CANCER. WHERE WE STAND

BY THE SAME AUTHOR

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CANCER. WHERE WE STAND

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With a Foreword by
The Right Hon. LORD HORDER, G.C.V.O., M.D., F.R.C.P.

Geoffrey Cumberlege

OXFORD UNIVERSITY PRESS

LONDON NEW YORK TORONTO

1950

Oxford University Press, Amen House, London, E.C.4

GLASGOW NEW YORK TORONTO MELBOURNE WELLINGTON

BOMBAY CALCUTTA MADRAS CAPE TOWN

Geoffrey Cumberlege, Publisher to the University

PRINTED IN GREAT BRITAIN BY HEADLEY BROTHERS
109 KINGSWAY, LONDON, W.C.2; AND ASHFORD, KENT

IN MEMORY

of

HECTOR A. COLWELL

M.B., M.R.C.S., L.R.C.P., D.P.H.

FOREWORD

By

THE RIGHT HONOURABLE LORD HORDER

G.C.V.O., M.D., F.R.C.P.

In accepting Professor Russ's invitation to write a short Foreword to his book, two considerations were implicit: Was the subject one which could be presented to lay readers, and was Professor Russ a man who could do this? In my own mind the answer to both questions was in the affirmative.

I have always held that in projecting a campaign against cancer, the help of the public should be sought and its efforts fused with the efforts of the doctors and the scientists. To secure intelligent help from any person or group, some knowledge of the thing they were 'up against' is essential. A policy of reticence in respect of a disease so widespread and so lethal as cancer has always seemed to me very foolish. Statesmen who adopt such measures when the body politic is in danger, whether from the enemy without or within the gates, are, and rightly, severely censured by the thinking citizen. So should we be censured if we allow a false delicacy to screen us from telling the public what is the real position in regard to this particular menace to its life and happiness, and from pointing out how it can help to achieve victory.

But the telling requires knowledge of the enemy and of the citizen. And it requires something more—the ability to make things clear without sacrificing verisimilitude; facts must not be distorted in order to 'write down' to the reader. Professor Russ has this gift. His approach to the subject is largely from the side of the physicist, but he is able to present the viewpoint of the biologist, the chemist and the clinician.

I regard this presentation of the subject of cancer as one of the clearest and truest that I have yet read. I think it will go far to enlist the help of the public in our ceaseless endeavours, by laboratory and clinical research, to reach a solution of this still baffling problem.

HORDER.

October 1949.
London, W.1.

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PREFACE

It has often been said that it is an unwise thing to tell people much about cancer, on the grounds that it would enhance their fear of the disease. But opinion changes with the years and it is an encouraging sign that people are much more ready than they were to be told unwelcome news, so that they may know how to meet it. This was exemplified to the full during the War, even in the darkest days.

It seemed a useful thing to present some facts about cancer down the years, to make an attempt at describing some aspects of the disease, to let the reader know what people at grips with this subject are doing, and to submit that the cancer problem, as it is often called, should not be looked upon as insoluble.

For centuries the only accredited method of treating cancer was surgical. A presentation of the gradual evolution of surgical practice lies far beyond the scope of this book or the competence of the author; but the introduction of chloroform as a general anaesthetic marked an epoch in surgery and a brief chapter has been attempted in tracing the trends of surgery since then in its application to the treatment of malignant disease.

For several purposes I have made use of historical matter prepared by my late friend Hector Colwell, whose death occurred in 1946; in some instances these notes had been written by him in preparation for a book of a rather different character which we had planned together, but unhappily this plan could not be carried out. He left me his writings and I have not hesitated to dip into them knowing that he would have allowed nothing in his pages which could not be verified. In Chapter XIII I have used his historical sketch of cancer from very early years up to the nineteenth century. If there be readers who have no taste for any sort of record of the past, their course is simple, but his writing is a piece of scholarly work which few people could undertake, and it seemed to me a great privilege to be able to make use of it in this way.

It is still true to-day that many people have such a dread of the disease that they go all too late for medical advice ; there is not only the testimony of the general practitioner to this effect, but over and over again in reports of treatment coming from the chief centres of radiotherapy does one find the lament that patients coming for treatment are found in an advanced stage of the disease ; this makes treatment very much more difficult.

If the reader should find the 'delay theme' that runs throughout the book a trifle wearisome, it can only be pleaded in extenuation that it is the chief reason for the book being written.

My thanks are due to Lady Schuster for the loan of two early radiographs and to Dr Brailsford for two modern ones, to Dr P. R. Peacock for the beautiful

microphotographs on Plate I, to Dr Merewether and Dr Currie for supplying me with new sources of information about occupational cancer, to Dr Percy Stocks and Dr Logan for their help with statistical data, and to my son John for a critical reading of the MS.

S.R.

London, *October 1949*.

CHAPTER I

THE NATURE OF CANCER AND THEORIES OF ITS ORIGIN

Cancer is a disease which extends throughout the animal kingdom and it has been authoritatively stated that there is no kind of cancer which is peculiar to man. The terms in common medical use in connexion with this disease may be given a place here. An alternative name is 'malignant disease' and the site of the disease is often referred to as a malignant growth; in those cases where the growth appears as an obvious swelling, the term malignant tumour is often used; the word tumour simply means a lump. The word 'malignant', which retains its everyday significance, namely malign or evil as opposed to good or beneficent, is of outstanding importance, for there do occur in the body what are known as benign tumours, and the term benign is no less significant, for though it might be going too far to say that benign tumours are harmless, yet the important thing is that they are not malignant.

Malignant disease may appear in practically any organ of the body; in some it is common, in others rare, but there is a very valuable rule about its first appearance in the body; it is that cancer arises from among the very cells[1] which compose the organ. If, for instance,

[1] 'Cells' *go to form* 'tissues' *which constitute the* 'organs' *of the body.*

malignant disease starts in the breast, then it starts from some typical cells of the breast; if it starts in the tongue, then from some typical cells of the tongue and so on. Some tumours consist of two or more kinds of cancer tissue, but they are rare. It is exactly as though some malignant change or process begins in some normal part of the body and this change continues from quite small beginnings until perhaps the whole organ becomes involved. But there is more malignancy in cancer than this, for if such a cancerous process is allowed to continue, it breaks its bounds and spreads into other parts of the body; this in fact, is the chief justification for the use of the term malignant. Here again it is highly significant that if a tumour arising say in the breast, continues to grow unchecked, it not only spreads by a process called permeation into the surrounding tissues, but by two other quite distinct processes. It can spread by means of the blood stream and thus be carried to quite distant parts of the body, or it can spread by means of what is called the lymphatic system. Arteries, veins and arterioles convey and distribute blood to every part of the body; lymph channels operating by way of an elaborate arrangement of lymph glands convey lymph, which is a colourless liquid, to practically every part of the body and it will be realized that if cancer cells once get into either of these systems and continue to thrive in them, there comes a time when they may be numerous enough to establish themselves in some organ where they can continue to multiply; thus they may constitute as grave or even graver danger to the patient than was the primary growth from which they started.

When malignant disease starts in the body it is referred to as the primary growth; when it has extended by way of the processes just mentioned, it is often referred to as the secondary growth, secondaries or secondary deposit or metastasis.

The reader will understand that the treatment of a primary growth localized in one part of the body presents a problem to the surgeon or radiotherapist which at any rate has definitely prescribed limits, even though there may be great anatomical or other difficulties to overcome in the course of any plan of action; but it is quite otherwise when there has been an extension of such a primary growth, not only into neighbouring structures of the body but into relatively distant parts. This is the main problem of malignant disease which makes it one of the most baffling diseases. We may well ask, how can surgery or the application of X-rays or Radium in such a case be expected to cope with the situation? While it is true that the *probable* paths of extension are, thanks largely to the pathologist, in many cases fairly well known, yet in any *actual* case they are often matters of conjecture. It is largely for this reason that those who have any long acquaintance with the disease see the one and only hope for dealing with *disseminated* cancer in the discovery of systemic methods. This means either the introduction into the body of some chemical substance or the initiation and establishment within the body of some process of resistance or immunization which will act specifically upon the malignant elements wherever they may exist in the body.

Malignant growths may, as mentioned, begin in almost any part of the body and reference is often made to them in terms which compare their states of malignancy; some will be termed very malignant, others as having not such malignant aspects. Malignant disease is often referred to as a disease of middle or old age; fortunately it is rare in young people, but the significance of the terms middle and old age is one which varies with the centuries. We are not now inclined to call our friends of forty middle aged or those of sixty as enjoying old age. It may be seen from the annual register of cancer deaths published in the Registrar-General's *Statistical Review* (1934), Table LXV, that the average age at death from cancer in the male was 64 and in the female 63.

It is generally found in medical writings on the subject that the word 'cure' is qualified in some way and the terms '5 years cure' or '10 years cure' mean that over these periods since treatment, the patient is apparently free of the disease. Such caution is only too necessary for, unfortunately, malignant disease may reappear or recur after long periods of time. For this reason it is unusual to speak or write of a 'cure' having occurred, but there is at least the consolation that the longer a recurrence is delayed the less likely is it to occur.

So much for the general nature of cancer. It is a formidable disease, like no other, a law unto itself in its general lawlessness, for cancer cells do not obey most of the laws of the organism in which they may thrive. By the time one reaches the adult stage of life, the general framework of the body has been formed, the bones do not continue to grow and practically every organ and structure of the body has reached that marvel of equilibrium, the normally functioning human being. It is quite true that damaged tissue is from time to time repaired and that the vital blood stream is continuously replenished from the bone marrow ; but by and large it is true to say that growth in the generally accepted sense of the word has come to an end when adult life is reached ; the hair and nails are not considered organs of the body. Yet, in the midst of this equilibrium, or ordered restraint, there is in malignant conditions, a complete disregard of this restraint by the cancer cells, for they continue to grow and divide and thus increase in numbers indefinitely. The rate at which they do so depends upon the particular variety of cancer they represent, also upon the situation in the body, the age of the patient and so on. In general we may say that the aim of the surgeon when he operates is to remove all cancer cells from the body ; on the other hand, among those who use X-rays or Radium, the aim is quite different. They hope, by the damage which these rays can do, to stop the cancer cells growing and dividing and eventually to cause their death ; but this is a gradual and not a sudden process. We may make a brief reference to the two terms carcinoma and sarcoma. This is the simplest and most elementary classification of malignant growths ; they are either one or the other according to the kind of tissue from which they arise ; tumours arising in the skin or the tongue, the stomach or intestines, for example, are called carcinomata, whereas those originating in muscle or bone or similar tissue are called sarcomata. But there are some organs of the body in which either a carcinoma or a sarcoma may arise. This is because the cells comprising the particular organ are not all of a kind. This simple classification is, however, quite inadequate for the purpose of the pathologist who is not only expected to be able to give an opinion upon what sort of tumour it may be, and from what organ of the body it arose, but to express an opinion upon its degree of malignancy and its likely response to radiotherapy, for example. For such decision a more detailed classification of tumours has gradually been evolved.

It is generally agreed that cancer is neither infectious nor contagious. Much has been written on the subject of predisposition to cancer and whether the disease is in any sense hereditary and reference will be made to these matters later.

A great deal of discussion has from time to time centred upon what are called 'cancer houses' ; this term conveys the idea that people were more likely to contract cancer in certain houses than in others. This question has been quite seriously considered and the conclusion has been drawn that there is nothing to justify the assertion that a certain type or build of house is in any way a 'cancer house'. It is quite true that more people have died of cancer in some houses than in others, but of what disease could not the same proposition be posed?

The cause of cancer, generally speaking, is unknown; there has to be a little qualification in the statement because it may be that in some cases we do know the cause of the disease and one of the best cases that could be quoted is that of benzpyrene which produces cancer among some of the mule-spinners in the cotton industry. These cases are often grouped together under what are called 'industrial cancer' and a brief chapter will be found on this subject. But mention is made of them here because although we do not know *the* cause of cancer in the usual sense of the term, we know of certain causative agents which when applied to man do in a percentage of cases result in the development of cancer.

However this may be, it is of great practical importance to know something about the *apparent* causes of cancer, for by adopting safeguards their potential action can be eliminated and thus at any rate we may do something to stop the beginnings of some varieties of cancer. That is well worth doing, though it must be admitted that in the great majority of patients suffering from malignant disease, the cause of the disease is unknown.

There is an impressive list of theories about the cause of cancer coming down the years to us. They have all had to stand a strong amount of criticism and have in no case been accepted by general medical consent. Nevertheless they are of great interest, for they show the extent to which people have bent their minds over a problem not yet solved, and all of such theories have their value in the speculation they arouse; in a spirit of wonder new ground of observation and experiment is worked over with valuable results. In his exhaustive work, *Occupational Tumours and Allied Diseases,* W. C. Hueper tabulates no less than eight theories about the cause of cancer, giving in each case a brief exposition of what was in the mind of the theorist. Some of them may be mentioned briefly here. The names of two pathologists, Cohnheim and Ribbert, are associated with the view that cancer starts among embryonic and other cells which have become, as it were, detached from their usual environmental controls and by virtue of this have unusual powers of proliferation. According to this theory cancer is potentially existent before birth. The next pathologist to postulate a theory was Virchow who looked to sources of chronic irritation as providing the necessary cause of cancer; the severest objection raised to this view is that it is only in a small fraction of cases subject to chronic irritation that cancer results. For a successful theory the exceptions to it must be exceptional and not the rule. The next theory arose from the consideration that the disease is more likely to occur in the old than in the young and this accounts for the name 'Senescence' given to the theory of Feyrter. The idea underlying this theory is that as the tissues of the body get older there develop among them certain degenerate features which gradually take on malignant characters and these changes are supposed to arise within the cells, independently of any outside agents.

On quite different lines are those theories advanced by the chemists, several of whom have suggested that foreign chemical elements, by virtue of their power of inhibiting or stimulating the growth and division of cells, can thereby upset the general rhythm of the tissues and induce malignancy.

We may turn finally to the virus theory of cancer. In the words of C. H. Andrewes: 'This theory postulates the existence of a virus or viruses, widely distributed in the animal kingdom ; that they are latent infections but are lit up by some stimulus such as the application of a carcinogenic (i.e. cancer producing) hydrocarbon.' The word virus is not used here with the dictionary meaning of 'foul, hurtful matter', but of a very small entity, something smaller than a microbe yet bigger than a moderate-sized molecule like that of haemoglobin, for instance. A virus was first suggested in cancer work as a result of an important discovery by Peyton Rous who found that he could transmit a tumour of the fowl by injection of a fluid suspension of the tumour cells after it had been passed through a filter.

This means that although anything as big as a tumour cell or microbe would be held back by the filter, the fluid that came through, perfectly clear to look at, contained something that could cause the appearance of a tumour in the fowl that was injected with it.

This was the starting point of a very extensive field of experimental work in many laboratories which continues up to the present time and will be referred to in a later chapter. The virus theory of cancer causation has many adherents who, however, are by no means unaware of the objections which can be raised to the view that *all* forms of cancer arise as a result of the action, direct or indirect, of a virus (or viruses). Very few people do hold this view, for cancer is a protean disease and it may be that different manifestations of it arise from different causes. Nevertheless it constitutes a great advance in knowledge when a causative agent can be associated with the onset or development of any variety of cancer, for therein lies at least a hope of its prevention.

It is noteworthy, though not surprising, that most of the theories of causation relating to cancer have been put forward by pathologists, but surgeons have contributed their quota. Butlin looked upon the cancer cell as a degenerate unicellular organism produced by reversion of the normal cells of the body to a primitive cell type ; one indeed not subject to the control of the body. Bland-Sutton expressed the view that the cause was a micro-parasite which stimulated the normal epithelial cells to multiply and produce cancer.

Of later years, the most important and sustained argument from the surgeons is probably that of Sampson Handley who, in 1932, published the *Genesis of Cancer*. The theory advocated is that the cause of cancer is lymph stasis, i.e. an arrest of the flow of lymph. The reader may be reminded that normally the tissues of the body are all bathed and indeed nourished by lymph. This fluid is conveyed and distributed throughout the body by means of the lymphatic system, which is just as elaborate and intricate a network as the arterial and venous systems. The lymphatics, i.e. the vessels containing the lymph, are of a rather delicate structure and comparatively easily damaged. Handley has shown that in some of the conditions before the onset of cancer, the pre-cancerous stage, there is a local blocking of the lymphatics and a condition of lymph stasis is set up. The old saying that 'nature abhors a vacuum' is rather difficult to defend since we know that the natural world about us consists of a nearly perfect vacuum with matter concentrated here and there, but nature abhors stasis in any circulatory system that she sets going ; if it stops, there is trouble ahead indeed. In the case of lymph stasis, Handley has shown some of the consequences of an arrest in the local circulation of this vital fluid, and has endeavoured to link them up with the present biochemical views about the various ways in which the life of the cell is maintained in the body. Handley's views are entitled to great respect in view of his contributions to the study of the ways by which cancer of the breast may extend from a small primary focus.

Lockhart-Mummery, in *The Origin of Cancer* (1934), put forward the idea concerning the origin of this disease that it is the result of a genetic change in the normal growing somatic cells[1] of the body. He does not discuss the cause of any such genetic change but comments on the fact that the previous attempt by Boveri in 1914 to construct a genetic theory of cancer was really a chromosome[2] transmutation theory. On this view an increase in the number of chromosomes should occur in malignant cells, but observation does not support the view. It is known that X-rays can occasionally produce genetic changes and that X-rays can, by repeated action over a long time, set up a condition in the tissues which leads to cancer, but whether there is any causative relationship between these two biological actions cannot yet be answered.

Few pathologists did more in their time for the advance of radiology in its bearing upon cancer treatment than Dr J. C. Mottram. He was the first to show how the susceptibility of cells to radiation varies with their state of activity; in particular that when a cell is in the process of active division it is most vulnerable.

[1] Somatic cells are those pertaining to the general framework of the body.

[2] A complex structure within the nuclei of cells; genes occur as distinct biological entities in the chromosomes.

He did crucial experiments on the production of tumours in rodents by means of synthetic tars and this led him eventually to formulate certain views about the nature and origin of tumours which he elaborated in *The Problem of Tumours* (1942). The views may be given a place in this chapter for they constitute a working theory of the origin of cancer and are based upon experimental work. This work was carried out upon small organisms known as Paramoecia; they are visible to the naked eye, live in fresh water and are easily propagated. Mottram exposed these organisms to several agents which are known to be causative (direct or indirect) of cancer, *vide* Chapter V. He asserts rather significantly that though these agents vary so widely among themselves, they yet have this cancer-producing capacity in common and herein may lie the key to the problem of tumour formation.

As a result of the elaborate studies which he undertook, Mottram was more and more convinced that the essential feature of these cancer-producing agents lay in their action upon the cytoplasm of the cell rather than upon its nucleus. He drew attention to the fact that many of the effects of X-rays and Radium upon living cells are seen in the cytoplasm (this is the part of the cell which surrounds the nucleus) long before any damaging effect can be seen upon the nuclear components. He showed experimentally that abnormalities, which could be produced by the agents in question, appeared to breed true, that is to say, they produced abnormal cells which in turn did the same. Here was a remarkable analogy with the cancer cell which is generally regarded by pathologists as an abnormal cell of the body.

The cytoplasmic theory of the origin of cancer is one that deserves not only consideration but development along the lines advocated by its author.

CHAPTER II

THE PREVALENCE OF CANCER AND THE PUBLIC ATTITUDE TOWARDS IT

Cancer is a disease which is widely discussed not only in medical circles. Interest is widespread because cancer is common; most of us know of relative or friend who has suffered from it, and cancer has, until recently, had the reputation of inevitably causing death to those who develop it. Moreover, the imagination is stimulated by the use in the treatment of the disease by Radium and X-rays, the full nature of which are not yet revealed to the scientific mind.

The prevalence of cancer in England and Wales is indicated by the data in Table I.

TABLE I

Year	*Population in millions*	*Deaths from cancer*	*Cancer deaths per million of population*
1937	41·0	64,943	1,583
1938	41·2	66,584	1,616
1939[1]	41·2	67,133	1,628
1940	39·9	68,740	1,723
1941[1]	38·8	68,974	1,780
1942	38·2	70,139	1,834
1943	37·8	71,814	1,899
1944	37·7	71,688	1,897
1945	38·6	73,753	1,933
1946	40·0	75,407	1,885
1947	42·2	77,649	1,840

[1] Excluding non-civilian males on and after 3 September 1939 and females on and after 1 June 1941.

The data are taken from the Registrar-General's *Statistical Review of England and Wales* for the year 1946, Tables, Part I, Medical.

When we try to compare these figures with those of other nations, difficulties occur because we do not know whether the methods of registration and classification of the deaths from cancer are identical. For this reason comparison is here restricted to the data to be derived from the Mortality Statistics of the Bureau of the Census, U.S.A., because their methods most closely resemble our own.[1]

TABLE II

Year	*Population in millions*	*Deaths from cancer*	*Deaths from cancer per million*
1936	128	142,000	1,110
1937	129	144,000	1,100
1938	130	149,000	1,140
1939	131	153,000	1,190
1940	132	158.000	1,200
1941	133	159,000	1,200
1942	133	163,000	1,230
1943	134	166,000	1,240
1944	132	171,000	1,320

The data in Table II give the number of deaths from cancer in the U.S.A. over a period of years, together with the population figures.

[1] Those who may wish to examine the figures for France and Sweden may be referred to the official *Publications Statistique du Mouvement de la Population*—Nouvelle Serie Tome XIX, and *Statistisk Årsbok fur Sverige utgiven av Statistiska Centralbryån.*

The same upward trend in the deaths from cancer per million of the population occurs as in the British figures.

The importance of the exclusion given in footnote to Table I is that since during the late war the average age of the civilian population was raised owing to the absence on war service of many young adults, the cancer death rates from 1940 to 1945 are a *little* higher than they would otherwise have been, since old people get cancer much more than young people. But, in spite of this consideration, the death rate seems to have been rising.

It is not an easy matter to tell whether there is a real increase in the incidence of cancer among the population, because an apparent increase could occur if a higher level of diagnosis were attained. Then again, the Returns of the Registrar-General are derived from the data in death certificates and it has been suggested that there used to be some hesitation in attributing death to cancer if heart failure or an intercurrent disease could serve official purposes. If this were true it was due to the quite misplaced view in the public mind that there was some stigma associated with cancer rather like that which is linked with venereal or mental disease. The statistical position appears then to be that there is a growing death rate from cancer in spite of considerable success in its treatment, but that this increase may be more apparent than real because of a greater readiness to assign deaths to their proper causes. It has to be remembered also that our population is becoming an older one ; people live longer, so since cancer is a disease that tends to come later on in life, there is a proportionately bigger fraction among the population of those likely to contract cancer and this likelihood is borne out in fact. But the increase in the death rate does not argue any general rise in the potency of malignant disease.

