found to be incriminated in the causation of cancer. Viruses, however, are definitely in the picture. In addition to the previously mentioned virus associated with the milk factor in mammary cancer of mice, there is the better-known Rous virus of sarcoma in fowls and the Shope virus of papilloma in rabbits and the virus identified with kidney adenocarcinoma of frogs. The electron microscope and the isotopic tracers will play a larger part in the newer investigation of viruses.

The Role of Injury

The old idea that cancer was caused by an injury, a blow or a bruise has, to all practical intents and purposes, remained unproven. To-day such a case would be hailed more as a coincidence. Normal rats which have been rotated and spun in uneven cages suffering trauma do not develop cancer in later life any more frequently than normal, control rats. A cancerous rat, on the other hand, similarly traumatized will develop metastases in many portions of the body.

The cancers which appeared on the bodies of many of the pioneers in radiology is ample evidence of the carcinogenic activity of unshielded X-rays. Proper precautions for the protection of workers who are handling the by-products of atomic fission is common knowledge and needs no further elaboration. It is perhaps less well known that prolonged, repeated dosage with ultra violet rays or sunlight will also induce a neoplastic reaction. The underlying basis for this change is not clearly understood. It is recognized that germinal cells suffer a true mutation under radioactive exposure, but there is no explanation of the carcinogenic change in non-germinal tissues like skin and mucus membrane when similarly exposed.

Cancer Cells Can Be Cultured Outside the Body

By a process known as tissue culture, cells can be grown in a test-tube containing oxygenated nutrient fluid. The body itself is not a "sine qua non" for the successful growth of these tissues. After growing normal mouse fibroblasts in a nutrient fluid, to which a carcinogenic chemical is added, for a period of about six days, the fibroblasts become cancerous. They can now be implanted into a mouse and a true cancer will develop. Further transplants of this cancer will also remain malignant. A permanent change has taken place in the cells. It is also interesting to note that at no time could any sudden change-over be observed as between normalcy and malignancy during the period of tissue culture.

The present stress in tissue culture investigation is directed toward the preparation of a nutrient culture fluid which will support the growth of cells but be chemically pure and free from biological products such as blood serum or other body proteins. Such a synthetic fluid would be a significant advance. New experimental elements could be added at will and in exact measurable quantities and thus the metabolism of tissue could be studied under constant control.

In recent years cancer cells have been cultured in the anterior chamber of the eye of a guinea pig. Many of the implants have regressed but many have also successfully grown. This method of cancer culture may prove to be a valuable tool in the diagnosis of rare tumours providing a biological filter for malignant cell differentiation.

The culture of mouse mammary cancer in the yolk sacs of fertilized eggs has been successfully used in many laboratories. Cancer cell mince can be transferred repeatedly from egg to egg without altering the malignancy of the original tumour. Multiple transfer of the tumour appears to step up its toxicity and the resulting early death of the embryo is associated with a marked anemia. This parallels cancer in the human patient where cachexia and anemia herald the termination of the malignant state.

Cancer and Diet

No article of diet has yet been proven to serve as a direct factor in the causation of cancer. The disease occurs in both flesh-eating and herbivorous animals and may also occur in fish, fowls and plants. In spite of the varied diets of these biological species it may yet be found that some article of diet may be indirectly involved in a chain reaction process.

It has been demonstrated that cancer growth can be inhibited by underfeeding but the host also suffers in the resulting malnutrition. No specific vitamin, enzyme or mineral excess or deficiency has as yet been proven to be a direct agent in cancer induction, but here too, an indirect factor may be shown to exist in future experiments.

Cancer Research Organization

No attempt has been made in this resume to correlate the general picture of cancer research in Canada. The subject ramifies throughout many sciences and hundreds of workers are involved. The National Cancer Institute of Canada and the Foundations, Institutes and Cancer Commissions in the provinces spend almost a quarter of a million dollars annually in the Universities where research personnel and equipment are available. These funds are supplied by the public through bequests, provincial governmental grants and the annual appeals of the Canadian Cancer Society. The public has wisely taken the attitude that this important work must be maintained as a long term project. Planning is being carried out not for a year at a time but for five year periods. Animals are bred, studied, re-bred and inoculated for many months before it can be proven that the factors being investigated are relevant or to be discarded. Men being recruited into cancer research cannot be retained in this exacting work without some assurance of more than year to year employment on catch-as-catch-can budgets.

While the ultimate goal may not be as far off as some persons think, nevertheless it would be foolish for anyone to predict a time when cancer may be prevented or quickly arrested. Research always precedes design and tooling-up comes before production. One thing is certain, i.e. that cancer research has vastly widened our understanding of the processes of life and growth. Each new morsel of evidence has whetted the appetite for more experiment. After all, the lives of fifteen thousand Canadians a year are at stake.

Conclusion

A cancer research worker may be likened to a man who has been requested to turn on the light in an unfamiliar house in the dead of night. He has been told that the switch in the basement is readily recognizable because it has been daubed with fluorescent paint. He enters and gropes his way to the basement. Not one, but many, points of light glimmer in the darkness for glow-worms have settled on the walls. His task is to systematically eliminate each point of light until he finds the switch. No will-o'-the wisp can be neglected. At the point of discouragement his fingers find a button and . . .