When we read the information provided in the annual Returns of the Registrar-General giving the number of deaths from cancer, we may well wonder how many people there are in the country suffering from cancer at this present moment. The Registrar-General does not tell us this number, but it is of importance as providing a guide to the scope and extent of the medical services likely to be required. In England and Wales at present, deaths number about 75,000 annually, and to arrive at the number who are actually suffering from cancer, some amount of guessing has to be done. Under these circumstances, it is a good plan to get the guessing done by a statistician ; in the present instance, Dr Percy Stocks of the General Register Office has been good enough to sponsor the following:

In an article entitled 'Illness from Cancer in the United States' (1944) by H. F. Dorn, Senior Economist in the U.S. Public Health Service, the relation between the number of people ill from cancer and those dying of the disease in that country has been studied. The evaluation was made of the number of new cases of cancer diagnosed for the first time in one year and of the number under treatment at a given time; from this information a ratio can be derived which, multiplied by the number of cancer deaths per year, gives an approximation to the answer required, that is to say, the number of people suffering from cancer at any moment within the period examined. Assuming that survival with cancer in general does not differ greatly in the two countries and applying this same multiplying factor to our own present yearly total deaths, we derive the approximate figure, 150,000, as representing the total number of people under treatment for cancer at the present time and the number of new cases of cancer seen yearly comes to approximately 100,000.

When the cause of a disease is unknown, conjecture is given full scope. Among many other questions about the occurrence of cancer the following ones may be picked out for comment:

(a) Whether cancer is more frequent in town or country?

(b) Whether there is any reason to believe that general climatic conditions influence its frequency?

(c) Whether any peculiarities in diet and cooking habits have any influence upon the onset of cancer?

(d) Whether there is definite proof that heredity plays any part in its incidence?

(e) Whether the frequency of cancer is related to social environment?

Several of these questions are discussed in a publication entitled *Regional and Local Differences in Cancer Death Rates* by Dr Percy Stocks (1947).

With reference to (a) the answer can only be given by fact-finding. This has been done to some extent by an analysis of the deaths due to cancer all over the country and it has been found that for cancer of all parts of the body in 1921-6, mortality was high for all ages in some counties in Wales, in Warwickshire and in an area north of London, whereas in the counties bordering the Severn and Bristol Channel from Worcester southwards, it was low.

Considering the country as a whole (England and Wales), the relative prevalence of cancer in town and country may be seen from the data in Table III.

TABLE III

Cancer of all parts of the body—death rates 1931-5 per cent of the corresponding rates for the whole of England and Wales.

	Males			*Females*		
	Under 65	*65–*	*75–*	*Under 65*	*65–*	*75–*
London A	121	114	113	102	101	103
County Boroughs B C	112	110	99	105	103	99
Small Towns D	95	99	98	99	101	102
Rural E	81	85	96	94	97	97
England and Wales	100	100	100	100	100	100

The figures in this Table are well worth studying. If they prove, as indeed they seem to do, that cancer in the male is relatively more frequent in town than country, this is not shown among females, the rates all ranging pretty well within a few per cent of the cancer death rate for the whole of the country. Why is this? To venture an answer would be to suggest that on the whole women live a more domiciliary life than men and that the home is the centre of their life whether it be in town or country. The case is not so for men; for them life in the country is an entirely different one from that in town and as far as cancer is concerned they seem to be all the better for it.

(b) General climatic conditions will include many more factors than the sun, the wind and the rain, for man in his urbanization has not yet found the way, or rather has not yet thought it worth while, to deal with the pollution of the air produced by smoke and noxious gases which take their heavy toll, especially among those with any lung affections, quite apart from cancer. Statistics show that the frequency with which cancer occurs in various parts of the body does change with the years very appreciably, but the cause of these changes is not known.

Perhaps the most outstanding case is the increase in the frequency of cancer of the lung and it is noteworthy that this increase is much more marked in town than in rural areas. Cancer of the respiratory organs was the certified cause of much higher death rates in urban than rural areas for the years 1921-30, and for lung cancer in males there was at every age a steep downward gradient from London through large and small towns to rural areas. It may be noted that this is not the only form of cancer which appears to be influenced by atmospheric conditions, for rainfall is apparently responsible for the fluctuations in cancer of the bladder death rates ; an expert fact-finding analysis has shown that the degree of mortality from cancer of the bladder in England and Wales corresponds generally with a condition of low rainfall. Comment upon this remarkable association will be made a little later in the text.

(c) Perhaps we have not yet recognized the importance which diet may have in the onset and in the course of malignant disease. Reference to Appendix I reminds us that nearly one half of cancer deaths in 1946 were due to its occurrence in the digestive system. This includes the oesophagus (gullet), stomach, small and large intestine and the rectum. There would seem to be a prima facie case for food playing some part in the incidence of the disease ; it has, however, to be borne in mind that cancer occurs throughout mankind and there is no need for emphasis as to the very varied character of the diet upon which man thrives. If, however, we confine attention to the peoples whose diet is catholic in diversity, it is noteworthy that, arising largely in the U.S.A., there has in the last fifty years been among them a growing use of tinned or otherwise prepared food in contrast to what is called fresh food.

About forty years ago Gowland Hopkins discovered what he termed ' accessory food factors ' and he was able to show that these existed normally in rather small quantities in practically all forms of fresh food such as milk, meat, vegetables and fruit. He was able to show that these vitamins, as they are now called, are to a varying degree diminished in their value by the high temperatures reached in cooking. It is now recognized that vitamins play an important part in the maintenance of health, especially in children—their diet is often supplemented by the addition of vitamins to their food. It has been proved that certain so-called deficiency diseases are brought about by lack of vitamins in the diet and that they can be successfully treated by restoring the vitamin balance. When Dr Stocks (see above) calls attention to the high incidence of cancer of the bladder in certain parts of the country having a low rainfall, one has perhaps to get over a certain element of wonder whether there is any intrinsic connexion between so little rain and so much cancer. But there is nothing more fantastic about it than, for instance, the statement that the level of starvation in some parts of the world rises and falls with the cycle of sun-spot activity. In the latter case, one goes further in the inquiry and notes that high sun-spot activity means good weather for wheat, which means abundance of food, which in turn can turn the scale in the right direction for those near the subsistence level. Returning to the question of cancer of the bladder occurring with greater frequency where rainfall is low ; with scarcity in water supply there will almost inevitably be an increase in the mineral and organic content of the drinking water, and if scarcity is acute, make-shift unhygienic methods have to be devised. There is no single factor that stands out clearly as a cause of the disease, yet the statistics should not be set aside, for they are not disproved because of our lack of knowledge of operating causes. Rather should the data serve as the starting point of investigation.

Some years ago a trial was made to see whether patients in the Cancer Wing of the Middlesex Hospital would benefit if they were put on a more spartan diet than the generous one to which they were accustomed. The investigation was continued for a period of six months, when it was concluded that as regards the course of the disease no improvement resulted among those who had suffered this restriction in their diet.

It is a painless matter for the mouse or rat to be put on a variety of diets in order to find out whether one can influence the growth of cancer in them. There are several varieties of tumour which grow in the rat. They can be transferred from one to another by the simple operation of removing a tumour, cutting it into small pieces and inoculating it beneath the skin. In the case of a very well-known tumour, Jensen's rat sarcoma, a small piece inoculated in this way into a susceptible rat will grow to the size of a walnut in three to four weeks. Miss G. M. Scott, at the Marie Curie Hospital, has recently found that if before the inoculation of small pieces of tumour the rats are fed on a liberal diet, including an extra quantity of the complex known as Vitamin B, the inoculations do not continue to grow as readily as they do in control batches fed on a routine diet.

Such experimental tests take a very long time before results appear, but it is quite likely that elaborate study of diet would throw some light on the high incidence of cancer in the digestive tract of man.

(d) We may now turn to a question which has some degree of interest to every one of us. Is cancer hereditary? For some this question will be answered once and for all in the affirmative should it be their experience to be intimately associated with a family an undue proportion of which has died of cancer. No statistical facts whatever will shake a conviction which is based upon what appears very stark evidence. It happens that there are many cases on record where a predisposition to cancer cannot be denied, yet directly we try to get evidence satisfactory to the statistician, the evidence seems to become very attenuated. The situation, though sounding rather paradoxical, is indeed no less than this, that if you want to find proof of heredity in cancer you will find it in carefully kept case records of patients ; if you wish for statistical proof that heredity plays any recognizable part in the general run of malignant disease among the population of England and Wales, then no such proof can be found.

It is, perhaps, hardly necessary to remind the reader that in using the term heredity in connexion with cancer, we do not intend to suggest that a hereditary tendency conveys the disease, but only that structural peculiarities in the tissues or body fluids may render certain organs more prone than usual to cancer.

Examples of a strong strain of hereditary predisposition to cancer are given by Lockhart-Mummery in *The Origin of Cancer*; the following is a quotation:

Wachtel has reported a case in which a woman, her mother, two aunts, three first cousins (daughters of one of these), the maternal grandmother and great aunt, all died of cancer of the left breast.

Power records a case of a man who died of cancer of the breast, and two of his three sons also died of cancer of the breast. When we consider the rarity of cancer of the breast in males, this case is important. Machlin reports the case of a man who had sarcoma of the neck, and five of his seven children also developed sarcoma of the neck. Gardner and Frazier mention a family in which through five generations, consisting of 217 persons, 38 had tumours of the acoustic nerve. Williams has recorded a family in which three sisters died from cancer of the uterus at the ages of 32, 36 and 53; their mother died from the same condition at 45, and an aunt and the grandmother also died from cancer of the uterus. Another remarkable case is that of the S. family reported by Warthin, in which there would appear to be two separate hereditary factors, one for cancer of the alimentary canal and one for cancer of the uterus.

At the time when the first report on this S. family was made, one parent had died of intestinal cancer. Out of his six children, four had died of the same kind of cancer and one of uterine cancer; out of six grandchildren, all of them had died of uterine cancer. This reads like a terrible indictment of the heredity factor, yet it must be remembered that such a record occurs very infrequently indeed.

We may probably conclude that although there are recorded cases of families in which there has been a greater frequency of cancer than the ordinary laws of chance would allow, yet in the main they are few compared with the great numbers of families in which single and not multiple members are affected by the disease. Cancer is a common disease and few families are unassociated with it but the total expression of cancer among us cannot be attributed to hereditary factors.

(e) A valuable contribution on the incidence of cancer has been made by E. L. Kennaway in a paper entitled 'The racial and social incidence of cancer of the uterus' (*British Journal of Cancer*, September 1948). The following excerpts are made from his summary:

> The comparative incidence of cancer of the uterus in Jewish and non-Jewish women has been studied on material from London, Munich, Amsterdam, Rotterdam, Vienna, Budapest, Sweden, Palestine, New York, Chicago, Rochester and Philadelphia.
>
> All of the twenty collections of data which have been found in the literature show an incidence of uterine cancer which is greater in non-Jewish than in Jewish women. . . .

The only numerical data on the *social* incidence of cancer of the uterus appear to be those of Bavaria forty years ago, and from England and Wales after the census in 1930-2. The liability to cancer of the womb increases with descent in the social scale and, in England and Wales, this is true of both married and single women. In cancer of the breast there is no clearly-marked evidence that incidence depends at all upon social scale.

Turning to another site of cancer, the mouth and throat, it may be seen from the data in Appendix I that cancer here is more than three times as prevalent in men as it is in women; it is not unlikely that this ratio is referable to the greater hygienic care to which women as a rule conform. It has been further maintained that the frequency of cancer of the mouth increases with descent in the social scale.

It would, however, be quite wrong to try to associate cancer as a disease with any one section of the community, though it is true to say that some varieties of cancer, notably those where personal hygiene may reasonably be a causative factor, do decrease in frequency with rise in the social scale.

PUBLIC ATTITUDE TOWARDS CANCER

It will be seen how doctors of the eighteenth century advised their patients to come for advice at the first signs of the disease. It is common knowledge that this advice is still being offered, but it is now given greater emphasis because clinical results are at hand, for all to see, which prove that the earlier a patient is seen the greater the chances of successful treatment; this applies for surgical, radiological or, indeed, any bona fide form of treatment.

It might be going too far to say that this advice is generally not taken ; probably people do go to the doctor on this account more readily because they are beginning to realize the need, if there is to be treatment, that it should be early. But it is very difficult to be sure of this in view of the large numbers of patients who are still seen for the first time in a comparatively late stage of the disease.

This reticence is due to a number of quite distinct causes and it would be a mistake to assume that it is wholly due to ignorance—the reticence is not confined to any one stratum of society and it is worth while considering the matter a little further. In the first place, cancer is a disease which is nearly always insidious but painless in onset and, with the exception of cancer of the skin, little or no certain naked-eye evidence exists until the disease is established. This will account for many cases of delay in seeking advice that cannot be attributed to casualness on the part of the patient. There are, however, large numbers of people who know that something is wrong but still defer the medical visit, and in the majority of these cases there is little doubt that the dominant underlying cause of their delaying action is the fear of the disease. This group consists of several quite different categories of people ; there is the really casual group, members of which are habitually careless about their person ; another group consists of people who have an instinctive dislike of being examined medically and with fear dominantly in their minds, they try to persuade themselves that 'it's nothing to worry about'. Then there are people who look upon malignant disease as having a stigma associated with it, like venereal or mental disease or as some kind of defect of the body; and, as with a deformity, the attempt is made to conceal it and fear once more is an accessory. This feeling probably has a very deep basis and it is going to be a difficult matter to rid the mind of it, especially in countries like our own that have a growing pride in physical fitness and all that it connotes. Finally, there are those who feel they dare not disclose what they fear to other members of the family—this state of mind is largely determined by economic surroundings.

Hence we see that there is quite a number of different causes which may account for reticence on the part of cancer patients; some of the causes can be countered, others will take time. In America during the last few years, a considerable effort has been made by the American Cancer Society to make people 'cancer conscious' and their efforts to do this have often been discussed in this country. There is not an unanimous opinion that they would only do good; some have expressed quite the opposite view in fact.

Among the activities of the National Cancer Institute of the U.S.A. was the initiation of a Cancer Detection Project in 1947. The object of a Cancer Detection Project is to examine apparently healthy people for early signs of cancer in the sites in which it most often occurs. In a report dated June 1948 a survey was made as to what public benefit was being derived from a project which is an expensive undertaking and it was realized that such projects were outside the realm of practicability for the average community. For instance, the cost of discovering a single cancer case in a detection centre at the Public Health Service of Hot Springs National Park, Arkansas, is estimated at 7-8,000 dollars and there is a note of realism in the comment upon this matter:

> It is true that human life is priceless, and that discovery of a case of cancer in a curable stage is worth any amount of money and effort. But this philosophy can be applied to only one person. If you apply it to everybody you run into the difficulty that time and money are available in only finite amounts and must be allocated to all the other essential things of living.

Even when these detection centres are maintained in cities where the supplementary medical services are at hand, the cost is still very high, for in New York City the expense involved at ten of such centres was well over 6,000 dollars per cancer patient.

At the Arkansas Centre, during the first six months of its operation, 1,500 women were examined and 22 were found to have cancer. Twelve of them had early cancer of the womb.

It was stated in a Moynihan Lecture of the Royal College of Surgeons, given in London recently (1949) by Dr Frank Adair, that one of the results of the widespread publicity campaign in America was to lengthen the waiting lists at many of the hospitals to a somewhat embarrassing extent.

Exactly what are the best steps to take in order to bring the cancer patient to the clinic in the early stages of the disease have, it seems, not yet been proved.

It must not be forgotten that the onset of cancer is, as a rule, painless and there are often no symptoms to guide one. This does undoubtedly account for the fact that a lot of people, quite mindful of their health and suffering from no marked reticence in consulting their doctor, first learn that they are suffering from cancer in a late stage of development. But when the fullest allowance is made for this, it is nevertheless true that a very large number of patients go to their doctors or to hospital with such obvious signs of cancer that they must surely have known that something was seriously wrong, yet they have put off the evil day. This is a situation largely brought about by fear which is costing many lives every year, and for this reason alone it seems worth while that attempts should be made to rectify a very tragic position.

CHAPTER III

CANCER THROUGHOUT THE ANIMAL KINGDOM

In attempting even a brief account of the incidence of tumours in animals other than men, there are a few points of outstanding importance which it is necessary to bear in mind.

In the first place, cancer is essentially a disease of the later period of life. Among domestic animals the great number which are slaughtered for food are not allowed to attain anything like old age. The vast numbers submitted to expert veterinary post-mortem inspection in, for example, the American stock yards are all comparatively young ; so that in this great mass of material only occasionally have the beasts reached the age at which one might reasonably expect to find cancer. Cattle, sheep and pigs will plainly be included in this category.

Of other domestic animals, horses, dogs and cats may live to a 'good old age', but it is probably rare even at the present time for a post-mortem examination to be carried out, at any rate upon scientific lines. The amount of material available from this source is, therefore, necessarily limited.

Among wild animals, quite apart from the question of how many become old or elderly, the measures taken by Nature for the removal of the dead are remarkably prompt and efficient. It must have struck the most casual observer how rarely one sees a dead wild animal or bird, except perhaps on a road or pathway. The smaller creatures are covered up by burying beetles, which, after making their own meal, lay their eggs inside the carcass, from which they then retire, and cover up their tracks. The eggs hatch out and produce larvae which complete the demolition of the corpse. Ants are, of course, well known for their consumption of animal remains. In countries with fauna of larger size, vultures, kites, jackals and other eaters of carrion perform the same service, while even here we have our carrion crows. Carnivorous beasts, birds and reptiles account for the disposal of multitudes of small fry ; the remains of defunct wild creatures are therefore seldom seen by man, while birds and animals which are shot for sport or snared and trapped for food do not usually come the way of experienced pathologists. The same will hold good for the millions of fishes which are used for food, and only an infinitesimal percentage of cases reach the laboratory. Indeed, most of our knowledge of the pathological conditions to be found in wild animals is derived from the examination of specimens in captivity in the various zoological gardens.

So far as can be ascertained, there is no form of human cancer which is not found in other animals ; and of the other animals it seems in the highest degree improbable that any is exempt. Certainly mammals, birds, reptiles, amphibians and fishes have all furnished examples of malignant growth. In one case there appears to be evidence of an animal suffering from a form of occupational cancer. The oxen used for drawing the native wagons in India are attached to them by a rope which passes round the base of the right horn, and after a time they may develop cancerous growths in this situation.

Among laboratory animals, rats and mice are kept in enormous numbers, reach maturity and old age in a comparatively short time and, moreover, are available for complete post-mortem examination by competent observers. Guinea pigs and rabbits are also available under similar circumstances, though not to the same extent.

Valuable observations have been made upon the occurrence of spontaneous tumours in very large numbers of laboratory mice, and the conclusions reached in this connexion are that a wide range of cancer is met in these animals. Most probably if we could examine similar populations of other animals the same or similar facts would come to light.

One thing that seems fairly clear is that the question of the influence of vegetarian or flesh diet as a *dominant* factor in cancer production must be ruled out. Mice, except when given meat or meat extracts designedly for experimental purposes, are vegetarians, and yet suffer, as we have seen, from all kinds of growths. Herbivorous animals which reach old age, such as horses and some cattle, also develop cancerous and other growths.

The usual site of new growths in different kinds of animals is variable. Carcinoma of the womb is one of the common forms of human cancer: in other animals it is, so far as can be ascertained, relatively infrequent. In this connexion it is of interest to notice that though cancer of the womb is more common in multiparous women than in others, yet although most other animals are considerably more multiparous than the human race, uterine cancer is relatively rare.

In horses uterine tumours are infrequent. This is especially striking in view of the fact that old animals of this species are common. In a series of 509 equine tumours of all kinds, only eight involved the uterus.

Dogs generally are particularly liable to cancer, but malignant disease of the uterus is very rare among bitches. In rabbits very few tumours have been found, in spite of the large numbers of laboratory animals which have been examined, but comparatively few rabbits are allowed to reach old age.

In a series of 123,000 wild rats killed in plague work, only 125 tumours of all kinds were found, of which only one was uterine.

Ground squirrels (*Citellus beechyi*) furnished another large collection of material for examination, since about 250,000 were killed in plague work and reported upon. Only eight tumours were found in this enormous series, with two uterine tumours of sarcomatous nature.

In a series of 39,000 laboratory mice examined by

Maud Slye, only twenty-two showed undoubted uterine tumours.

Fish are not exempt from the disease; at rare intervals an angler will come across a fish which, to his expert eye, has something wrong with it. Few will go to the trouble of examining the abnormality.

Reptiles have been found suffering from malignant growths but the records are scarce.

Cancer, then, is a disease which seems to operate throughout the animal kingdom and it is much more likely to occur in old than in young animals, exactly as in man. Whether cancer occurs in the vegetable world has often been discussed and some specimens of the tumour-like formations not infrequently seen in trees are certainly suggestive parallels to animal tumours.

Recent experiments in the U.S.A. have shown that certain bacteria provoke, in plants, tumours similar to those in man; the crown-gall is now considered to be a true plant cancer.

CHAPTER IV

OCCUPATIONAL CANCER

There are certain occupations, now fewer in number than they were, in which an undue frequency of cancer may occur. Once association is proved, precautions are taken in the light of acquired knowledge to avoid, if possible, any repetition of these occurrences. The first cases recorded were among miners and a book was written on the subject and published in 1567. The miners in question were at Schneeburg and some of them had contracted lung tumours. Another mine in which such tumours occurred was at Joachimsthal. The silver for which the mines were worked was regarded as of specially fine quality; owing largely to wasteful methods, the supply was practically exhausted by the end of the sixteenth century. Mining of bismuth, cobalt and other minerals was still carried on, though on a diminishing scale, until about the middle of the nineteenth century, when more extensive operations were started for the extraction of uranium, which is present mainly in the form of pitchblende. The discovery of radio-activity by Bécquérel in 1896, almost immediately after the discovery of X-rays by Röntgen in November 1895, re-awakened interest in the Joachimsthal deposits, since it was in compounds of uranium that radio-activity was first observed. This, as is well known, led to the discovery of radium by the Curies, the element occurring along with uranium in pitchblende and other uranium ores. A great deal of attention was thus directed to the little mining centre, but although the workers complained of the same symptoms as had been noticed in the Schneeburg miners, their complaints attracted no practical attention from the responsible authorities. This fact is remarkable since, as early as 1879, when they had already demonstrated the nature of the disease which was known to the Schneeburg miners as Bergsuch or Bergkrankheit, Haerting and Heese made definite inquiries regarding the possibility of the existence of malignant lung tumours among the Joachimsthal miners. They received an answer in the negative; and what is even more surprising is that the same reply was made as late as 1921, in spite of the fact that Professor Hlava of the Czech University of Prague had, on several occasions, pointed out the possibility of malignant pulmonary growths as the reason for the Joachimsthal miners' ill-health. It was not until 1926 that the researches of Rostoski, Saupe and Schmorl finally established the identity of the pathological conditions underlying the symptoms of both Schneeburg and Joachimsthal workers.

The next form of industrial cancer to be described was chimney sweeps' cancer; its true nature was pointed out in 1775 by Percival Pott, the famous surgeon to St. Bartholomew's Hospital. After referring to the painters' colic as especially connected with those engaged in certain trades where white lead is in common use, he proceeds to the description of chimney sweeps' cancer, which up to that time had not been recognized as having any direct relation with their particular employment. He describes it as a superficial, ragged, painful and ill-looking sore, with hard and rising edges, known in the trade as the 'soot-wart'. Since it was rarely seen before puberty it was commonly regarded by doctor and patient as venereal in character, and consequently treated by the liberal use of mercury, which only made the condition worse. Pott describes the rapid local spread of the disease, the involvement of the testicle and invasion of the abdomen by way of the spermatic cord. He proceeds to give a description of the conditions under which chimneys were swept in his day, and indeed, long afterwards.

> The fate of these people seems singularly hard; in their early infancy they are most frequently treated with great brutality, and almost starved with cold and hunger; they are thrust up narrow and sometimes hot chimneys, where they are bruised, burned and almost suffocated; and when they get to puberty become liable to a most noisome, painful and fatal disease.

The Chimney Sweeps' Act was passed in 1783 in an effort to protect these children, but with little effect.

Pott emphasized the necessity for free and early excision as giving the patient his only possible chance of life, and referred to the tendency to early and extensive recurrences which took place even when the operation had at first seemed to be successful.

Butlin, in his lectures on chimney sweeps' cancer (1892), mentioned that in addition to twenty-nine chimney sweeps admitted to St. Bartholomew's Hospital at various times for cancer of the scrotum, there were ten other patients similarly affected. Of these, three followed the occupations of gas-fitter, tar-worker, and pitch and asphalt worker respectively, while three were barge and boat builders who, in the course of their employment, would come in contact with tar.

The association of pitch with cancer production was first brought to the notice of the Committee on Compensation for Industrial Diseases, in connexion with the severe skin symptoms shown by patent-fuel workers in Swansea and Cardiff. The matter had been made rather prominent by the death from skin cancer of an alderman of Swansea who was, or had been, a pitch-worker. The matter was investigated by Legge, who 'found a true bill, not only in the case of the briquette workers, but also in the case of those using "coal oil" in the manufacture of grease'. The condition is of very slow development, but once started on its course, even giving up the work will not arrest its development. 'It is really a centuries-old malady,' continues Legge, 'but was thought to be confined to chimney sweeps.' Regularly the Registrar-General's *Decennial Supplement on Occupational Mortality* brought out the high mortality from cancer of the scrotum among chimney sweeps, but his classification of occupations failed to show what it enabled him to prove in his supplement published in 1927, namely, that persons in other occupations using tar, pitch, mineral oil or paraffin, or any compound, product or residue of any of these substances, also suffered in the same way, especially mule-spinners in the cotton industry.

The high incidence of mule-spinners' cancer is most probably accounted for by the gradual change, in the 'sixties and 'seventies of the last century, from animal and vegetable to mineral oils for the purposes of lubrication. It is noteworthy that skin cancers from tar, pitch and mineral oils take a long time for their development. Legge states that, taking industrial skin cancers generally, less than five per cent begin to show any signs of the disease under 30 years of age; the average age of incidence in mule-spinners is 52 years; while less than three per cent exhibit the condition in a dangerous form under twenty years' work—forty years represents the approximate average.

In Table IV, the data are taken from the *Annual Report of the Chief Inspector of Factories* for the year 1947.

TABLE IV

	No. of cases	*No. of deaths*	*Percentage of deaths*
Pitch	98	2	2·04
Tar	75	3	4·0
Paraffin	1	—	—
Oil	29	15	51·72

The differences in death rates are very striking. They are explained as being due, not to differences in the carcinogenic (cancer producing) powers of the materials handled but to the fact that only a few of the cases among the tar distillers and gasworks operatives are reported, whereas nearly all of the patent-fuel and shale oil workers are sooner brought to notice, so that treatment is adopted in the early stages of the disease.

The patent-fuel and shale oil industries are concentrated in particular areas ; the disease is known to the medical practitioners and to the workers themselves, who are fully aware of the importance of obtaining early treatment for apparently trivial skin troubles, without waiting for them to develop into the more severe forms. It is one more example of the truth which cannot be insisted upon too strongly in relation to cancer, namely, that treatment at the very earliest possible date is imperative.

Shale oil was first distilled on an industrial scale from bituminous shale in Linlithgowshire about 1860, and several cases of cancer, mainly affecting the arms, have been reported. The definite causal relation of paraffin to cancer was first pointed out by Bell of Edinburgh in 1876.

Cancer in Arsenic Workers

Hutchinson, in 1888, reported on several cases of skin cancer following the medicinal use of arsenic ; and it is, indeed, probable that, in other cases where carcinoma was reported as following upon skin treatment, arsenic had been administered, probably over long periods.

Modern industrial arsenical poisoning occurs in two forms, either as the result of the inhalation of arseniuretted hydrogen gas or as the result of the deposition of arsenical dust either upon the skin or within the respiratory tract. It is with the second of these conditions alone that we are at present concerned. Arsenical dust is extremely fine and light, so that it 'flies' very easily, and tends to lodge on those parts of the skin where there are folds, as around the nose and mouth, upon moist areas such as the groins and axillæ, and upon the scrotum, in which both conditions are combined. The dust is highly irritant and sets up an eruption, which tends to become extensively ulcerated. Various other conditions may be associated, but the skin manifestations are the most marked.

Aniline Dye Workers

Tumours occurring in the urinary bladder of those engaged in the manufacture of intermediate dye stuffs, including aniline, were first noticed by Rehn in 1894. Subsequently 117 similar cases were reported at Hochet am Maine, the centre of the aniline colour industry. The tumours may be either benign or malignant. Usually the duration of employment before any symptoms occurred was from ten to twenty years or more, but they are stated to have been noticed after only three years' employment. They have also been found several years after the patient has given up the work.

In this country about a hundred fatal cases of cancer which occurred in synthetic dye workers have been recorded. Of late years an effort has been made by the Association of British Chemical Manufacturers to obtain more exact knowledge of the harmful chemical substances which may cause this effect on the human bladder.

X-RAY AND RADIUM CANCER

The first case of cancer being produced by X-rays was reported in 1902; the patient was a worker in a factory where X-ray tubes were made. Part of his duties were no doubt to test the tubes after their manufacture and as a result a malignant growth formed on the back of his hand. Succeeding years brought an increasing number of victims, some of them being medical men who had taken up the use of X-rays professionally. Gradually precautions were taken to ensure that the users of X-rays did not share in the doses of X-rays they were giving their patients or using for the purpose of diagnosis. This involved completely new designs in X-ray apparatus and in methods of manipulation and in this country the situation was viewed very seriously indeed, for, by the year 1921, it was estimated on reliable evidence the world over that more than one hundred people had contracted cancer as a result of undue exposure to X-rays and Radium. In that year the

British X-ray and Radium Protection Committee was set up and has continued to keep a watchful eye on developments and on the increasing extent to which X-rays and Radium are used. The Committee has recently (December 1948) issued the seventh edition of their Recommendations, which are sixty-eight in number and cover all of the risks as far as they are known at the present day.

In recent years one more association of cancer with occupation has been reported by A. J. Amor. It refers to the occurrence of cancer of the nose and lung among some men engaged in the manufacture of copper sulphate and the refining of nickel by the carbonyl process. The copper was abstracted with an arsenical sulphuric acid and the arsenical residue was subject to a process of grinding and calcination. As a result, dust containing copper and arsenic was present in the working atmosphere. Bearing in mind the role which arsenic (*vide supra*) can play in the production of cancer, Amor is inclined to attribute the occurrence to arsenic and not to the metal nickel. Accordingly, arsenic has been in recent years eliminated from the process and the whole régime fundamentally changed to conform to modern industrial hygiene.

Asbestosis is a term used to denote a diseased condition of the lung associated with workers in the asbestos industry; the particular hazard is the breathing of asbestos dust. It is a very serious condition and in some cases malignant disease is associated with it. In the

Annual Report of the Chief Inspectors of Factories for 1947, it is reported:

> During the twenty-three years 1924-46 inclusive, 235 deaths either caused by Asbestosis or in which Asbestosis has been proved at autopsy have come to our notice. Cancer of the lungs and pleura was found to be present either as a cause of death or as a concomitant in 31 of these cases.

The term chronic irritation has often in the past been used to indicate a process in the production of cancer by quite other means than those under consideration and it is significant that in the cases of industrial cancer so far considered, the poisonous or irritating agents have continued over long periods before cancer resulted. We may refer to the action of a few kinds of chronic irritation which, though not associated with any particular occupation, have probably been directly or indirectly responsible for the onset of cancer.

Some of the inhabitants of Tibet carry a small fire basket, the Kangri burner, beneath their flowing garments and as they walk about with this contrivance it tends to chafe their skins; in the course of time, cancerous lesions may appear in just those places where long-continued chafing has been going on.

Chewers of the betel nut get into the habit of tucking it away in the folds of the cheek; the juice of the nut is very astringent and it sometimes damages the soft tissues. In the course of time a malignant growth may appear in the parts which have been so misused.

A clay pipe is said by some to be the choicest of all pipes but the stem is very apt to stick to the lower lip, the skin of which becomes lacerated and if there is complete indifference to such matters, the clay pipe smoker may pay for his carelessness by a malignant growth supervening upon such a 'chronic irritation' sore.

We may at this stage recall a remark attributed to King Edward VII about tuberculosis. 'If it is preventable why not prevent it?' It could apply with singular point to some of the varieties of cancer, the contributory causes of which have been touched upon in this chapter. It is one of the duties of the Ministry of Labour to maintain good working conditions in those establishments or workshops which come under the rulings of the Factory Acts. The reader may rest assured that directly any agency, be it a substance or radiation or industrial process, comes under suspicion that it is causative, directly or indirectly, in the production of cancer, then precautions are formulated for the benefit of those whose calling may involve participation in such work. In this way, the most strenuous efforts are made, both officially and otherwise, that existing knowledge of hazards be put to immediate service in ways and means of protection.

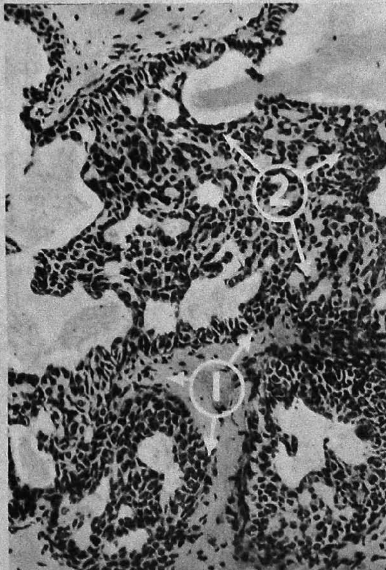
One of the finest examples of pre-vision of dangers to come was shown during the last war. The 'Manhattan Project', which produced the first atom bomb, was a project which involved the handling of quantities of radio-active material thousands of times greater in quantity than anyone had previously experienced. The American doctors, physicists and engineers, to their great credit, envisaged the dangers involved and instituted a splendid régime of safety measures which were obeyed by all. The benefits of this régime did not cease when the end of the war came, for it was seen that these same safety measures could be put to service, not only in industry, but in hospital X-ray and Radium practice. The result is that all handling of Radium and work with X-rays is now subject to a much finer degree of scrutiny than formerly.

The reader may well wonder at the apparent paradox that while X-rays and Radium have been shown to produce cancer in man, they can yet justifiably be used in order to treat the disease. The paradox is explained by reference to the time involved in the two sets of conditions. Cancer has, as a rule, only been produced in man by these agents after prolonged and intermittent exposure to quite small doses, often extending into many years, whereas treatment is of very limited duration. In some skin cases, for example, treatment is complete at one sitting, though in other cases it is extended into several weeks, but the point is that in no X-ray or Radium treatment does it ever become a form of chronic irritation. A bucket of cold water over the head can be a good corrective to certain forms of malaise, but a well-directed series of drops to the crown of the head is a form of torture.

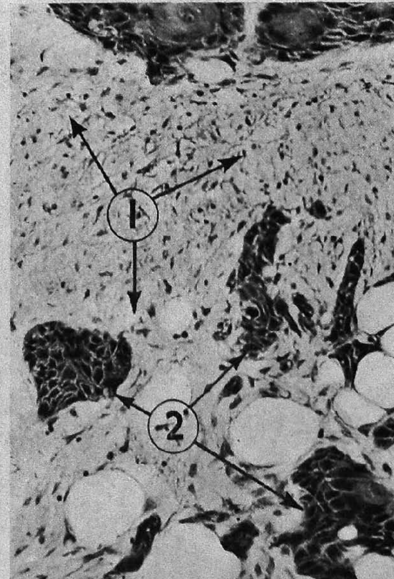
CHAPTER V

THE DIAGNOSIS OF CANCER AND THE DEVELOPMENT OF SURGICAL METHODS

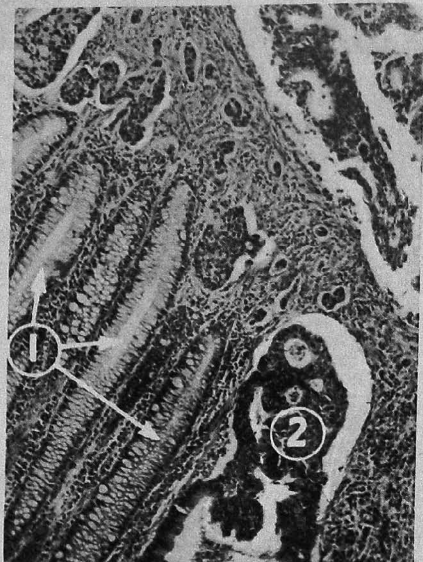
Two discoveries about the middle of the last century marked an epoch in surgery. They were the anaesthetic powers of ether and chloroform and the far-reaching discoveries of Pasteur. But it would be a mistake to suppose that these discoveries created surgery where it did not previously exist; as a matter of fact, there was at this time a high level of surgical skill among those who practised it extensively and this had been brought about very largely by the paramount need for speed, for patients had to undergo these ordeals without an anaesthetic. They were not, however, as a rule, fully conscious during operations, for in many countries there had been found drugs and other narcotics which certainly diminished pain and in some cases induced a general state of insensibility. Nevertheless, it was a momentous year when the American, Crawford Long, in 1842, showed that ether could be used as a general anaesthetic. This discovery was taken up by surgeons rather slowly but by 1846 it had spread from America whence it derived. In particular, Sir James Simpson used it as an anaesthetic in childbirth but within about a year of this date he introduced



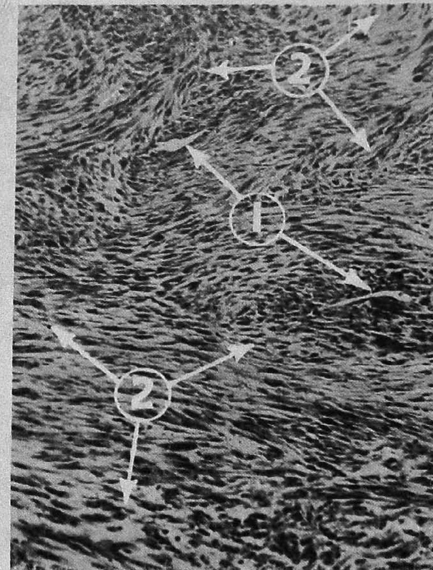
A. Human breast cancer.
1. Normal healthy tissue.
2. Cancer cells.



B. Cancer of the skin.
1. Normal healthy tissue.
2. Cancer cells.



C. Cancer of the rectum.
1. Normal healthy tissue.
2. Cancer cells.



D. Cancer of connective tissues in a sarcoma.
1. Normal healthy blood vessels.
2. Cancer cells.

chloroform. His first experiments, with his two assistants, resulted in their being found unconscious beneath the table at which they had been inhaling the vapour of chloroform. The adoption of chloroform as a general anaesthetic was rapid and was at the service of Lister when he initiated the method of antiseptic surgery in 1865. Founded upon Pasteur's discoveries of the part micro-organisms could play in disease, the methods of antiseptic surgery advanced with sure strides; but, restricting ourselves here to the effects which the new surgical methods were to have in cancer treatment, we have to take into account the great simultaneous advances made in the pathological knowledge of malignant disease. Following upon the ingenious method of cutting sections and counter-staining,[1] pathologists, among whom Virchow was especially prominent, seized upon these two new technical devices and developed them with amazing results. Microscopical examination was made, not only of the diverse and normal tissues of the body, but of the different varieties of malignant growths. These studies proved of the first importance; not only could surgeons become acquainted with the general structure (Plate I) or pattern of the malignant growths they were excising, but more than this was to follow, for pathologists and surgeons, in collaboration, were able to study the methods by which cancer invades the tissues which surround or are otherwise in contact with the malignant

[1] This is the staining of sections of tissues by means of dyes.

cells. These studies were largely made by means of microscopic examination of stained sections of portions of the malignant tumours. In some cases the whole of a tumour was, with infinite pains, cut, section by section, no thicker than $\frac{1}{1,000}$ inch, and stained for microscopic examination; a notable example of this was Lenthal Cheatle's whole examination of the breast; the information so obtained was vital to a more enlightened method of excision. It is not only necessary to remove the obvious tumour but to decide what more should be done in extirpating the spread of the primary growth into neighbouring structures. Armed with this new pathological knowledge the aim of the surgeon was widened; he had changed *antisepsis* into *asepsis* and surgical methods became a ritual in which obvious cleanliness was enhanced by a scrupulous avoidance of bacterial access to the patient. Further, an operator had much greater confidence in the avoidance of shock, not only by the use of general anaesthetics but by the application of new knowledge gleaned by physiologists. Hence the advent of what became known as 'radical' operations in cancer, which meant the eradication by the knife wherever possible of *all traces* of cancer. Some distinguished names are associated with these radical operations, as, for instance, Halsted in America for breast cancer, Wertheim in Germany for uterine cancer. In this country mention may be made of Harmer for cancer of the larynx, Miles in malignant growths of the rectum, Victor Horsley for the first operations upon cancer of the brain tissue and Sampson Handley for a still wider operational basis for cancer of the breast than that of Halsted and for relief of some of the most painful symptoms.

Surgical methods in the treatment of cancer had for the most part gone as far as they could by the early part of the present century and when Radium and X-ray treatment began to prove itself of value, there had to be some adjustment of mind to a new situation. How far was it justifiable to continue to operate *if* as good results could be obtained by radiation treatment? Another consideration was, to what extent can these two methods of treatment be combined with advantage to the patient?

There is no quick and easy reply to such questions, for it depends very largely on the individual outlook of the surgeon, gynaecologist or radiologist. And so it is to-day that we find certain centres of treatment where the dominant outlook on treatment is surgical—at other centres of equal repute it may well be radiological, and it will be some years before any general agreement is found on what is best for the patient.

Until the years when pathologists were able, by their research, to put vital information at the service of surgeons and physicians, they had to rely on ordinary visual examination in order to diagnose cancer. With the advent of the new methods of microscopic examination of tissue which have already been described, there opened up a new era in diagnosis. Great reliance is now placed upon the report of the pathologist, when a tumour suspected of being malignant is in question, and with some surgeons it is their practice to obtain this report at the time of the operation.

Another era in the diagnosis of cancer began soon after the first medical use of X-rays. Their obvious use was in the examination of fractures and in the location of foreign bodies. The bones of the body are the most opaque of all parts of the body to the passage of X-rays. In Plate II may be seen four radiographs, two very early and two modern ones, and they serve to show how modern technique has resulted in much clearer outline in the radiographs of the parts of the body. In the two examples of this modern technique in Plate II, a certain amount of fine structure in the bones is seen.

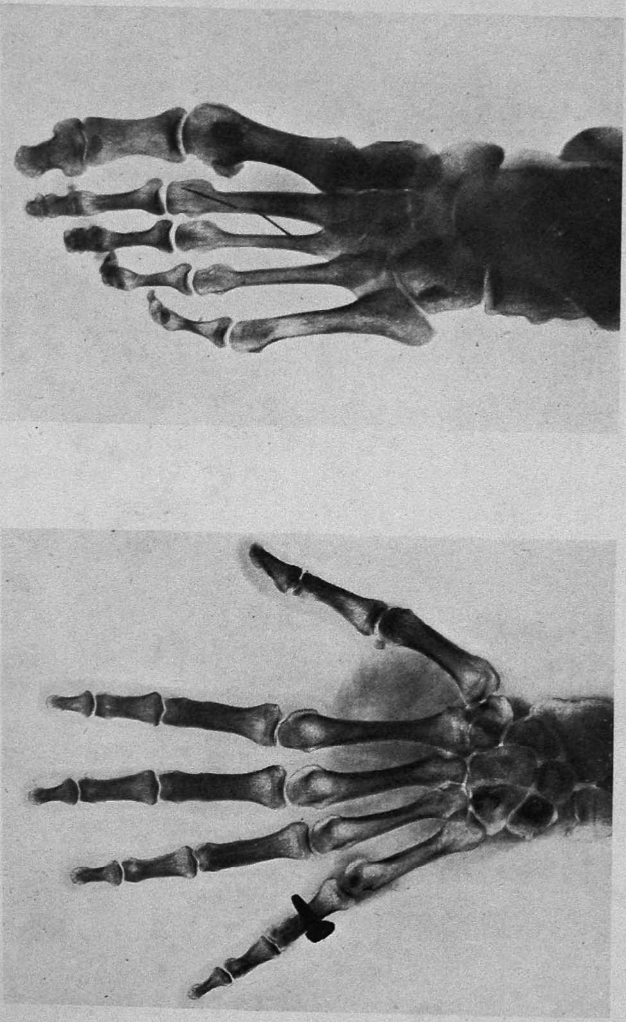
If one took a radiograph of the whole body (it has been done), the picture would strongly resemble a skeleton, because of the outstanding opacity of the bony framework ; but massive organs like the heart and liver would also cast appreciable shadows and the expert eye would detect the outline of the kidneys and the spleen. The lungs would show an unusual lightness of shadow because of their air content ; air is very transparent to X-rays.

Cancer may occur, as we have seen, in a very considerable proportion of all the tissues of the body and there is practically no difference in the density of cancer tissue and the particular tissue from which it arises—so that, on the face of it, there did not seem to be any special

Plate II

A. Copy of the first radiograph taken by Röntgen. The left hand of his wife.

B. Radiograph by Professor Schuster, January 1896, of a needle in the foot.



C. Modern technique showing the fine structure of the bones.

place for the use of X-rays in diagnosis affecting the soft parts of the body ; yet ingenuity has been exercised in this direction with very valuable results.

One of the most valuable ways in which X-rays have been used to diagnose cancer is in what is termed 'internal' cancer. The whole of the digestive tract, for instance, is covered by this term and when it is seen (*vide* Appendix I) that cancer of this tract causes about one half of the total deaths from cancer, it will be realized that any new method of assisting diagnosis in this connexion must stand high in importance.

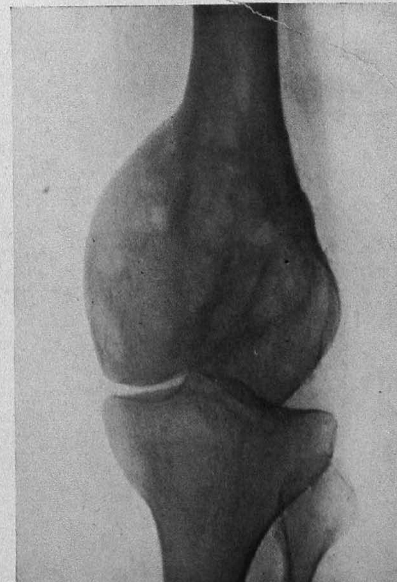
Before the use of X-rays in the diagnosis of cancer of the digestive tract could be properly developed, a large amount of preliminary exploratory work had to be done. If a patient stands in front of an X-ray viewing screen and swallows a glass of water or milk, it is only with great difficulty that this can be traced on its way down the gullet into the stomach. This is because there is little difference in the opacity of the liquid and the soft tissues through which it is passing ; but if to a basin of bread and milk a small amount of barium or bismuth is added and the patient tries again, then the act of swallowing the 'opaque meal', as it is called, can be observed by the radiologist looking at the X-ray fluorescent screen, on which appears a highly differentiated picture ; the opaque meal stands out quite clearly.

This technique, which was started by Kastle and followed by Krause of Bonn in 1908, was used to detect signs of ulcer in the stomach and intestines, but in the course of time and as a result of refinements in method, radiodiagnosticians were sometimes able to detect the existence of malignant growths in parts of the main digestive tract which were, except for a direct operation, not open to visual examination at all.

Another region of the body, the lung cavity, cannot normally be inspected. The diagnosis of tuberculosis is often aided by X-ray examinations, hence the development of what is known as Mass Radiography. Tubercular lesions in the lung give rise to X-ray shadows which are not given by the normal organ ; but an undue shadow may also be given by a malignant growth in the lung. The expert can generally tell to which disease the shadows are due, especially when there are other clinical signs to help him.

Perhaps the most obvious use of X-rays in the diagnosis of cancer is throughout the bony framework of the body. Cancer of any bony part will tend to destroy the regular contours of the joints or the flowing line of a limb and these features are generally well exhibited in the radiographs. But the service of X-rays does not end here, for if the malignant growth is treated the general course of treatment can be studied in the same simple and direct way. One of the most striking features of successful radiation treatment of cancer in bone is that in the course of time the bone, in spite of extensive damage, may become restored to its normal shape and function.

A. X-ray diagnosis of bone cancer.



B. X-ray treatment of cancer diagnosed (A) by means of X-rays.

Plate III shows a radiograph of cancer of the leg which was treated by means of X-rays ; the result was the apparent disappearance of the cancer process. We may remark upon the unique character of X-rays as a medical aid for they here serve the double role of diagnostic and therapeutic agent upon the same patient. The rays that penetrate the tissues affect the photographic plate, those that are absorbed by the tissues exert the beneficial action of treatment.

The claim that one could diagnose cancer by means of tests upon the blood of the patient has been made over and over again. These tests fall into two categories ; one in which attention is chiefly directed to the cellular content, that is to say, the red and white cells of the blood ; the other in which the fluid part of the blood is the focus of interest. The red corpuscles of the blood have two main functions to perform, to carry oxygen to the tissues and to discharge carbon dioxide via the lungs, but the issue is much more complicated when the role of the white cells is examined. There are no less than ten different varieties of leucocytes (white cells) which are enumerated in an ordinary blood count and the proportions in which they occur vary between limits which are fairly well known. It is for the haematologist to say when variations above or below these normal limits are sufficient to become of diagnostic importance.

The concensus of opinion among physicians is that at present there is no diagnostic guide to the presence of cancer in a patient by the aid of simple or even elaborate methods of making blood counts.

When we turn to the other aspect of blood examinations, namely, that of the fluid content of the blood, recent work suggests that there may be some diagnostic value in careful determinations of coagulation temperatures.

If the finger be pricked with a needle and blood, drop by drop, collected in a test tube, it is found that after a few minutes the blood clots, the solid clot shrinks and fluid separates (about half and half); this is called blood serum and it is generally straw-coloured. If, however, as the blood is collected, it is allowed to drop into a certain strength of salt solution (physiological saline) there is no clotting and the red and white cells remain suspended in the fluid. But they can easily be separated from the fluid by means of a centrifuge; after a few minutes spinning at high speed the cells accumulate at the bottom of the container and the fluid above can be collected free of any cells; this fluid is called blood plasma.

In collaboration with others, C. B. Huggins of the University of Chicago has recently (1948) shown that the blood serum of cancer patients coagulates much more readily on heating than normal serum; this change is attributed to some alteration in the albumin content of the serum.

Delayed coagulation is also shown with serum from some patients with lung tuberculosis or acute infections, but these conditions are not likely to be confused with cancer. The test does not locate cancer, neither does it determine the type of growth present, but it puts the examining physician on his guard and this should prove of great value in early cases of malignant disease.

CHAPTER VI

EARLY DAYS IN X-RAY WORK

With the vast modern improvements in X-ray apparatus and technique, it is difficult for us to realize the conditions under which radiological work has been carried out down the years since 1895. The earliest form of X-ray tube was of the type used by Röntgen when he discovered the rays; this was a pear-shaped glass bulb, no longer[1] than the span of one's hand, with a side piece of glass tubing which led to an air pump used to evacuate the bulb of its air. Within the bulb was mounted a flat piece of aluminium about the size of a shilling; on the far side of this a wire was sealed through the glass which allowed contact with one end of an electrical induction coil, the other end of which was connected to a wire sealed into the side piece of glass tubing. When put into operation, electrical action started inside the bulb and a stream of electrons was sent out in all directions from the aluminium surface; where this struck the glass X-rays were produced. The photographic plates were wrapped in black paper so as to exclude light, and the object to be photographed was placed between the tube and the plate, and in as

[1] One may compare this with the million-volt X-ray Plant installed at St. Bartholomew's Hospital, London, in 1936; the overall length of the X-ray tube is about 30 feet. (Plate XII.)

RÖNTGEN
Discoverer of X-rays.

close contact with it as possible. With such an apparatus the first X-ray pictures were produced. Professor Schuster of Manchester University and Mr Campbell Swinton made the first ones in this country in January 1896; the time of exposure required in order to get an X-ray shadow picture of one's hand was about twenty minutes; as early as February 1896, A. W. Porter of University College, London, pointed out that satisfactory results could be obtained with an exposure of only four minutes, using a coil with a spark-gap of three inches and worked with three small accumulator cells.

But this bare recital gives the reader little idea of the difficulties of running these early X-ray tubes. They often ran for only a few minutes before breaking down and even when they were got to work the output of X-rays was erratic and a lot of coaxing was required on the part of the experimenter who, indeed, required endless patience.

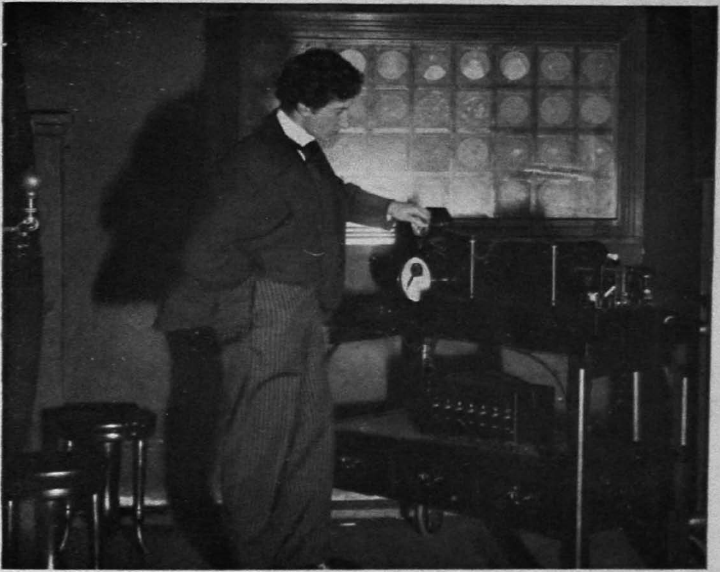
At a meeting of the Paris Academie des Sciences, held on 27 January 1896, Lannelongue, Barthélemy and Oudin read a communication on the utility of X-rays in human pathology. They found that in diseases where there is either over-growth or deficiency of bone the X-rays confirm the previous diagnosis. In Paris, experiments were made with X-rays upon the discharge of electrified bodies, an aluminium screen being interposed between them and the source of the radiations; the results were communicated to the Academie in

February 1896 by Benoist and Hurmuzescu, and at the same time Chabaud published the results of his experiments on the transparency of different metals to the rays. The last observer used photographic plates and confirmed the results stated by Röntgen in his original memoir, which had been obtained by using a flüorescent screen only. Chabaud points out that, of the series of metals examined, the two which were most opaque to the rays were those of the highest atomic weight, platinum and mercury, while the most transparent was aluminium with a low atomic weight. Very early in the application of X-rays to surgical diagnosis it was found that iodoform was very opaque to the rays, and had on some occasions given rise to mistakes when used as a surgical dressing. The opacity is due to the high atomic weight of the iodine which it contains.

In this country the first skiagram[1] of a gunshot wound was taken by Oliver Lodge at Liverpool, and recorded in the *British Medical Journal* of 22 February 1896, and in the same issue appeared a report of the first use of the rays in London for diagnostic purposes, when a fractured finger-bone was satisfactorily demonstrated at St. Thomas's Hospital.

Towards the end of February 1896, Campbell Swinton described the results obtained by using a fluorescent screen of barium platinocyanide mounted at the end of a stout pasteboard tube. The apparatus

[1] The term skiagram was introduced by Rowland and has never been improved upon.



Middlesex Hospital X-ray outfit, 1896.

consisted of a tube of opaque pasteboard, with a simple aperture at one end to which the eye was applied. The other end was provided with an opaque diaphragm of double black paper upon the inner side of which was laid a piece of blotting-paper impregnated with platino-cyanide of barium in a crystalline state. A purse, or other object, was held against the diaphragm with the Crookes tube beyond it, so that the rays from the latter cast a shadow of the coins, through the leather and black paper, upon the inner impregnated screen. The platinocyanide fluoresced brightly under the stimulus of the rays on those portions of the screen on which no shadow was cast, and consequently the form of the metallic objects was made clearly visible. Non-metallic objects were also seen, though more faintly owing to their greater transparency to the rays.

The most important advance in tube construction at this time was made by Herbert Jackson, who, in a communication to the Chemical Society on 5 March 1896, described his 'focus' tube. Hedley referred to this as 'the greatest, and almost the only great advance made in radiography since the beginning'. In this tube the cathode is a concave aluminium disc and the cathode stream issuing from it strikes a flat platinum plate, which also serves as anode, placed opposite to the cathode and inclined at an angle of forty-five degrees. It is here that the Röntgen rays are produced, and are directed to the wall of the tube, which they penetrate. The great improvement, both in rapidity of action and clearness of definition, caused the universal adoption of tubes of this type in practical diagnostic work.

One of the first workers to obtain plates showing the soft parts of the body was John Macintyre of Glasgow, who succeeded in demonstrating the heart shadow, as well as the larynx, hyoid bone and tongue. His note was published in May 1896. At the Royal Society's Conversazione, held in the same month, Rowland exhibited a number of skiagrams dealing with subjects of medical and surgical diagnosis. Some fifty cases were shown, of which about 20 per cent had reference to the detection and localization of foreign bodies, including one of a coin lodged in the intestine. Part of the exhibit consisted of various deformities and ankyloses of the bones and joints of the limbs. It may be stated here that the proper representation of the X-ray shadows of the soft tissues of the body remains, even after fifty years, a matter of great difficulty. The importance of this from the standpoint of diagnosis in cancer by means of X-rays need not be emphasized. In most cases there is no difference between the densities of normal and malignant tissues and, therefore, no visible difference in their X-ray shadows.

At another conversazione of the Royal Society, held in June 1896, X-rays were again one of the main attractions. Stereoscopic skiagrams were exhibited as well as Macintyre's pictures of the human heart under both normal and pathological conditions. Macintyre also exhibited some 'instantaneous' skiagrams; the actual duration of exposure was less than a second.

The credit of starting a systematic investigation into the diagnostic possibilities of X-rays must be given to the British Medical Association, which commissioned Dr Sidney Rowland to undertake the necessary work. This he carried out with remarkable thoroughness and his reports to the *British Medical Journal*, beginning on 8 February 1896, give an exhaustive account of the possibilities of the rays with the equipment then available. Fractures, dislocations, the detection of foreign bodies and the examinations of various pathological conditions are all dealt with, and as all members of the British Medical Association had been invited to send suitable cases for investigation, there was abundance of clinical material. At the same time, Rowland was editing the first journal entirely devoted to the subject of X-rays: the *Archives of Clinical Skiagraphy* appeared in May 1896, and its first illustration shows the method then used for obtaining a skiagram of the leg. The title of this journal was soon changed to the *Archives of the Roentgen Ray*; it is now the *British Journal of Radiology.*

In October 1896, Downie and Sewell of Glasgow noticed vesication of the skin and baldness consequent upon attempts at X-ray diagnosis of the cervical spine; and from time to time various lesions due to exposure to X-rays were reported from this country, from the Continent and from America. Waymouth Reid contracted dermatitis after working on demonstration skiagrams; and in January 1897, more cases were reported from America, including two of considerable severity from Edison's laboratory.

This country was apparently the first in which a Röntgen Society was formed. The first meeting was held on 3 June 1897, and Professor Silvanus Thompson was elected the first president. Soon after the invention of the focus tubes had furnished more powerful sources of X-rays it was noticed that frequent exposures to them sometimes resulted in severe local inflammation of the skin, accompanied in some cases with destruction—at least temporary—of the hair, which fell out, leaving bald patches.

We know from recorded experimental evidence that X-rays were actually produced in vacuum tubes that were tested after Röntgen's discovery, and which had previously been in use; indeed, a skiagram of a grid composed of platinum, silver, copper and aluminium was made by Sir William Crookes in 1896 with a tube which he had used in 1879. The irony of such an observation was not missed by the man who got so very near to the discovery of X-rays.

In 1897, N. Tesla recommended that aluminium gauze or thin aluminium sheet should be placed in front of the focus tube as a protection against the X-rays and in 1898 R. Hughes of St. Louis suggested covering the part to be X-rayed with a layer of rubber.

It soon appeared that there was yet another very practical danger to be apprehended. In France, damages to the amount of 5,000 francs were claimed in consequence of ' alleged X-ray injuries ', and in England three exposures, each of. forty-five minutes' duration (made to diagnose the condition of a hip after an accident) produced a large wound which was considered to be responsible for the death of the patient. Another case was reported from Paris, where a patient had three exposures, the first of forty minutes, the second of forty-five and the third of one hour and a quarter. The injuries were severe, the pain intense, and gangrene was feared. The patient and her husband sued the radiographer for the equivalent of £200. A letter from the head of the laboratory of the Pitié Hospital was read by counsel for the defence ; in this the writer stated that, if any responsibility is attached to the use of the Röntgen rays they cannot be utilized at all. He concluded by saying that the susceptibility of patients to the influence of X-rays varies like their susceptibility to drugs. The court decided that a medical commission should be appointed to decide as to the duration of an examination which would be considered safe. Judgement was postponed.

Yet one more example, this time from Chicago. A patient of the Roentgen Ray Laboratory claimed 25,000 dollars for injuries received during treatment there. He had sought relief from stiffness of the leg, but the treatment resulted in three amputations, ' besides injuries to his sight and hearing'. He was awarded 10,000 dollars damages.

One of the first, if not the first, cases of malignant disease treated was a small cancerous ulcer of the mouth, in which pain was reported to be diminished and narcotics rendered unnecessary by prolonged and frequent exposure to the rays, the number of exposures having reached two hundred when the patient died of pneumonia (*Lyon Med.*, 16 July, 9 August, 28 December 1896). A case of cancer of the stomach was treated 'in this way' and it was considered that a general improvement resulted—an absolute disappearance of the pain and a diminution in the size of the stomach. Freund treated a case of pigmented hairy nævus covering the neck, back and upper part of the arm. Daily exposures were given, each of two hours' duration; after the eleventh the hair began to fall out, and the result was a complete clearance of the occiput, neck and back.

In July 1897, W. S. Hedley gave an account of the diagnostic work accomplished by means of X-rays up to that time. Among the items to which reference was made were the localization of a bullet in the brain, of a needle in the tonsil and the position of a Murphy's button in the intestine. A dilatation of the oesophagus was diagnosed by making the patient swallow bismuth subnitrate 'cream'. Vesical calculi were clearly shown and measured. As regards renal calculi, Henry Morris stated that 'owing to the position of the kidneys close to the vertebral column, the depth of the cavity and the thickness of overlying tissue' it had so far proved impracticable to obtain a skiagram of renal calculi. Four months before this was written, Macintyre had already found (11 July 1896) 'an obliquely placed elongated deposit, evidently of a calcareous nature' in the position of the kidney, and had also expressed to the surgeon the opinion that a well-formed stone would not be found. On operation, at the bottom of an old cicatrix from a previous operation for renal calculus, there was found an ill-defined calculous mass which was removed with a spoon.

This record of what had been achieved in some eighteen months of work, starting absolutely from the beginning, is one of which the pioneer radiologists might well feel proud. It is obviously impracticable in a book of this character to continue a record of progress chronologically; but there is little doubt that this quick realization by the medical profession of the possibilities of using X-rays with advantage in diagnosis and treatment ensured the adoption of radiological methods throughout the world. They were not to be deterred by difficulties and hazards; not only so but their zeal quickly began to be supported technically. Efforts were made to improve the output of the X-ray tubes which were fashioned more boldly so that they would work more reliably and at higher electrical tension. Physicists and engineers were drawn into these problems and one by one the rather primitive appliances were replaced by instruments of precision and reliability. At the present day the whole set-up in a diagnostic or therapeutic X-ray department is a highly finished accomplishment on the part of electrical engineers.

CHAPTER VII

RADIUM AND ITS USE IN CANCER

A discovery which has had far-reaching consequences throughout science, medicine and the body politic, was made in 1896 when Henri Bécquérel showed that uranium was radioactive; he gave it this name because it emitted 'rays'[1] spontaneously. The photograph in Plate VII was taken by means of the rays given out from a small lump of pitchblende which is rich in uranium; the mineral was laid upon an ordinary photographic plate which was wrapped in a light-tight envelope, it was left for about an hour and then the plate was developed. The result was an autophotograph.

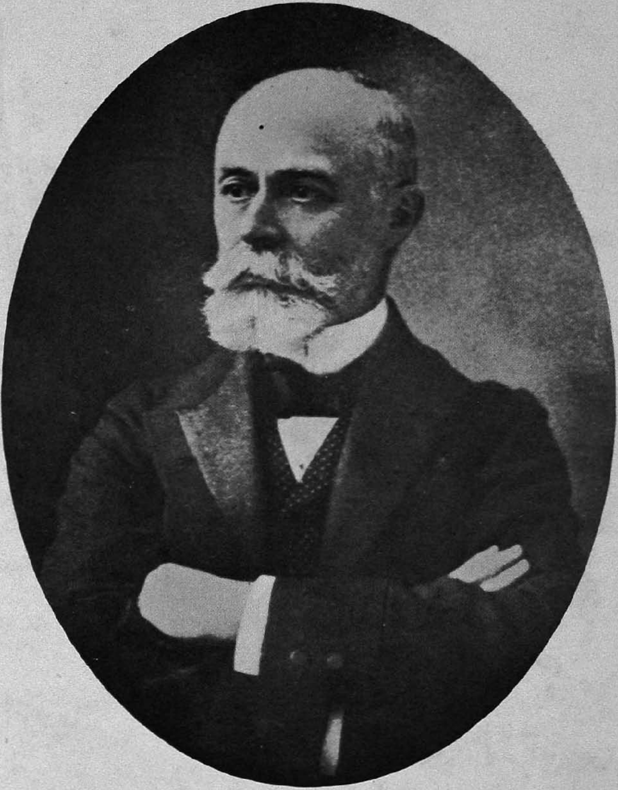
From Bécquérel's discovery the science of radioactivity began and for the first few years the outstanding figures were Professor and Madame Curie who began a systematic research upon uranium and the various minerals in which it is found in the earth. As a result of an extremely arduous piece of work which continued for four years, two new radioactive elements were found, one polonium, named after Madame Curie's native country, the other Radium.

[1] The word 'ray' in radioactivity covers three distinct varieties of radiant energy; one called alpha which consists of positively charged atomic particles, beta which consists of sub-atomic particles known as electrons and gamma which is an electromagnetic radiation like light, but of very much shorter wavelength.

The way in which Radium was isolated from pitchblende is a story that has often been told, but it does not stale in the telling for it was only achieved after excessive labour, and the crowning glory of the achievement was the gift to the world of the whole of the chemical process involved. Had this process been patented, great riches would have fallen to the discoverers, but they decided otherwise. The labour of four years had resulted in a pure salt of radium being extracted from pitchblende. Some idea of what this process involved may be gathered from the fact that from a ton of hard refractory material, there came not as much crystalline powder as would fill an ordinary salt spoon. The crude material had to be crushed and boiled and filtered and precipitated and fractionated and crystallized until at long last a new element was given to the world.

The discovery of Radium by Professor and Madame Curie in 1900 soon made it possible for people to have the use of considerable quantities of radioactive material with which to work. Discoveries of the greatest importance were made in physics; in medicine a new system of treatment, based on the use of the rays emitted from preparations of Radium, was begun.

Actually the rays emitted by Radium itself are not used in this so-called Radium Therapy; the gamma rays are those that are most commonly used, and they come from a substance called Radium C but this is produced *in situ* wherever Radium is sealed up for use.



BÉCQUÉREL
Discoverer of radioactivity.

It is quite true that use is sometimes made of the alpha and beta rays, but it is very restricted in scope because of their lack of penetrating power. So that when we speak of Radium or Radium rays in association with the treatment of malignant disease, we nearly always mean the gamma rays coming from one of the *products* of Radium.

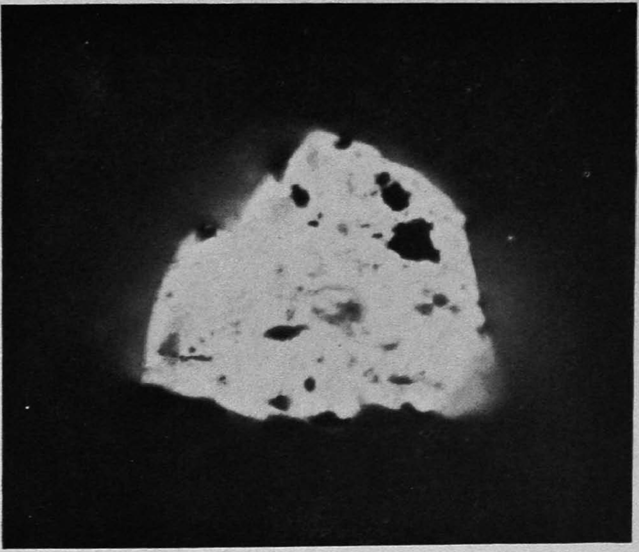
Although Radium was actually used in such treatment for quite a number of years before its physical properties were fully explored, it was used in a more definite, precise and quantitative manner when these properties became more fully known. This was only achieved after investigations which rank very high in boldness, insight and ingenuity, had been made by the many physicists who took up these studies.

It is impossible to go very far in these discoveries by the physicists without mentioning the name of Rutherford. Although the home of radioactivity was France, the focus of attention between the years 1900 and 1937, the year of his death, was upon Rutherford wherever he might be; first at McGill University, Montreal, then at Manchester University and finally at the Cavendish Laboratory, Cambridge. It was directed upon him because of the outstanding discoveries which he made.

To-day there are literally hundreds of radioactive bodies known to science, for it is possible now to *make* commonplace substances, common salt for instance, radioactive, but over the years when Rutherford was so outstanding, the studies were upon natural radioactive substances and their radiations. There are two characteristics which a substance must possess before it earns the name 'naturally radioactive'; it must have the power of emitting 'rays' and it must change its character atomically; both of these are spontaneous. When they occur otherwise the substance is called an 'artificial radioactive substance'. We are here concerned only with the natural varieties because the fundamental discoveries were made with them.

One of Rutherford's first contributions was to sort out the different kinds of rays emitted by Radium and its products and they were called alpha, beta, and gamma rays. His next epoch-making piece of work was to show that thorium, a natural radioactive substance discovered by Madame Curie and Schmidt, spontaneously produced a radioactive gas; he called it thorium emanation. Very soon after this it was found by Dorn that Radium did a similar thing and the new gas was called Radium Emanation. These gases are now known as thoron and radon; it is the latter only that is of interest in medicine.

Radium is generally prepared in the form of a salt of the metal either as radium chloride or bromide when we want to put it into solution, or as radium carbonate or sulphate when required in insoluble form. In all of these cases what we handle is either a white or light brown powder, in no way remarkable to look at, except that preparations of any strength are visible



Autophotograph of a specimen of pitchblende.

in the dark. The quantities in medical use range from about 1 milligramme (about a thirty-thousandth of an ounce) to about 10 grammes, rarely more.

If we take some of the powder, put it into a thin glass tube and seal the tube off, the glass will soon become discoloured, brown or violet, owing to the action of rays on the glass. The gas radon is being produced all the time that Radium exists, we cannot hasten it nor can we stop it; eventually the Radium will be completely changed into radon, but it will take thousands of years, so we do not generally have to take into account this 'decay', as it is called, when we are using Radium. But it is quite otherwise with radon, for it changes comparatively quickly into another substance, solid this time, called radium A, and this kind of atomic change goes on through a whole series of substances, ending up rather prosaically with ordinary lead. The whole process goes on continuously, the emission of rays and the change from one kind of atom to another.

Each radioactive substance has its own distinctive properties and rate of decay. This rate is generally expressed as the time required for a substance to diminish to one half of its value at any moment. As examples, uranium I takes nearly 5,000 million years to do this, radon takes about four days: radium C^1 takes only about one millionth of a second, and, incredible as it may seem, there is a substance, Thorium C^1, which has a shorter life than this.

Radon is a very important gas because it can often be used more conveniently than Radium, so that there are two main ways of using these substances in cancer treatment. One is called Radium Therapy, the other Radon Therapy, but the distinction need not be insisted upon because, as it happens, exactly the same kind of rays are used in the two cases. Radium for treatment purposes is generally put straight into fine platinum-iridium tubes or hollow needles, the latter having sharp pointed ends to ease their insertion into the tissues; they are sealed hermetically and very carefully manipulated in every way; direct contact with the fingers, if often repeated, causes damage. An alternative method of using Radium in treatment is to have much larger quantities in specially protected containers, and the rays emerging from a container are directed upon the patient from a distance of several inches or more. This technique in France is called Tele-Curie-Therapie. A photograph of a 10 gramme Radium Unit may be seen in Plate X.

One of the advantages of radon is that it allows for a more flexible use of the radioactivity; once Radium is put into platinum tubes or needles there cannot be any quick redistribution to some different shape or length or radium content that may be required in treatment and this is where the use of radon can be of great service, for a gas can be run into a tube or hollow needle or applicator of any shape or size to suit the particular clinical need. The manipulation of radon

PROFESSOR AND MADAME CURIE
Discoverers of Radium.

is a rather specialized technique because it means not only dealing with extremely small quantities of gas but, the gas being radioactive, safety precautions are required at every step in a number of quite different processes.

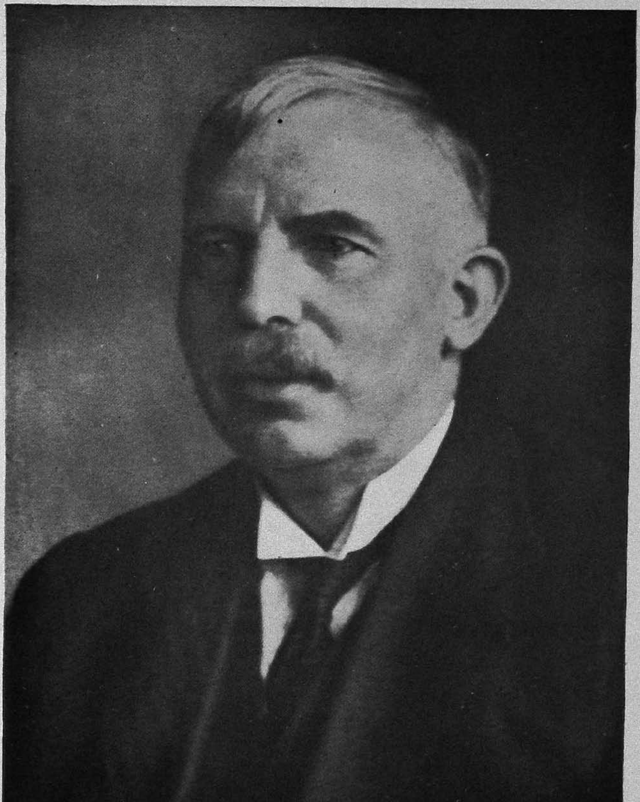
An ordinary soda-water bottle is operated by allowing the compressed gas at the top to force the liquid out of the bottle, the gas remaining behind, except the fraction that goes into solution. Radon is, however, collected in just the opposite way ; the Radium solution half fills a flask which connects up at the top with a vacuum pump. As the radon is produced by the Radium it collects in the top half of the flask, some remaining in solution down below ; now, provided the gas pressure is big enough, the radon and other gases which have been allowed to collect there, too, will pass over into the vacuum pump when the intervening tap is opened, the liquid Radium solution being left behind. This is the beginning of operations and once having secured the radon the next process is to purify it, and in this way the volume of gas we have to deal with can be made very small indeed, and it can then be passed into minute glass or gold tubes making what are called ' seeds '.

During the war years, a radon plant was set up in the country in tunnels a good many feet underground for reasons of security. There were three purification plants in operation five days a week and with a supply of over four grammes of Radium. Even so, the total quantity of radon collected over a period of three years, when purified as carefully as possible, gave not enough to fill an ordinary thimble. Yet so potent is radon that this quantity served for the treatment of several thousands of patients (*vide Medical Research Council Report*, 1948).

When Radium or radon is sealed within any kind of metal container and left for a time to reach what is called an equilibrium, there is a most complicated issue as regards radiation going on inside the container, but a comparatively simple one as to what comes out, and we shall restrict ourselves to this. The rays that emerge through the walls of the container are almost entirely gamma rays; these are identical with X-rays of great penetrating power. So that when a choice has to be made in the radiation treatment of a malignant tumour it is entirely on technical merits that a decision between X-rays or gamma rays is arrived at. There is no hard and fast rule about it and the choice of one or the other is a matter for the judgement of the radiotherapist.

The Founding of Radium Institutes

With the growing use of Radium and radon in the treatment of disease there came the recognition of its highly specialized character; it was certainly not a form of treatment which could be undertaken, with advantage to the patient, by anyone unless they became acquainted with certain physical and biological principles which form the basis of the use of these elements. In due course a Radium Institute was founded in



RUTHERFORD
Co-discoverer of Laws of Radioactivity.

London and a little later the Holt Radium Institute in Manchester, to which reference is made in another chapter.

The name of Curie will always be associated with such work, for the man and wife did two things which placed the world in their debt ; they discovered Radium and they made public their method of its chemical separation from the mineral pitchblende. Had they kept this process secret, a fortune would have accrued to them, but at the time when they were free to do this they realized the use which Radium might be in the treatment of cancer and played the nobler part.

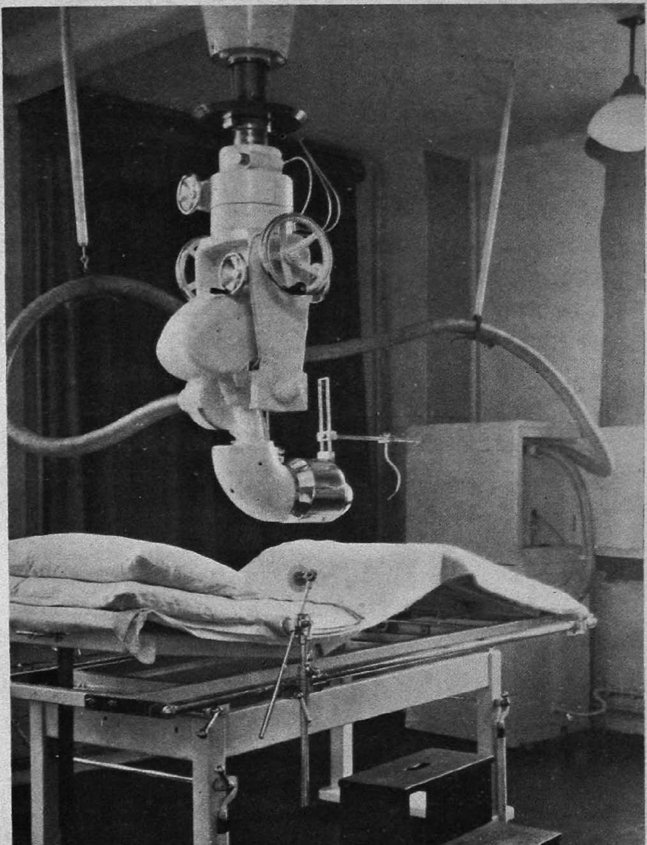
The idea of forming a Radium Institute[1] in Paris was the result of a kind of remorse in intellectual circles, and even among the general public, when it was learnt that Pierre Curie, one of the greatest men of learning ever produced by France, whose discoveries had transformed the evolution of science, had died on 16 April 1906 before he could obtain a research laboratory where he could have expended all his energies in work or come by the barest necessities for the pursuit of his experiments.

In 1909, the Pasteur Institute and the University of Paris agreed together to build a Radium Institute, at their joint expense, on a part of the land recently acquired by the University between the rue d'Ulm and

[1] The author was favoured with a brief historical note upon the foundation of the Institut du Radium in Paris by Professor Antoine Lacassagne, who is its present Director.

the rue St. Jacques. This Institute was to consist of two parts: (a) a laboratory devoted to the study of the physics and chemistry of radioactive substances which would be under the direction of Madame Curie and subsequently of her successors in the Chair of General Physics and Radioactivity of the Faculty of Science; (b) a laboratory for research on the biological phenomena of radioactivity and their application to the treatment of disease, which would be directed by the Pasteur Institute. This was under the direction of Professor Regaud. Some years later Regaud established the Fondation Curie. Since 1936 this has consisted of a modern hospital of eighty beds near the Institut du Radium, for the treatment of cancer by means of surgery, Radium and X-rays. The direction of the Laboratory Curie of the Institut du Radium is in the hands of Madame Joliot-Curie and that of the Laboratory Pasteur is under Professor A. Lacassagne.

The influence of the work of this Institute has been far-reaching for not only is it the guiding influence for radiotherapy at all of the Anti-Cancer Centres of France, but its experimental research is of the highest order.



General view of 10 gramme Radium beam unit.

CHAPTER VIII

OFFICIAL AID AND INTEREST IN CANCER

In this country progress in radiology has had very considerable support from bodies such as the Medical Research Council, King Edward's Hospital Fund for London, the British Empire Cancer Campaign and the Radium Commission.

This support may be said to have begun in 1920 when the Medical Research Council, entrusted with several grammes of Radium, decided to encourage experimental and clinical research by lending Radium free of charge to those who had a warrant for its use. A few years later they arranged for a quantity of Radium to be put into solution for a supply of radon. The need for this was felt especially among those who were devising new lines of technique in the treatment of cancer, and the proof that this was a productive and progressive step is shown by the fact that by 1939 there were no less than nine radon installations in the country preparing supplies very largely for medical needs.

The technique for the production of radon is exacting, the skill required in the manipulations is considerable and the cost of production is large. With the outbreak of war on 3 September 1939, the London installations were shut down and the Radium was deposited for safety[1] in bore-holes; but radon centres were soon operating in the country with a reasonable degree of security from air raids.

The support given to Radium therapy by the Medical Research Council began to show itself in the years 1920 to 1928. Year by year the publication, *Medical Uses of Radium*, showed not only a development of the various technical methods of treating malignant disease but the results of treatment.

There is little doubt that in 1928 the time was ripe for an inquiry into the warrant for further national support for Radium treatment and this was carried out by a Radium Sub-committee of the Committee of Civil Research.

On the basis of the findings of this Committee (Cmd. 3303, 1929) a national appeal was made for the purchase of larger quantities of Radium. The result was that a sum of over a quarter of a million pounds (partly subscribed by the Government of the day) was available for the purpose. Two bodies were set up, the National Radium Trust and the Radium Commission, the duty of the former being to administer the fund and of the latter to see that the Radium was used to the greatest advantage. The membership of the Commission was drawn from a wide medical and scientific

[1] This was not so much on account of the precious commodity, Radium, but for the safety of the public, for any Radium actually dispersed by bomb action would have disastrous effects upon people who might breathe it in the form of dust.

circle and the policy was adopted of concentrating the Radium at Clinical Centres where the fullest facilities for treatment could be found and maintained. Beginning with the large cities, the Medical Faculties were found to support the plans that had been envisaged by the Commission, and as time progressed, further Regional Centres were formed so that Radium treatment could be given still wider scope.

Simultaneously with this development, King Edward's Hospital Fund for London, benefiting from a large gift by Sir Alfred Beit for the purchase of Radium, put at the disposal of many hospitals within the Metropolitan area, Radium for their use, in many cases augmenting the supplies which many of the voluntary hospitals already possessed but found quite inadequate to their needs. As time went on the Fund and the Radium Commission collaborated in a general plan for improvements in the co-ordination of Radium work, persuading those who carried out the treatment to institute special systems of clinical records and statistical presentation of their results. These additional burdens on the hospitals were for the most part cheerfully borne as it was realized what an important part they play in the adequate treatment of such a disease as cancer.

A sequel to the formation of the National Radium Trust and Radium Commission was the initiation by the Ministry of Health of 'An Inquiry into the extent to which (Cancer) Patients receive Treatment'. This Inquiry was published in 1939. The Radium

Commission had stated in their seventh Annual Report that the facilities for X-ray and Radium treatment of cancer patients were inadequate, when the needs of the country as a whole were taken into account. The Inquiry of the Ministry was made in order to attempt a more direct assessment of the situation. In general the Inquiry confirmed the opinion that had been expressed by the Radium Commission and in submitting conclusions to the Minister, the Principal Medical Officer put emphasis on the need of wider provision of facilities for treatment and for early diagnosis. There was indeed some need for emphasis, for the significant fact emerged that the proportion of patients who attend for treatment at hospitals which are known to be equipped with *full facilities for modern treatment*, is small, just over one quarter.

Parliamentary action followed fairly quickly upon the heels of this Inquiry and in 1939 a Cancer Act was placed upon the Statute Book. Its provisions are of great interest and the scope of the Act will be appreciated when we quote one or two of them. We may start with the duties of local authorities:

> It shall be the duty of every Council of every county and county borough in England and Wales* to make arrangements to secure that the facilities for the treatment of persons suffering from cancer are adequate for the needs of the county or borough and so submit its arrangements for the approval of the Minister within one year from the commencement of this Act or such longer period as the Minister may in any case allow.

So much for the provision of facilities. The days of quackery in the treatment of cancer are over, we hope, but the Ministry have thought to make certain of eliminating those of the breed who advertise their nostrums, for we read:

No person shall take any part in the publication of any advertisement:

(a) Containing an offer to treat any person for cancer, or to prescribe any remedy therefor or to give any advice in connexion with the treatment thereof; or

(b) Referring to any article, or articles of any description, in terms which are calculated to lead to the use of that article, or articles of that description, in the treatment of cancer.

Exception is made in cases where it is reasonably necessary to draw the attention of registered medical practitioners, nurses, etc., to a remedy or article concerned with cancer treatment.

The public has had to wait long for an Act such as this. In order to implement the Act a large increase in facilities, both diagnostic and therapeutic, was to be set in operation. The coming of war in 1939 made it impracticable for this to be done straight away; in fact, only by the greatest efforts of those who at that time were engaged in such work, could active treatment for cancer be continued.

The chief aim of those directing the British Empire Cancer Campaign, which started in 1924, was to further investigations into the cause or causes of cancer and at the same time to assist those who were trying (by one means or another) to apply the results of experimental investigation in the laboratory to the treatment of the disease. Hence they assisted by money grants not only those institutions which had big staffs at work on experimental problems and individuals devoting themselves to specialized work, but they arranged for loans of Radium and X-ray plant in cases where these were urgently required. Active collaboration between the British Empire Cancer Campaign and the Medical Research Council was secured by the appointment of a joint Radiology Committee with Sir Cuthbert Wallace as Chairman.

The foregoing survey, brief as it is, may give the reader a general idea of the way in which cancer research work has been assisted by the co-ordinated action of a number of corporate bodies. Typical of the best traditions of the country, these bodies have, in giving their support to institutions or individuals, allowed them the greatest freedom of action compatible with the obligations involved in dispensing public monies. It is not reasonable to expect that grants of money, apparatus or Radium should be made without restrictions, but these have, in the field under survey, been made as little irksome as possible.

CHAPTER IX

RESEARCH IN CANCER

Those who engage in research are compelled by an insatiable curiosity ; the ways in which they seek satisfaction are indeed very variable for while some are content to seek an answer to the problems that Nature presents in naked-eye fashion all about us, others contrive by experiment to unravel secrets that Nature seems as it were to keep to herself. The outstanding example in the latter category is perhaps the electron, for there is certainly no naked-eye evidence of its existence, yet it is the most universal entity in the material world about us.

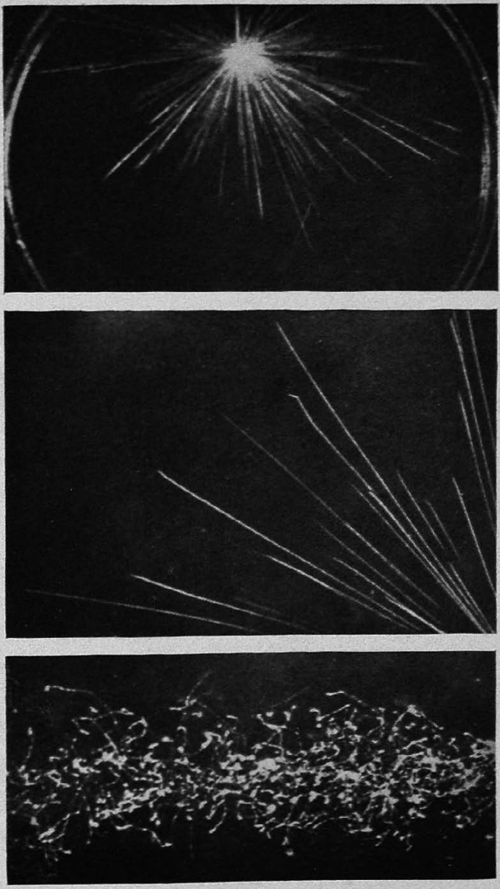
The ways of the experimentalist are very diverse, but it may be said with little fear of contradiction that the outstanding and fundamental discoveries of physics were made by men using a very modest extension of apparatus ; the epoch always begins on a very small scale whereas records are later broken by means of devices of massive scale. The apparatus by means of which X-rays were discovered could all be put on an ordinary laboratory table and the simple yet delicate device by which atoms were first disrupted by man would not require all of the space of an ordinary writing table. The subject of study often gives no hint concerning the form which the resulting discovery may assume.

No better example of this could perhaps be given than that of C. T. R. Wilson upon the behaviour of water vapour. If we take an ordinary glass bell-jar and put it face down on a flat table the air inside it will be the ordinary air of the room, and will contain some moisture and a little dust. It would be an easy matter to get rid of all of the moisture and leave the dust; we will suppose, then, that the jar inside contains only air with just the ordinary small amount of dust. We now introduce a small flat vessel containing water; at once it begins to evaporate into the air inside the bell-jar. In a matter of a few minutes no more water evaporates, and the air inside is said to be saturated; there is nothing to show for it, but if the temperature is quickly lowered a cloud inside will form because the air cannot hold the same amount of water vapour as it did before; the lower the temperature, the less water vapour air can retain without becoming saturated, and when it is saturated, any excess comes out of it as a cloud of very fine droplets of water. Wilson showed that if the air was first cleared of its dust, then it did not form a cloud as readily as it did before, in fact the air could become super-saturated. He explained this by supposing that the minute invisible particles of dust acted as foci or nuclei which made it easier for the water vapour to condense upon and so form the water droplets which constitute the cloud. He then went on to show that if some of the molecules of the air in the bell-jar were electrified they could act in just the same way as the fine particles of dust. Water vapour would condense on these electrified molecules, or 'ions' as they are called, while it would not do so on the ordinary molecules. The drops formed in this way, though very small, are much larger than molecules; they are little spheres of water big enough to reflect and absorb light. The next step taken by Wilson was to photograph these drops at the moment they were formed. Let us suppose that a fine pencil of X-rays is made to pass through the air in the bell-jar—in this invisible pencil the air is electrified, ions are formed in very large numbers, yet there is no visible change for the ions are too small for vision. A sudden lowering of the temperature, however, converts the ions into drops of water. Wilson arranged that immediately this happened a flashlight photograph was taken, with the result that the whole path of the pencil of X-rays was shown up as a vivid conglomeration of small water droplets. Thus on the instant the ions were made visible; the instrument is generally known as the Wilson Cloud Chamber and by its means 'ion-tracks' are revealed. It is difficult to over-estimate the importance of this instrument in the developments of modern atomic physics; Rutherford called it the most wonderful physical instrument ever devised. Yet it started with an apparently academic study of the behaviour of water vapour. Plate XI shows a typical example of ions made visible.

It may seem a far cry from such studies to what many people may try to visualize as research in cancer. But in fact it is not so, for present-day methods of research, whether it be in pathology, or radiology, or biochemistry, are all based on some basic forms of research which at the time they were carried out were of an academic character. Getting to grips with any problem connected with the cause, prevention or cure of cancer, means getting hold of the particular basic discoveries which provide a firm footing and then putting one's imagination to the test of experiment.

The study of cancer in its widest sense implies a threefold effect; to find the cause of the disease, to bring about its prevention, and, failing this, to produce its cure.

Cancer is a protean disease; it can occur in almost any part of the body and this carries with it the implication that it can occur among any of the widely different types of cells of which the body is composed. This is a most important consideration, for the whole medical classification of the different forms of cancer is based upon the fact that cancer appears to arise from the normal tissues, but the general cause of this agency is at present unknown. In some cases, a specific agent can be made to produce, within a limited field, a variety of malignant growth, but in the wide field of cancer as it occurs spontaneously in man we do not know the cause or causes of the disease. Since cancer can occur in almost any part of the body and since there is such an abundant variety of cells in our bodily structure, there is an almost corresponding variety in the types of



Photographs of experiments by C. T. R. Wilson, showing the tracks of *alpha* and *beta* particles.

cancer that can occur. In classifying these, the work may be said to be now practically completed by the pathologists; though occasionally there will be some difference of opinion as to the origin of a malignant tumour. It has always to be remembered that the tumour has its origin in some normal tissue of the body and something has caused a breakdown in the normal routine of this tissue's functioning and often of its structure; the first of the new malignant cells are modified normal cells and it is the task of the histologist to recognize the particular type of normal cells from which the modified ones have arisen. We need *not* be surprised if differences of opinion sometimes arise in such debate. The verdict as to the histological type of cancer present is of the greatest importance, first in giving the clinician some indication of its malignancy and second in providing evidence which will help to decide upon the best method of treatment. We might well say that the histologists are the great experts in studying and recognizing the different *patterns* presented by stained sections when seen under the microscope. It has already been explained how a section is prepared from part of a malignant growth; after the section has been obtained it is stained by some appropriate method. The result is a pattern of great variety and one which requires a very long experience to interpret. In order to give the reader some idea of the pattern of malignant disease, four different varieties are represented in Plate I.

It is, as a rule, on evidence of this sort that the opinion of the pathologist is based ; he may, however, seek other information from the clinical side to help him to come to a decision but this is a matter of choice for the individual. The serious nature of cancer is largely, though not wholly, due to the fact that the tumour cells invade parts of the body other than those in which they arise. Did cancer but remain localized it could, in the majority of cases, be removed surgically or resolved *in situ* by means of X-rays or Radium. But, unfortunately, this is quite exceptional behaviour on the part of malignant tumours—the general rule is that they eventually break bounds, they invade the surrounding tissues, they upset the protective mechanism of the body and malignant cells or small clusters of cells can be carried to distant parts by means of the lymphatic system or occasionally by the blood. It is this character of a malignant growth that makes its treatment so difficult whether surgically or by radiation ; the great hope is that some systemic cure will be discovered, some substance which can be tolerated by the patient and yet prove harmful to the malignancy within.

A laboratory is a place for experiment and test. So we find that in the study of any disease there is a dual activity among pathologists, some who study the disease as it is found and others who carry out experiments designed to shed a fuller light upon the problem. It may surprise the reader to learn that thirty-five years ago the number of laboratories in the United Kingdom at which experimental research was being made into the obscure problem of cancer could be counted on one hand; though we may unwittingly be omitting some few free lances (all honour to them) who were pursuing their own plans unassociated with well-known laboratories. The laboratories we have in mind were those of the Imperial Cancer Research Fund, the Middlesex Hospital, the Cancer (now Royal) Hospital, the Christie Hospital, Manchester, and the Royal Cancer Hospital, Glasgow; the list is enough to show how limited although inspired these efforts must have been.

Experimental work at these centres varied with the outlook of those generally responsible for its direction. At the Imperial Cancer Research Laboratories the early years were devoted to a wide survey by Dr Bashford, its first Director, to cancer throughout the animal kingdom and he initiated in this country what Ehrlich had done in Germany, namely the propagation of animal tumours by implanting a small piece of tumour as big as a pin's head under the skin—mouse cancer grows in mouse, rat cancer in rat, man cancer in man. Bashford wrote: 'Cancer can only be transmitted experimentally by processes which allow of the continued growth of the tumour of one animal in other animals of the same species'; he considered it a waste of time to seek for the cause of cancer outside the life processes of the cells. A succeeding Director, W. E. Gye, however, spent a great part of his scientific life in looking for just such a cause. We may quote Gye as to the significance of recent experimental results which he records in the Forty-sixth Report of the Fund (1948-9). He says: 'The apparent gap between filtrable and non-filtrable tumours is fictitious; the difference between chicken tumours and mammalian tumours is quantitative and not qualitative . . . It is sufficient to say that the negative results obtained hitherto in attempts to achieve non-cellular propagation of tumours mean precisely that the methods were not good enough for the task and that they do not warrant either the pessimism of the past or the rather wild popular speculations of the present.' In the last few words the writer, no doubt, had in mind the fairly general belief that once the cause of a disease is found, the cure will probably follow. This may well take time, but there is no doubt whatever about the value of discovering the cause of any disease.

Dr Gye has brought forward experimental evidence which has led him to believe that the cause of cancer in mice and rats is a virus. So far there is no proof that any virus acts as a generally causative factor in cancer as it occurs in man, but there is a mass of evidence to show that a virus plays some part in spontaneous tumours of the fowl. Here, however, it must be added that according to P. R. Peacock of the Royal Cancer Hospital, Glasgow, sarcomas can be made to occur in the fowl by treating the tissues with chemical carcinogens (cancer-producing substances) devoid of any virus.

At the Royal Cancer Hospital (London) laboratories, the problem of causation has been one of the main experimental lines of investigation. There is a great deal of significance to be attached to those cases where the production of cancer in man follows upon the prolonged action of an irritant. Professor Kennaway, when at the Royal Cancer Hospital, devoted many years to the synthetic production of tars which will produce cancer in animals ; the full implications of this work cannot even yet be realized. Further reference is made to the work of these laboratories in the chapter on Chemical Treatment in Cancer.

The work of the Cancer Research Laboratories of the Middlesex Hospital was for many years devoted to a study of the way in which X-rays and Radium act upon malignant growths. This trend of experimental work was probably a natural one at a hospital which initiated the first cancer ward in Europe (in 1792). It is a significant fact, showing the way in which X-rays and Radium have altered the outlook for anyone suffering from cancer, that up to recent times, patients admitted to these wards could only expect to be looked after kindly, or to be 'released by death' which was the alternative to 'cure by science'. This is set forth on the plaque commemorating the endowment of the permanent beds in the old Cancer Wing at the Middlesex Hospital. Cure by science was rather an illusory hope years ago, for the majority of the patients had passed beyond the operable stage on admission and there was no form of treatment alternative to surgery.

After a period of trial, beginning seriously about the year 1920, X-ray and Radium treatment had justified itself to such an extent that by the year 1939 no patient was occupying a bed in the Cancer Wing of this hospital to whom some active form of treatment was not being given and for the most part that treatment was by means of X-rays or Radium.

The adoption of X-ray and Radium treatment for cancer called for experimental work upon the nature of their actions, not only upon cancer cells but upon the healthy tissues of the body. Elaborate studies to this end were made, as far as possible upon quantitative lines, and it was found that as a general rule the rays have a destructive action upon all living cells and structures of the body, but that some of these are more sensitive to radiation than others ; in fact, that there is an enormous range of sensitiveness. Moreover, within itself the living cell exhibits a range of sensitiveness which depends upon the activity and function of the cell at the time it is irradiated. Some of the earliest of this work showed that when a cell was in the act of division (mitosis) it was more affected by a dose of X-rays or Radium than when it was in the so-called resting stage ; it could be as much as eight times as sensitive. Professor Lazarus-Barlow made an important study upon the way in which different kinds of cells responded to a given dose of gamma rays. By selecting two kinds of tissue growing side by side in the animal, he showed that one variety was more affected by giving the dose of radiation in a very short time while the other responded more markedly when the time was extended. This had obvious implications in treatment. Another example of individual sensitiveness to the rays was found during studies upon the effects of X-rays upon the circulating blood ; it was found that the lymphocytes were very much more sensitive than any of the other varieties of blood cells. It may be that as such studies are extended we shall find just as big a range of 'selective action' of X-rays and Radium among the cells or organs of the body as is shown when drugs are administered.

The reader will not be surprised to learn that the different types of cancer also exhibit a range of sensitiveness to X-rays or Radium, so that the therapist, in treating a patient, has two ranges of sensitiveness to bear in mind, one relating to the healthy tissues and the other to the malignant growth. What he aims at is to give the malignant cells a lethal dose of radiation without causing undue damage to the neighbouring normal cells or to the body as a whole. The technique of treatment is elaborate and there is a considerable tendency in the bigger centres of treatment now for the line and detail of treatment to be the result of collaboration between physician or surgeon, radiologist, pathologist and physicist, all hoping that out of a multitude of counsel the best for the patient will prevail.

Another line of investigation was to find out the fate of cancer cells after they had been given various doses of X-rays or Radium. The dose that must be given to a group of cancer cells so as to ensure their subsequent death was called the lethal dose; this does not kill them immediately for it has been shown that after much more than a lethal dose, mouse tumour cells could persist in the body for as long as a week without showing any marked microscopical changes; after that, however, degeneration and dissolution set in. What is aimed at in treatment is a dose of radiation which will not cause the *immediate* death of the cells but is large enough to damage the cells so much that they will all eventually die. If the amount of radiation is unnecessarily large irreparable damage may be done. On the other hand if the dose is not large enough some of the cells may stop growing for a time but eventually renew their vigour and flourish in a state more resistant to radiation than they were originally. In the very early days of Radium treatment these points were not fully realized. The body mechanism plays a part in all this, but it is difficult to disentangle the different stages of a process which goes on continuously while observation must of necessity be intermittent. The intention is to use the rays so that they do not kill at once; if they were so used they would be badly used, for X-rays and Radium constitute about the worst cautery in the world. Working with several different strains of tumour, experiment has shown that when an animal tumour (mouse or rat) has been X-rayed long enough to ensure that the tumour will gradually disappear, then the animal is generally quite resistant to a new inoculation of the same strain of tumour.

An unexpected line of development in chemotherapeutic research was the use of 'stilboestrol' in the treatment of carcinoma of the prostate. This was produced after some ten years of continuous research on synthetic 'oestrogens'[1] and was the result of the joint efforts of a team at the Courtauld Institute under Professor E. C. Dodds and in the Dyson Perrins Laboratory under Sir Robert Robinson. This substance was found to be highly active when taken by mouth. It was first used by Huggins in America in 1941 for the treatment of carcinoma of the prostate. After a number of years experience, it would appear that practically all cases are benefited in the first instance, even to the extent of a complete disappearance of symptoms due to primary and secondary growths. Unfortunately the beneficial effects appear to wear off in a certain percentage of cases which become refractory to the use of oestrogens. It is difficult to assess the final position of this form of treatment.

The Strangeways Laboratory at Cambridge has, since about 1920, made notable contributions in the study of cancer. These studies began from a radiological point of view with an investigation upon the ways in which living cells, maintained in what are known as tissue cultures, respond to X-rays and Radium. The cultures were obtained very largely from fertilized hen's eggs

[1] Substances naturally produced in the body.

and the technique was to dissect out from the unhatched chick the particular kind of tissue required for study, and to culture this in a sterile glass slide, feeding it periodically with chicken broth. In this way groups of living and multiplying cells form excellent material for observation under the microscope. Among other tissues studied were groups of animal tumour cells and when enough information about the damaging effects of the rays had been accumulated, the time came when Dr F. G. Spear and Dr Glucksman felt justified in linking up their findings with the work going on in radiation treatment. This was done in collaboration with several hospitals and one of the chief aims was to try to forecast the general trend of treatment as it proceeded. When a malignant growth is under treatment by means of X-rays the patient is under close clinical scrutiny over the whole time, but the aim here was to supplement this by taking small pieces of the tumour (biopsy) for microscopic examination of the change occurring in it. If these were found to be of a favourable character the routine treatment was continued. If, however, the general trend of cellular changes were otherwise, a cautionary attitude would be taken about a renewal of radiation treatment, and the possibility of operation considered as an alternative. Whatever measure of success the method may have in the future it is at present the only one, apart from observation in the clinic, which attempts to forecast what is likely to be the ultimate response of a malignant growth to a course of X-ray or Radium treatment.

The brief description in the preceding pages of experimental research on cancer does scant justice even to those whose work is mentioned, and there has been no reference to kindred work beyond our shores. It would, however, be unpardonable if no mention were made of the outstanding radiological work of the Institut Pasteur under the direction of the late Professor Claude Regaud and his successor, Professor Antoine Lacassagne. National pride in the discovery of radioactivity may have played some part in determining the role which Madame Curie and Professor Regaud played in 1919 in attempting to place radiotherapy upon a scientific foundation. The classical publications from this centre—*Compt. Rend. Acad. des Sciences*—were carried on until the outbreak of war twenty years later.

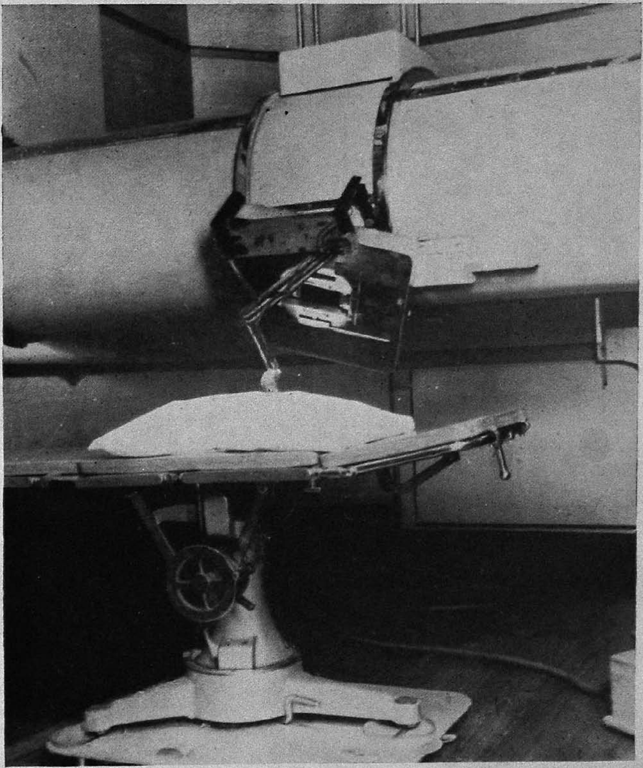
In the wide fields of cancer research there have been notable contributions from America, and special mention should be made of the work of Peyton Rous who discovered a filterable virus associated with a tumour of the fowl ; of Dr Woglom of Columbia University whose contributions to the study of tumour growth rank in importance with those of the Imperial Cancer Research Fund, and of Dr Murphy at the Rockefeller Institute of New York who has made many ingenious attempts at inducing a state of resistance in animals to the growth of malignant tumours implanted in them.

It would take us too far to pursue further the development of experimental work at different laboratories. It should, however, be mentioned that the circle of research workers was enlarged shortly after the formation of the British Empire Cancer Campaign in 1924. Owing to a generous public the Campaign was able not only to give substantial grants to recognized cancer research laboratories, but to men and women attached to other Institutions who wanted to engage in the problem.

Turning to X-ray and Radium therapy, it should be stated at the outset that treatment did not begin as a result of any urge to action by research people, but as a result of the courage and curiosity of the clinically minded, and in a few years their curiosity at least was shared by experimentalists interested in the cancer problem. So it came about that the treatment of cancer started on an empirical basis, but this basis has gradually been underpinned, buttressed and internally strengthened by the application of biological and physical discoveries.

The early days of X-ray treatment have been dealt with in a previous chapter. The subject has grown so gradually that looking down the years it is exceedingly difficult to mark down particular years or even people in those years that could be considered as epoch-making. And yet to the reader it may seem rather invidious in selecting for mention people in the experimental world while we remain silent about those who have been doing such excellent work in the clinics. The only way out of the difficulty seems to make a brief survey of therapeutic developments with reference to where they originated. The first recorded X-ray treatment came from France and the first Radium treatment from the same country. At first the small X-ray tubes could only be run for a few moments, they often broke down and they were difficult to manage. Gradually they became more robust, contrivances were devised to prevent the parts from getting too hot, the voltage applied to them was kept steadier, and it was then raised so that X-rays might be used which penetrated deeper into the body ; this made it necessary for the tubes to be bigger, still more robust and, with more energy being used to operate them, more heat in the tube was produced so that artificial cooling had to be introduced; so radiating fins were mounted on the metal parts while water or oil under pressure was pumped round through parts of the X-ray tube so as to dissipate the heat. And all the time the voltage on the tube was mounting so as to get more and more penetration of the rays—from 100 to 200 kilovolts from 200 to 400 kilovolts, then up to a million and beyond. Perhaps it would be correct to say that the main developments in the construction of X-ray tubes occurred in Germany and America while the ingenuity in devising methods of stepping up the voltage came very largely from the U.S.A. Also the U.S.A. is the country to which one would go to study the developments in what is called super-voltage. Not that this country has stood still in such matters, far from it, as our illustration of the million volt X-ray department at St. Bartholomew's Hospital shows. This was installed in 1936. (Plate XII.)

The methods of using higher and higher voltages seem to have been evolved on lines of sheer necessity. If one employs X-rays generated at say a quarter of a million volts, added dangers to patient and operator arise so that inevitably the rays had to be filtered to screen off those that would play no useful but possibly a dangerous part in treatment. Further considerations of safety made it necessary to protect the staff from the rays while treatment was being given to patients, so in the end an elaborate safety ritual was developed. Modern X-ray hospital departments are now well protected; this is generally done by enclosing the X-ray tube in a holder which is practically ray-tight except for an aperture which can be modified at will. But protection has to go further, because when X-rays strike upon any surface they are scattered in all directions and people have to be protected from this radiation as well as from the direct beam. In treatment with X-rays, protection is generally secured by having one room for the X-ray apparatus and the patient, while an adjoining room is devoted to the necessary controls of the X-ray apparatus, and the radiological staff; the two rooms are usually separated by lead-lined partitions which reach from floor to ceiling. The floor of the X-ray room is covered with sheet lead so that people in



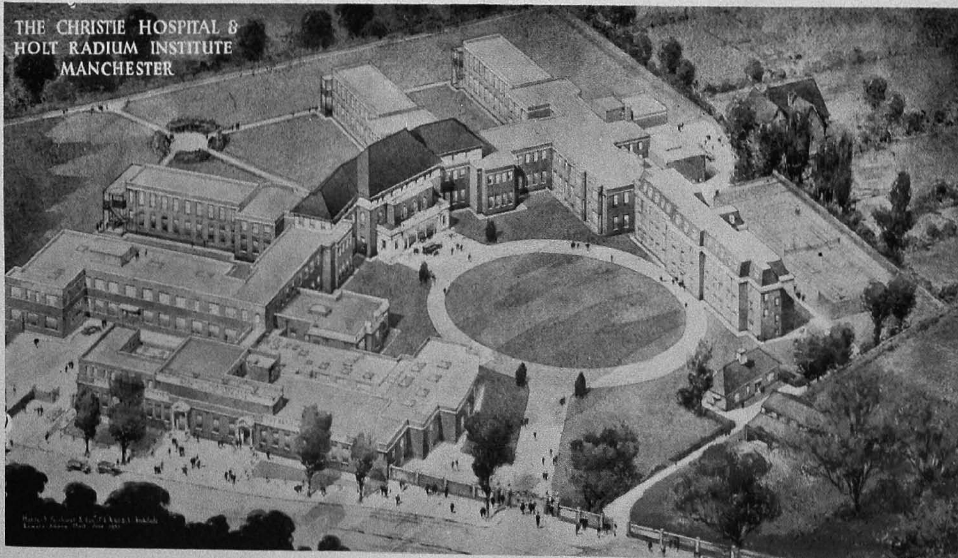
Million volt X-ray tube at St. Bartholomew's Hospital.

the rooms below receive none of the downward radiation. The degree of protection to the staff is almost complete for it is difficult, even by the aid of delicate electrical instruments, to detect any stray radiation at all in such working quarters.

From the foregoing it will be seen that X-ray work has become a rather complex undertaking and this has brought with it the realization that it can best be done at Institutions which have the space and resources which will allow them to keep pace with a subject which so persistently enlarges its boundaries of usefulness. The lay-out of an X-ray department requires a great deal of planning if the best is to be made of the possibilities in front of the governing body. A notable example of planning is the Holt Radium Institute at Manchester under the direction of Dr Ralston Paterson. Views of this centre, at which surgical X-ray and Radium treatments are given, are shown in Plate XIII.

Radium treatment made rapid progress after 1919. In the very early days of Radium treatment the amounts of radium used were very small ; they were put up in plaques and applied superficially, or sealed in platinum tubes and needles which were easily inserted into the cavities or tissues of the body. One of the more important later developments was the use of large quantities of Radium in specially designed and carefully screened containers. These were applied from a distance of a few centimetres rather after the manner of an X-ray tube. The contents ranged from one to as much as ten grammes in recent times and were sometimes called by the inappropriate name of bomb, but more correctly gramme units, one, two five, or ten gramme units according to the content. This form of Radium treatment originated in England in 1920, and was extended in France, Belgium and America.

The Medical Research Council has made two noteworthy attempts at developing the therapeutic use of large Radium gramme units; the first was in 1920 when they placed at the disposal of the Middlesex Hospital 2½ grammes of Radium for a therapeutic trial. The results obtained after about a year and a half are embodied in a publication entitled *Medical Uses of Radium. Studies of the effects of gamma rays from a large quantity of Radium, 1922.* There is no doubt that the investigation would have been continued had it not been for two things, one, the acute shortage of Radium at that time and the other the urgent request that was made for Radium to be split up into smaller quantities so that other centres could develop its possibilities. This was done by using the Radium surgically in small sealed platinum tubes, which held quantities varying from 1 to 50 milligrammes for the treatment of cancer at various sites. The second attempt at initiating work on gramme unit lines was made by the Council in co-operation with other bodies, at the Radium Institute, London, when larger quantities of Radium were available. A team of qualified men and women was concentrated on the problem of how best to use a single



The Christie Hospital and Holt Radium Institute, Manchester.

unit of 5 grammes or more at a time and to examine what cancer cases would be benefited by such treatment and how the results of X-ray and Radium treatment compared with one another. The work of the ' Radium Beam Therapy Research Unit ' was interrupted by the outbreak of war in 1939, but it was started again as the Medical Research Council Radiotherapeutic Research Unit at Hammersmith Hospital in 1942, where it continues at the present time, under the direction of Dr Constance Wood.

Since the year 1935 the subject of artificial radioactivity has developed with truly enormous strides, for it is now known that all substances can be made radioactive. If, for instance, phosphorus is exposed to a kind of intense irradiation a small fraction of it becomes radioactive though chemically this fraction has exactly the same properties as ordinary phosphorus. It is called a radioactive isotope, the word isotope was coined by Professor Soddy; it means that the new substance occupies the same place in the Periodic Table of Elements as the original one.

These new isotopes are often called Tracer Elements because since their atoms are radioactive they can be traced wherever they go, in the body for instance, by delicate electrical means. A growing field of research is in fact widening year by year, both in physiology and in the treatment of disease by means of the new isotopes.

In the ordinary ways of Radium treatment of cancer the element itself does not come into contact with the tissues, it is only the rays which emerge through the walls of a container (needle or otherwise) that affect the tissues, but in the new radioactive isotope form of treatment this is not so, for the actual substances, certainly a very dilute form, are inoculated. The hazards have to be very clearly visualized but the investigations are carried out with a scrupulous regard to the safety of the patient. One of the greatest safeguards is that the substances used do not last very long, they have, in fact, quick rates of decay and when they have decayed the end products are harmless. The subject is as yet too young to say what its value may be in the treatment of cancer.

Soddy
Co-discoverer of Laws of Radioactivity.

CHAPTER X

THE HERITAGE OF PHYSICS AND ITS APPLICATION IN CANCER

Modern treatment of cancer is very largely based on the natural and medical sciences; something has already been said about the development of the latter. When we come to inquire which branch of the natural sciences has so far contributed most towards the present-day treatment of cancer, the answer is physics and this is most clearly seen in the widening scope, year by year, of radiodiagnosis and radiotherapy. Doubtless in the next decade we shall see chemistry assuming a more and more important role. To many readers there is something rather intangible about the whole subject of physics; electricity and magnetism, for instance, are two forces in Nature that still retain a great deal of mystery and though they are controllable to some extent, yet there remains something inscrutable about them and this trend of thought may well lead to the conviction that their study can have little practical value in cancer treatment. Yet such is far from the case and what follows in this chapter is an attempt to trace the chief lines of thought and of experimental research in those parts of physics which bear directly upon the subject of radiology. At first hearing there seems to be very little connexion between theories about the nature of radiation and the results of X-ray treatment in cancer, yet speculation about the nature of X-rays and of the way in which living cells react to their influence, lies at the very foundations upon which the whole superstructure of radiation treatment is based.

With this assurance in mind, the reader may well be able to see for himself the relevance of classical researches in physics in the growth of some of the scientific methods of treating cancer. The men and women who have become world figures are here brought to memory by photographs; the term 'world figure' is used because their names are known not only to physicists but to the world at large. In the subjects of surgery and pathology it would be just as easy to select men who had been giants in their subjects and whose work has been of the greatest value in the study of cancer: Halsted of U.S.A., Virchow and Ehrlich of Germany, Pasteur and Regaud of France, and so on, but, with the exception of Pasteur, we should hesitate to accept them as world figures in the sense in which the term has just been used.

Discoveries are sometimes but not often the work of one man, and no greater mistake could be made than to suppose that the discovery of X-rays came, as it were, 'out of the blue'. This is not to deny that it was a remarkable and surprising discovery—remarkable because of the power X-rays have of penetrating human tissues (and this still remains their most remarkable property, for they are not, generally speaking, a very penetrating kind of radiation); a surprising discovery because X-rays had been generated for years in the type of vacuum vessel known as a Crookes tube, yet they had not been detected.

It was about the middle of last century that the foundations were laid for three outstanding discoveries of 1895-7, namely, X-rays, radioactivity and the electron. We shall not go far wrong in saying that the discovery of electromagnetic induction by Michael Faraday (1837) and the electromagnetic theory of light by Clerk Maxwell (1861-2) were the outstanding achievements in physics in this preparatory period.

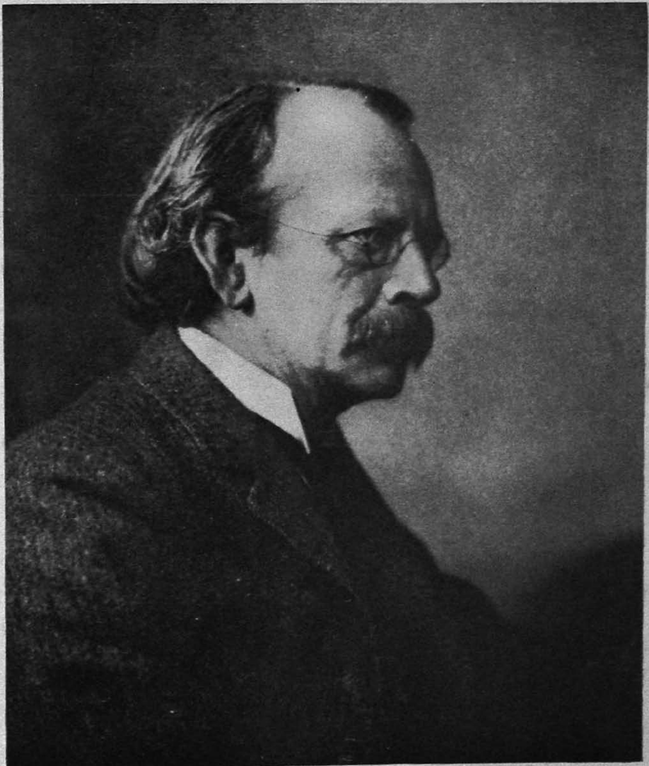
Faraday was not only an experimental genius of the first order, but a man of great imagination. The following note by Faraday in 1819 is, in view of subsequent developments, of such interest to warrant its inclusion here. Faraday had been dealing with various states of matter, solid, liquid and gaseous, and to these he suggested the addition of a fourth state, *radiant matter*. Its existence he admitted was unproved but he submitted a series of analogies which, he considered, rendered such a conception not only possible but probable. It was realized in 1897 by the discovery of the Electron by J. J. Thomson.

I may now notice a curious progression in physical properties accompanying changes of form, and which is perhaps sufficient to induce, in the inventive and sanguine philosopher, a considerable degree of belief in the radiant form with the others in the set of changes I have mentioned.

As we ascend from the solid to the fluid and gaseous states, physical properties diminish in number and variety, each state losing some of those which belonged to the preceding state. When solids are converted into fluids all the varieties of hardness and softness are necessarily lost. Crystalline and other shapes are destroyed. Opacity and colour frequently give way to a colourless transparency, and a general mobility of particles is conferred. The immense differences in their weight almost disappear; the remains of difference in colour that were left, are lost. Transparency becomes universal, and they are all elastic. They now form but one set of substances, and the varieties of density, hardness, opacity, colour, elasticity and form, which render the number of solids and fluids almost infinite, are now supplied by a few slight variations in weight and some unimportant shades in colour.

To those, therefore, who admit the radiant form of matter, no difficulty exists in the simplicity of the properties it possesses, but rather an argument in their favour. These forms show you a gradual resignation of properties in the matter we can appreciate, and they would be surprised if that effect were to cease at the gaseous state. They point out the greater exertions which Nature makes at each step of the change, and think that, consistently, it ought to be greatest in the passage from the gaseous to the radiant form.

Maxwell was the first Professor of Physics at the Cavendish Laboratory in Cambridge and it remained for his three immediate successors, Rayleigh, Thomson and Rutherford, to make discoveries which bore immediately upon the three major discoveries of the end of the century. Rayleigh discovered argon, the first of the so-called inert gases. His collaborator,



J. J. THOMSON
Discoverer of the electron.

Ramsay, went on to discover neon, xenon, krypton, and in doing so developed the technique of manipulating minute volumes of gas which was put to good use in radioactive studies. J. J. Thomson not only discovered the electron (1897) but laid the foundations of our knowledge of the various ways in which electricity is conducted in gases and first proposed an electrical structure for atoms. Rutherford was the great explorer in the fields of radioactivity. One might without offence call him the navvy of science, to judge by the way in which he broke new ground practically every year between 1900 and 1937, the year of his death. This work was not restricted to the subject of radioactivity, but like the master workman that he was, he turned to the particles which he had discovered and made them his tools, using them as projectiles to penetrate the almost forbidden fields of 'within the atom'. Rutherford was the first to do this and *make* something atomic emerge from the atom ; then he started to build up a conception of atomic structure which still holds the scientific mind. The word 'conception' is deliberately chosen here, for there can be no certainty in anything so venturesome; how uncertain is the life of an atomic model can be deduced from the fact that three new particles which all have their place somewhere within the atom have been discovered since Rutherford's conception of the atom was first propounded.

It is a remarkable fact that no nation other than our own has a record of four geniuses in physics holding a single Chair in succession. There is no overstatement in maintaining that the four Cavendish Professors have led the world in experimental physics for three-quarters of a century—they have gone their own way, for the wind bloweth where it listeth, and the way of their going was good. Their vision may be contrasted with the blindness of the fanatics who would seek to compel the man of science, be he genius or not, to toe some chalk line in a laboratory prison.

X-rays are of similar nature to light, though the essential nature of this is still a riddle. Newton first ventured on a theory as to the nature of light with his prime conception of corpuscles and Huygens had countered with waves, a conception enriched by Young, who actually made the waves, like ripples on a pond, interfere with one another. Maxwell had the immediate heritage of Faraday's work, fresh from the mint of the Royal Institution. Faraday's magnetic and electric fields were woven into a single garment that covered the universe; for this electromagnetic field was the substance of light.

A word might be added here on the meaning attributed to the word 'field' among physicists; it is any region of space where the particular force referred to is operating. There are four of these 'fields' which continue to engage the mind of experimentalist and theorist; they are the gravitational, electrical, magnetic and electromagnetic. Though Newton did not actually use this term, it cannot be doubted that he thought of the forces of gravitation extending throughout space. Faraday invented the term field when he attempted to visualize the electric and magnetic effects which he explored so successfully; he supposed that the space in which electrified bodies attracted or repelled one another was permeated by lines of force which constituted the electric field. In a similar way, wherever magnetic forces have play, he visualized lines of force permeating the space between (and indeed throughout) the magnetic bodies; far beyond the reach of any airman the magnetic effects of the earth spread outwards into the field. So with the electromagnetic field of Maxwell; wherever light or X-rays or gamma rays, or heat, or wireless may go, the regions of space concerned are the electromagnetic field.

All of these conceptions represent in one way the supremest flights of imagination of the physicist; they do not, however, explain the *nature* of gravitation, etc. Physicists still have problems that baffle them but inquiry does not stop on that account.

In Maxwell's day the spectrum extended for about two octaves, one occupied by light, a half octave by ultra-violet, the other half by heat radiation (infra-red). He predicted the existence of rays in the part of the spectrum that we now call wireless. We have it on the authority of Sir Arthur Schuster who worked with Maxwell that, so great was his prestige, no one at the Cavendish Laboratory thought it was worth while to produce the predicted radiation! Shortly after

Maxwell's death, the thing was done by Hertz, and for many years the term 'Hertzian waves' was used to denote the new extension of the spectrum. One of the first questions asked, among others by Röntgen himself, was, 'Are X-rays electromagnetic waves in the Maxwellian sense?' He formed the opinion that they were not, but his own countrymen, Laue, Friedrich and Knipping, have shown that they are.

As we have stated elsewhere, only a few months separated the discovery of X-rays and radioactivity. In this case Bécquérel, the discoverer, was at pains to show that the rays emitted by uranium had nothing akin to X-rays, but later research showed that the alpha, beta and gamma rays from radioactive substances have their immediate counterpart in the canal rays, electrons and X-rays generated within an X-ray tube.

Physicists the world over were quick to investigate the properties of X-rays, though it was not until eighteen years after their discovery that their wave character was revealed. The four outstanding physical properties of X-rays are the production of fluorescence in various crystalline substances, photographic action, 'ionizing' power, and the property of penetrating substances ordinarily opaque to light, for example, thin sheets of metal, black paper and the tissues of the body.

These properties of X-rays were recognized by their discoverer, and whereas the first two properties named did not constitute new phenomena, it was quite otherwise with ionization and penetrating power. Ordinary air is a very bad conductor of electricity, but when a beam of X-rays passes through it the conductivity may easily rise many thousandfold. The passage of X-rays through the air causes ions to be formed in the track of the rays; these are positively and negatively electrified atoms, molecules or molecular clusters which can move freely under electric and magnetic forces. The ions can, in fact, be made to register the passage of X-rays, for it is found that the electric current flowing through the air is proportional to the number of ions formed, and this number is proportional to the intensity of X-rays. The intensity of a beam of X-rays is generally measured by an electric current due, directly or indirectly, to the ions formed by the rays as they go through the air or other selected gas. It is true to say that, were it not for this ionization, we should not have a fraction of our present knowledge of X-rays or, indeed, of radioactivity. The detection of ions has become one of extraordinary delicacy and, by way of illustration, we may refer to the 'spontaneous' ionization of the air. The adjective implies that this occurs in the air without any effort or interference on the part of man, but he has been busy for the last twenty years trying to find out the cause of this spontaneity. The fact that even the driest and cleanest air always contains some, even though very few ions, was realized by C. T. R. Wilson and by Elster and Geitel as early as 1900, and Wilson suggested that it might be due to radiation coming from the cosmos, the world surrounding us. But it was not till 1929 that experiment indicated that the so-called 'cosmic' *rays* were charged *particles*, and this view is the one now generally held. One cubic inch of air (N.T.P.) contains about 10^{20} molecules, yet if one of them is ionized per second it can be picked out from its neutral neighbours by delicate electrical detectors and made to register an electrical current. Rutherford was so much at home with the ways of ions that in lighter moments he would refer to alpha rays, which are great producers of ions, as 'jolly little beggars'.

The term 'ion' was coined by Faraday to describe the wandering character of electrified particles which are the active agents when a current goes through a liquid or a gas. They cease to wander when an electric field is applied to them, for they speed quickly under such an influence, and the bigger the voltage difference the greater the speed of the ions. Townsend saw that such a process might have a very important consequence. A person moving slowly through a crowd need knock no one down, but let a madman loose and there are casualties. Townsend found that if he made the gaseous ions travel at great speed through the air they produced many more ions, and this he termed 'ionization by collision'. One ion can thus make thousands of others, and so we get an amplifying action ; this is the basis of action of instruments found not only in physics laboratories, but in the clinic.

Physicists in their X-ray studies were primarily concerned with the ionization set up in gases. This phenomenon was the stand-by of all their measurements and it is worth while glancing back to this period of years, if only to realize what a mass of knowledge accumulated about the nature and properties of X-rays, though it was years later that the nature of the radiation was at least partly disclosed.

The outstanding contributions to our knowledge of X-rays before 1913 were made by Barkla. Without going into detail here about his experimental methods we may mention that if a primary beam of X-rays falls on a metal like silver, it is found that the metal gives off secondary X-rays. Barkla found that these secondary X-rays from metals are characteristic of the metals ; we now say that they differ in their wavelengths.

It was quickly found by medical men as well as physicists that as the voltage operating in an X-ray tube was increased, the penetrating power of the rays generated increased too; this could be realized in radiographs and naturally the voltage on the tube was increased when greater thicknesses of bone or of the body generally were under examination. The physicist measures the penetrating power of a beam of X-rays by finding out what percentage of its energy is absorbed when it passes through a definite thickness of some selected metal. We may say in fact that Barkla sorted out the beams of X-rays by finding out the different degrees to which they were absorbed by thin sheets of metal.

The fact that we get more penetrating X-rays the higher the voltage on the X-ray tube is put to direct service in medical radiology. If one wants a radiograph of the hand there is no need to use very penetrating rays and an X-ray tube running at 50–60,000 volts is adequate; but for radiographs of the shoulder or thigh this would be stepped up to 100–120,000 volts. In X-ray *treatment* the considerations are much more complicated.

There are two chief aims in treating a malignant growth with X-rays or Radium, one is to give the cancer cells a dose which will cause them so much damage that they will degenerate and eventually die ; this is the lethal dose. The other aim is to cause as little damage as possible to the normal healthy cells of the body. If a deep-seated tumour is being treated by means of X-rays applied to the surface of the body it is evident that a thickness of tissues above the tumour will get more radiation than a similar thickness of the tumour because the X-rays are gradually absorbed as they penetrate the tissues. This handicap is to some extent lessened by the technique known as 'cross-fire', and it is quite frequently arranged that there are four ports of entry in the direction of the tumour, one front and back and two laterally. In this way and other ways the normal tissues are spared undue irradiation.

The need to get an adequate 'depth dose' is one which accounts for the important steps which have been taken in the last fifteen years to increase the penetrating power of X-rays used in treatment and here the electrical engineer has, in a way, taken over from the physicist. High tension X-ray apparatus, working at a million volts has, however, not been very much used in this country, though extensive use is being made of such apparatus in the U.S.A. In 1936 a million-volt X-ray plant was put into operation at St. Bartholomew's Hospital, London, and the reports which have issued from the department in question give the fullest justification for its continued use. It is likely enough in the near future that X-rays at even higher voltages than this will be put at the disposal of radiologists in their treatment of malignant disease.

It should, however, be understood that these higher voltages are, generally speaking, designed and used for one purpose only and that is to increase the penetrating power of the X-rays. This necessitates larger scale, sometimes very large-scale, apparatus but it is not to make the beam of X-rays used a stronger one; there are plenty of rays from X-ray tubes run at a quarter of a million volts, but there is rather a lack of penetrating power in them when they are used for treating any condition at a depth in the body.

This chapter may be closed by brief reference to the part which physicists now play in the treatment of cancer by means of X-rays and Radium. The main lines of any such treatment are determined by the medical radiologist, but the details of dosage and technique are matters in which the physicist collaborates. Since 1928, when an International Unit of X-rays was agreed upon, the dispensing of X-ray doses has been an act which is prescribed just as rigorously as a dangerous drug would be and this attitude of precision among those now carrying out radiotherapy is reflected in the degree to which the Hospital Physicists' services are used. In large therapy centres there are often several physicists engaged and it is unusual for radiotherapy under modern conditions to be carried out without their assistance. A Hospital Physicists' Association was formed in 1943.

CHAPTER XI

THE RESULTS OF X-RAY AND RADIUM TREATMENT OF CANCER

After any method of treatment has been used over a period of years it is but rational to review the value of its effectiveness, and this has been done from time to time in the case of X-rays and Radium. These agents are so often complementary to one another in treatment that the results of their action may with advantage be considered together; when the question arises as to which is the better form of treatment the answer is that Radium is more suitable in some cases and X-rays in others, while for some malignant growths a combination of both is best.

The use of these agents is of outstanding interest and importance in the treatment of cancer, though there is a wide field for them also in non-malignant disease. Their importance in the treatment of malignant disease arises from the fact that before their advent there was no other form of treatment than surgery, and surgeons are not silent in their opinions about the limitations which beset them in trying to eradicate malignant growths by means of the knife; if they can be completely removed by this means then the prospects for the patient are good, but if not, recurrence must be expected.

It may be said that X-rays and Radium have fully justified their use in the treatment of some types of cancer ; this statement is not to be taken as a mere expression of personal opinion ; it is better to let the facts speak for themselves. It is now recognized that these agents are more effective than surgery in the treatment of cancer of the tongue, and mouth, and of the womb. In the case of breast cancer it is true to say that the results with radiotherapy are no better than those obtained in surgery, and, in some cases, they are not so good. Research continues on the response of other forms of cancer to X-rays and Radium, but it would take us far beyond the general scope of this book to deal with this subject over the whole variety of cancer in the body.

Significant facts about the results of treatment have been accumulating in this country during the last fifteen years, largely due to the work of the Medical Research Council, the Radium Commission and many individual hospitals where these have had well-organized centres of radiotherapy. Valuable data have been collected in the Council's yearly publication, *Medical Uses of Radium*, and some selection has been made from them in the following pages.

In the treatment of cancer of the womb, there are two conditions which receive quite different consideration ; in one the disease originates in the neck of the womb (the cervix uteri) and it is quite localized in the early stages ; in the second condition the body of the womb is the site of the growth. Both types, if left unchecked, spread into the neighbouring structures. As mentioned before, in this disease the more localized it is, the better the chances are of adequate treatment; once extension from the .primary site begins, these chances diminish very significantly. So well are the various stages of cancer of the cervix uteri known and recognized that it is usual to classify patients in four stages, the first indicating that the growth is purely local, the second that extension has begun but the case is still considered operable, the third that the growth has become so extensive that it is non-operable, and any classification into stage four signifies that the condition is a very grave one. Nevertheless, it is often treated radiologically to relieve symptoms and results show that by this means life is sometimes prolonged and pain alleviated.

Cancer of the body of the womb is much less frequent than cervical cancer. In her book, *Cancer of the Uterus*, the late Dr Elizabeth Hurdon, who was at one time in charge of the work at the Marie Curie Hospital, London, stated that during the years 1932-7 the number of patients treated for cancer of the neck of the womb was 807, while over the same period the number relating to the body of the womb was 221.

The data in Table V are taken from and refer to the results obtained in the Radium treatment of cancer of the cervix uteri; in some cases supplementary treatment by means of X-rays was given. The classification of the Stages is often referred to as the League of Nations Classification.

No emphasis should be laid upon the actual percentages when the numbers in question do not actually reach the figure one hundred.

TABLE V

Five-year Survival Rates at the Marie Curie Hospital.
Cases treated between October 1925 and December 1939.

Stage	*Number of patients*	*Five-year survival rate*
I	40	34 = 85·0 per cent
II	170	104 = 61·1 " "
III	459	147 = 32·0 " "
IV	133	11 = 8·2 " "
I-IV	802	296 = 36·9 " "

It is maintained by statisticians that significant variations in percentage results can occur when the numbers provided do not amount to as many as four hundred. More reliable statistical information can be obtained by collecting data from a number of hospitals which have adopted the same method of grouping their cases according to the severity of the disease, in the manner already described.

In Table VI are collected the returns over a period of years from the following ten hospitals:

Aberdeen, Royal Infirmary.
Birmingham, General Hospital.
Cardiff, Royal Infirmary.
Dublin, St. Anne's Hospital.

TABLE VI

Cancer of the Cervix Uteri.

L. signifies Living; D., Dead.

Year	Interval since irradiation (years)	No. of patients treated	Stage I		Stage II		Stage III		Stage IV		Total	
			L.	D.	L.	D.	L.	D.	L.	D.	L.	D.
1930	8	296	22	25	26	55	25	104	5	34	78	218
1931	7	298	23	30	18	57	24	93	3	50	68	230
1932	6	296	32	24	27	47	24	102	3	37	86	210
1933	5	301	25	19	28	54	31	95	5	44	89	212
1934	4	321	25	32	30	57	39	94	5	39	99	222
1935	3	359	33	17	55	59	46	107	5	37	139	220
1936	2	332	44	17	60	43	42	85	5	36	151	181
1937	1	386	58	24	84	30	93	70	5	22	240	146

King's College Hospital.
Marie Curie Hospital.
Middlesex Hospital.
Royal Free Hospital.
St. Bartholomew's Hospital.
University College Hospital.

Taking the year 1933 we see that out of 301 patients treated by means of Radium often supplemented with X-rays there were:

44 patients in Group I:	19 died,	25 survived 5 years.
82 " " " II:	54 "	28 " " "
126 " " " III:	95 "	31 " " "
49 " " " IV:	44 "	5 " " "

Bearing in mind the warning of the statistician, the percentages work out among the different groups as 56·8, 34·1, 25 and 10·2 respectively. Three facts may be particularly noticed, one is that if a patient is in Group I, the chances are rather in her favour that she will be living at the end of five years, the second is that nearly as good results may be obtained with Radium treatment among patients of Group III as Group II. The reader may find this difficult to reconcile with the data in Table V; it is most probably explained by inevitable differences of opinion among clinicians as to how particular evidences of the disease are to be classified. The third fact which compels attention is that of the 394 patients in Group I treated in the year 1937 only 82, i.e. *20·8 per cent, came for treatment* *when the disease was in its early stages.* Facts like this should become more widely known and so help towards breaking down the barrier which still seems to prevent women seeking early medical advice, even when signs they know only too surely tell them that all is not well.

X-ray and Radium treatment of the breast is faced with formidable difficulties, and they have not been overcome. It is expecting too much of these agents and of those who use them, to think that the treatment of this problem can easily be solved. If a small nodule in the breast is discovered quite early, then there is a good chance that if it is surgically removed in its entirety there will be no recurrence, but in the vast majority of cases of patients who seek medical advice on this matter, other manifestations are evident, for the original tumour has begun to spread. The tumour may spread but still retain contact with the original tumour or it may disseminate into other regions of the body, and this constitutes its greatest menace ; if it has already spread to the glands in the armpit it is serious, if to some glands localized in the upper parts of the chest it is still more serious, and with dissemination farther afield such as to the liver the condition becomes well-nigh hopeless. With every advance in this process from the primary growth the difficulties of radiotherapy mount up.

We shall expect, therefore, to see good results only in the early stages of cancer of the breast, and in view of the fact that this has also been attained by surgical means, the question arises as to whether one method is preferred to the other. This is answered later in the text.

There are few surgeons who now operate on localized cancer of the tongue, not only because the results of Radium treatment are good but because the operation is of necessity a mutilating one. The results obtained in Radium treatment of cancer of the tongue, mouth, lip, cheek, larynx, pharynx and oesophagus at the same group of hospitals are collected in Table VII.

So far the data presented have, except in the case of the Marie Curie Hospital, been drawn from general hospitals where the treatment of cancer is but one of many activities. We may now turn to the work of a centre designed for the treatment of patients suffering from cancer and organized so as to serve not only the city in which it stands, but a large part of the surrounding country. The Christie Hospital and Holt Radium Institute, Manchester, was formed in 1933, by the fusion of the Christie Cancer Hospital and the Manchester Radium Institute. At this centre all varieties of cancer are referred for opinion ; if the interests of the patient are best served by surgery then that form of treatment is advised, for although this Institute specializes in radiotherapy designed and carried out under the best conditions, other forms of treatment are given if they are considered more suitable.

We may begin with the Radium treatment of cancer of the cervix uteri and it should be understood that the

Data collected in the year 1938.

Table VII

Cancer of the Mouth, Nasopharynx, Larynx and Oesophagus.

Year	*No. of cases treated*	*Tongue*		*Floor of mouth*		*Palate tonsil and fauces*		*Lip*		*Cheek*		*Larynx*		*Pharynx, naso-pharynx and pharyngeal wall*		*Oesophagus*	
		L.	*D.*	*L.*	*D.*	*L.*	*D.*	*L.*	*D.*	*L.*	*D.*	*L.*	*D.*	*L.*	*D.*	*L.*	*D.*
1925	42	1	8	0	2	0	6	1	2	0	3	0	5	0	5	0	9
1926	49	0	8	0	7	0	7	1	2	0	2	0	7	0	4	0	11
1927	61	0	20	1	4	0	8	2	4	0	2	0	7	0	1	0	12
1928	111	1	48	0	7	1	14	5	3	0	6	0	9	0	3	0	14
1929	141	6	43	0	19	2	9	7	11	0	2	0	7	0	9	0	26
1930	349	11	101	7	35	1	33	10	37	3	18	1	31	2	24	0	35
1931	366	12	85	6	34	4	33	29	43	2	11	0	24	2	33	0	48
1932	376	18	100	6	25	8	48	36	34	4	10	1	24	2	24	0	36
1933	391	13	85	13	19	11	48	42	45	10	15	0	23	1	43	0	23
1934	460	20	102	7	29	6	47	65	47	8	22	6	27	2	27	1	44
1935	560	25	110	25	29	15	63	72	58	12	16	5	49	3	31	0	47
1936	558	44	99	21	35	19	55	116	50	14	10	9	37	4	13	0	32
1937	586	59	79	28	37	31	41	138	28	18	12	14	42	10	21	3	25

Radium is often supplemented by X-ray treatment, though not expressly stated in every case, *vide* 1945 Report.

Five-year results may be seen in Table VIII.

TABLE VIII

Cancer of Uterine Cervix.

Treated by Radiation, showing stages and number of patients alive and dead five years later.

(Includes recurrences after treatment elsewhere.)

Stage	*Number treated* 1934-8	*Alive*			*Dead*		*Not traced*
		No evidence of cancer	*Cancer present or indeterminate*	*Total*	*Cancer present or indeterminate*	*No evidence of cancer*	
I	48	28	2	30	16	2	—
II	292	114	2	116	159	13	4
III	241	58	3	61	169	6	5
IV	245	14	1	15	228	—	2
Total	826	214	8	222	572	21	11

Number of cases too advanced for treatment 73.

Something has already been said in the preceding pages of the special problems presented by cancer of the breast. We may quote from the Report of the Holt Radium Institute here:

At this Centre surgery continues to be regarded as the method of choice in the treatment of early cancer of the breast. This does not mean that radiotherapeutic methods are not successful in the early cases but the treatment is, if anything rather more trying for the patient than surgery, and the results are no better. There is therefore no reason to exchange the well-tried method of complete excision for a new one which up to the present seems to offer no special advantages.

Unfortunately, in spite of its accessibility, cancer of the breast is *often first seen at an advanced stage*, the main reason being the painless onset. At this point operation is no longer possible and yet either Radium or X-ray may prove successful.

Because of this policy the group of cases analysed contains a very high preponderence of late cases and any sample designed to show the real treatability of breast cancer would also have to include the early surgically treated cases to get a true balance. In order to make this point quite clear the following Table is presented which indicates the results of good surgery in cases still easily operable or just operable. The information is taken from the Report No. 51 issued by the Ministry of Health in 1939.

TABLE IX

Lane-Claypon Table (British Centres Only)
(non-statistical cases deducted).
Surgical treatment of cancer of the breast.

Stage	*Number treated*	*Five-year survival*
I	334	71%
II	485	32%
III	397	21%

It should be noted here that the staging is rather different from that hitherto given but not enough to prevent comparisons being made.

TABLE X

Radiological Treatment of Cancer of the Breast, Christie Hospital and Holt Radium Institute.

Showing the number of Patients alive or dead five years after treatment (includes post-operative recurrences (staged) and prophylactic irradiation (unstaged: bottom row)).

Stage	Number treated 1934-8	Alive			Dead		Not traced
		No evidence of cancer	Cancer present or indeterminate	Total	Cancer present or indeterminate	No evidence of cancer	
I	69	28	7	35	29	5	—
II	99	28	9	37	58	4	—
III	245	27	17	44	190	10	1
IV	342	8	6	14	327	—	1
—	863	126	45	171	666	21	5

The information in the preceding pages does not cover the whole field of radiation treatment of cancer; the particular sites have been chosen deliberately, not because they show radiation therapy in its best possible light (the treatment of skin cancer would for that purpose have been given prominence) but because in two of the categories chosen, surgery has largely given place to Radium and X-rays, and in the other, namely cancer of the breast, the position is rather that surgery is still the method of choice in early cases, with X-rays and Radium a valuable supplement. Though it is not possible here to go farther into the results for other forms of cancer, we may include here Table XI from the Holt Radium Institute 1945 Report giving the survival rates for *all patients* suffering from cancer who received treatment in the years 1934-8.

TABLE XI

Cancer—all sites grouped together, treated by Radiation, showing stages and number of patients alive and dead five years later. (Includes post-operative recurrences (staged) and prophylactic irradiation cases (unstaged).)

Stage	Number treated 1934-8	Alive			Dead		Not traced
		No evidence of cancer	Cancer present or indeterminate	Total	Cancer present or indeterminate	No evidence of cancer	
I	1,727	1,162	19	1,181	169	330	47
II	1,862	692	39	731	902	196	33
III	881	152	24	176	663	33	9
IV	1,722	100	21	121	1,574	16	11
—	188	80	6	86	87	10	5
Total	6,380	2,186	109	2,295	3,395	585	105

It has already been mentioned that differing medical opinions will account for the fact that patients suffering from cancer are classified in order of severity of disease in a manner which varies from one hospital to another. In the same way a differing medical outlook upon the best form of treatment for individual cases accounts for the fact that a patient may be advised at one hospital to submit to surgical treatment and at another that radiotherapy is the method of choice. We cannot say that the advice of one is right and the other wrong, for it is inevitable that such differences in outlook exist; even in a single hospital there may co-exist differing *bona fide* opinions on the best mode of treatment. For this reason, among others, the following information is taken from the records of the Middlesex Hospital, a hospital which has for many years maintained a high interest in cancer and its treatment.

Treatment of uterine cancer is classified in the categories of Surgery or Radiation, and the data that are recorded in the following Tables refer to 179 patients suffering from this disease who were seen at the Middlesex Hospital during the years 1931-4 and who had received no previous treatment. Each patient was seen in the first instance by the surgeon, and only those who were inoperable because of their general condition were referred for X-ray or Radium treatment.

Readers will remember that patients thought to be operable form Stages I and II in the League of Nations Classification. The results of surgical measures among 64 out of these 179 patients are seen in Table XII.

TABLE XII

Results of Surgical Treatment.

	Number treated	*Died of operation*	*Died of*		*Un-traced*	*Five-year survival*
			Cancer	*Other causes*		
Glands not invaded	46	6	16	3	2	19
Glands invaded	18	5	8	1	0	4
Total	64	11	24	4	2	23

Turning now to X-ray and Radium treatment, the data in Table XIII refer to 104 patients; 11 out of the total number received neither surgical nor radiation treatment.

It scarcely need be said that patients in Stages I and II of the disease are better subjects for treatment with

TABLE XIII
Radiotherapy.

Stage	*Number treated*	*Treat-ment mortality*	*Died of*		*Un-traced*	*Five-year survival*
			Cancer	*Other causes*		
I	12	0	5	0	0	7
II	13	1	7	1	0	4
III	43	2	27	1	0	13
IV	36	2	32	0	0	2
Total	104	5	71	2	0	26

X-rays and Radium than patients in the latter stages, just as they are for surgery and so there need be no surprise at the fact that a higher five-year survival rate has resulted from surgical measures among this group of patients than from the other method. The object has not been to compare the results of surgery and radiation, this has already been done. But to state this and leave the matter would be to miss a very important point of the record; for had the group of 179 patients presented themselves at this same hospital before the advent of X-ray and Radium treatment, 64 of them might well have been operated upon, but what of the remaining 115? *There would have been no other form of treatment for them.*

The foregoing brief recital of some significant data relating to cancer treatment should not be taken to represent the extent of radiological treatment to-day. Though surprising perhaps, some of the marked successes are those we hear least about; this is because their numbers are small. In a review like the present one, a sense of balance necessitates the selection of those sites of cancer which affect a considerable fraction of the population, and so there would be no justification for any but the barest mention of these rare successes. Even so the reader should know that several blood diseases, cancer of the bladder and the cancerous invasion of bone are often greatly relieved by timely radiotherapy. Finally, brief mention has to be made of some non-malignant conditions which may cause great suffering and mental misery in women; the haemostatic action (i.e. the arrest of bleeding) of Radium and X-rays can bring complete relief in these conditions when treatment is carried out by the expert.

Some forms of cancer are more successfully treated by surgical than by radiological methods. An outstanding example is cancer of the rectum and the degree of success in treating this disease is very considerable; this has only been achieved by a combination of surgical skill and pathological study. In order to give the reader the present position, the following information has been taken from W. B. Gabriel's book on *Rectal Surgery* (1948). The extent of the disease is indicated by Groups A, B and C, which represent early, middle and late cases and as in other sites which have already been considered, the earlier the stage at which the case is seen the more likely is success to attend treatment. In Table XIV are collected data relating to 247 cases of cancer of the rectum treated by surgical methods by Gabriel and it will be seen that 50 per cent of these patients survived five years.

TABLE XIV

Five-year survival rate after Perineo-abdominal Excision of the Rectum.

Group	*Number of operation survivors*	*Died in less than five years*	*Alive at end of five years*	*Per cent of five-year survivors*
A	36	9	27	
B	81	30	51	
C	130	85	45	
Total	247	124	123	50

The data so far on the treatment of cancer have been collected from important centres in the British Isles; it is inevitable that they will be of more interest to most of our readers than data selected from the wide world. Yet it would be unfitting to say nothing of the efforts made by people outside our own country to advance the radiological treatment of cancer. France, Sweden, Germany and the U.S.A. have made notable contributions in this respect. Almost immediately after the 1914-18 war the Institut du Radium, Fondation Pasteur, came into being, and the work for many years was linked with the names of Madame Curie and Professor Regaud. The rest of France, through its Centres Anti-Cancereux, looked to the Institut for guidance in X-ray and Radium treatment. The results at the Central Institut compare favourably with those of any centre in the world.

We may make a comparison between the results of radiation treatment of cancer of the neck of the womb at the Institut du Radium, Paris, with those which have already appeared in the text. The results are given in Table XV and refer to large numbers of patients *five years* after treatment was completed.

TABLE XV

Among the 1,430 patients treated between 1929 and 1941, 598 (41%) were alive and well, with variations from one year to another of 33·3 to 51%.

13 were alive, but had recurrence of the disease.
754 were dead, due to the disease.
40 had died of intercurrent disease, after less than 5 years.
25 were lost trace of.

Grouping according to the Stage of the Disease the results were:

Stage I. 228 patients treated.
148 (64%) were alive, with variations from one year to another of 37 to 81·2%.

Stage II. 652 patients treated.
297 (45·5%) were alive, with variations from one year to another of 35 to 67·5%.

Stage III. 421 patients treated.
134 (31·8%) were alive, with variations from one year to another of 10 to 41%.

Stage IV. 129 patients treated.
19 (14%) were alive, with variations from one year to another of 0 to 35%.

Once again reference must be made to the small proportion, *228* out of a total of *1,430*, i.e. only 16 per cent of the patients, in the early operable Stage I of the disease. This compares with 20·8 per cent returned by the British Hospitals (*vide* p. 127); so we are at least no worse off in this serious matter than our neighbours.

In Sweden, Professor Forssell, combining his radiological knowledge with his diplomatic abilities, was responsible for the allocation of money, subscribed by the people as a gesture of affection for their King, towards building and equipping a fine treatment centre known as the Radiumhemmet in Stockholm; here again the results published yearly go to show that they are on about the same level as the best in this country. In the U.S.A. the biggest technical advantages have been in the domain of X-rays generated at very high voltages. When sufficient time has elapsed, results of treatment with high voltage can be compared with those in the preceding pages. Should it be proved that, other factors being equal, high voltage X-rays give better results than can be achieved with comparatively low voltages (less than a quarter of a million), then all the effort and expenditure will be justified.

The world-wide efforts to treat cancer by means of X-rays and Radium have been abundantly worth while. It is difficult to know exactly what perspective the reader may individually bring to bear upon the subject of treatment. If he scans the data at a time when extravagant claims about radiotherapy are being made, it is easy to see that the results may fall short of his expectations ; if, on the other hand, he happened forty years ago to walk through the cancer wards of a big hospital, and saw that the patients, all inoperable, were receiving no *active* medical treatment whatever, his reaction will be profoundly different. For there is no doubt whatever that life is often saved by radiation treatment ; when it is not saved it is often prolonged, and even when it is not appreciably prolonged it can be made more bearable by the timely and judicious use of X-rays and Radium by people specially qualified to use them. This is, indeed, the consensus of opinion among the chief centres of radiological treatment of cancer throughout the world.

Radiology was slow in becoming a recognized speciality in Medicine. This was perhaps partly due to the fact that there was no distinction of an academic character by which the radiologist could be recognized as having some claim to the status of a specialist.

In 1922 the University of Cambridge initiated a Diploma in Medical Radiology and Electrology (D.M.R.E.), the candidates for which had to be medically qualified before they could enter the course of instruction. This was twofold in character, the shorter course covering the ground of physics especially relating to the two subjects and the other including both diagnosis and treatment by means of radiological and electrical methods.

This was a very important step in many ways. It gave status to the two subjects, and it ensured that those deciding to take up this sort of medical work had definite courses of instruction in general working principles.

The example set by Cambridge was quickly followed by Liverpool and by Edinburgh Universities. Later on the University of London and the Conjoint Board of the Royal Colleges decided to institute Diplomas in Medical Radiology. So widening are the boundaries of Diagnosis and Treatment that each has now a Diploma to itself at the last-named Institutions. Even so, specialization is not entirely met by these Diplomas, for the radiologists in recent years decided to institute a Faculty of their own, one of whose activities is to make a further recognition of advanced knowledge on these subjects by examination for their Fellowship.

It will be easily understood, therefore, that from a strictly professional point of view it is not expected that anyone medically qualified will undertake the radiological diagnosis or treatment of a patient unless he can show that he has every warrant for doing so. This does not mean that a surgeon or gynaecologist is not entitled to use X-rays or Radium, but it does imply that the surest and best ways of doing so are in collaboration with a radiologist; this is fast becoming the usual practice in this country.

CHEMICAL TREATMENT OF CANCER

We have seen how the discovery of a way of cutting very thin sections of the tissue of a tumour and the staining with dyes of these sections opened up an epoch of great importance in the diagnosis of cancer. The pathologist was able to classify the different kinds of malignant tumours by their characteristic patterns revealed by microscopical examination of these stained sections of tissue. The varied pattern is not only evidence of their complicated structure but also of the differing chemical affinities among the normal tissues of the body as well as among malignant tissues. This chemical affinity is shown by the fact that the tissue is stained by the dye, the dye is indeed fixed by the cells and as the study of this process went on a kind of micro-chemistry was evolved.

This subject had a great deal to do with the growth of a new science, bio-chemistry, by which we understand the study of the chemical processes involved in living matter. The staining of a section is not a bio-chemical process because the staining is carried out when the tissue in question is dead; but nevertheless a knowledge of the staining reactions did show at an early stage (100 years ago) that there was a great diversity in the chemical affinities among the cells and tissues of the body.

In the course of time the chemistry of respiration and of excretion were studied in great detail, then tentative steps were taken on some of the more difficult problems in the vast subject of metabolism. This term is used to denote the innumerable changes that occur in the various organs of the body for its general maintenance. Food is taken in by the body, it is digested and assimilated and somehow or other nutrition of the whole organism is brought about. Metabolic studies have allowed an accurate estimate to be made of the nutritional value of the various components that enter into our normal diet.

The body is served by glands which have been called the great regulators of the body. Some of these glands have ducts by which the fluid produced by the gland is discharged into the body; others are called ductless glands and the products of these glands are called hormones.

The study of glandular products has grown to very big proportions, and it is noteworthy that within recent years attention has been drawn to the possibility that since they in many cases control or regulate important functions of the body, including actual growth, they might influence the growth of a malignant tumour in the body. One instance of this has already been mentioned in the use of a synthetic oestrogen called stilboestrol in the treatment of cancer of the prostate.

In the Chester Beatty laboratories of the Royal Cancer Hospital, under the direction of Professor Haddow, elaborate studies of a bio-chemical character have been carried out with a view to their application in cancer. As Professor Haddow reminds us, ventures in chemotherapy long antedate the *modern* developments in surgery, for at different times in the past fifteen hundred years, there have been applied such diverse agents as belladonna, aconite, mercury, antimony and arsenic. It has been a policy for many years at the Middlesex Hospital to examine the claims of those putting forward cancer 'cures' and provided certain guarantees were forthcoming, trials are made of these so-called cures. In a publication, *Cancer Research at the Middlesex Hospital, 1900-1924*, Sir Henry Morris contributed the following lines upon this subject:

> It is the duty of the surgeons of the Hospital to try all remedies stated to be cures for cancer provided they are not secret preparations, and that their known composition is a guarantee that they will not act poisonously or harmfully on the patient. Hence in our respective wards, de Morgan, Nunn, Hulke, Lawson, and I tested a goodly number of reputed 'cures'. Acetic acid slowly injected through a capillary tube, bromine, cocaine, conduranga, chian turpentine, thyroid extract, high-frequency electric currents, cancroin, violet leaves and escharotics of arsenic were each given a trial.

The verdict upon any method of treatment of cancer is not given by any one individual, it is given by Time. We must conclude, in view of the fact that not a single one of the substances listed by Haddow or Morris is now in use as a means of 'curing' cancer, that the claims have not been upheld in the course of time. Yet it would be wrong to state that they were useless for in fact some of these agents did bring local relief, very often in the way of clearing up some local infection.

Modern methods in chemotherapy are highly scientific in the sense that no one can expect to take part in their laboratory development without specialized chemical knowledge. Those engaged in this way are under no illusions about the difficulty of the problem and it requires a fine degree of intellectual integrity to write dispassionately upon one's own selected life work, as Haddow does in *The British Medical Bulletin*, Vol. 4 (1947), pp. 417-26:

> The fact that the cancer cell is but a modification of the normal somatic cell holds out little prospect of a *chemotherapia specifica* in Ehrlich's sense, whereby chemical substances which, on the one hand, are taken up by certain parasites and are able to kill them, are, on the other hand, tolerated well by the organism itself or at any rate without too great damage. Further, the conversion of a normal into a malignant cell is possibly brought about by a reorientation of enzyme constitution of such a kind as would not necessarily involve any great change in protein structure or immunological specificity.

The reference to Ehrlich is in his discovery of salvarsan in the treatment of syphilis ; this was a drug which killed the spirochaete (the cause of the disease) without unduly damaging the tissues of the patient. There is no doubt that this discovery of Ehrlich raised high hopes that a similar discovery would be made for cancer; if for one disease, why not for the other? It is just in this connexion that we do well to remember that cancer is not like other diseases for it arises from the healthy tissues of the body and not as a result of some infection from without; for this reason biochemists look upon a malignant tumour as composed of tissues not very different in their chemical interchanges from the normal cells of the body.

Again to quote from the same author:

> Cancer is no ordinary disease, but rather the unique development of a new and specific cell-type in response to unfavourable conditions; this again is one of the inherent difficulties besetting any attempt at chemotherapy, namely, that we are in effect expected to undo what can almost be regarded as a natural process, which proceeds in one direction with facility, but must from its essence be considerably more difficult to reverse. In the writer's opinion the best prospects of success, and certainly the most satisfying intellectually, should come from persistent investigation of the mode of action of carcinogens, so that by increasingly exact and quantitative knowledge of the process as it occurs in one direction, we may estimate at any rate the feasibility of its deliberate reversal. While this may seem a counsel of perfection, the indications are that the problem is very likely just soluble, even although success must depend upon a very considerable extension of our present knowledge, particularly in the direction of a comparative assessment of the specific growth-requirements of normal and malignant cells. If, however, such a solution were to be looked upon as an unattainable ideal—and it is true that we do not yet know any chemical substance capable of producing permanent regression—it is entirely possible that useful

therapeutic effects may be brought about by substances powerful enough to inhibit the mechanism of cell-division in tumours (directly or indirectly), without affecting the normal tissues unduly. It is perhaps a measure of progress that while we knew of no such substances even a few years ago, we now have three examples—in the treatment of cancer of the prostate with oestrogens, in the action of chloroethylamines in certain cases of Hodgkin's disease and other lymphadenopathies, and in the effects of urethane upon the immature cells in leukaemia. Admittedly, all these examples have very manifest imperfections as practical measures, since none of the drugs is curative and their effects are usually temporary. There is, however, no doubt at any rate of their theoretical importance, as showing that the cancer cell is more susceptible to specific interference than was thought to be possible less than ten years ago.

An excellent example of the relief of symptoms by means of a drug is in the use of the nitrogen mustards (chloroethylamines). In a Report (1948) from the Royal Cancer Hospital, details of this treatment were given. Forty-one cases of cancer of the bronchus which were unsuitable for any other form of treatment, were given injections of one or several varieties of chloroethylamines, and relief of symptoms and objective signs of improvement were noted in approximately one half of the patients. Over half the patients had relief from their most distressing symptoms and anyone who has experienced pain 'deep in the chest' will realize what relief from such pain can be, to the mind as well as the body.

We shall do well to keep Haddow's statement in mind: 'None of the drugs is curative and their effects are usually temporary.' No reputable chemotherapist claims that he has a drug which can cure cancer, yet drugs are in use for treatment for very good reasons; they can alleviate symptoms and often keep the disease in check.

CHAPTER XIII

HISTORICAL NOTES ON CANCER AND ITS TREATMENT

There is now a general consensus of opinion that the civilization of Ancient Egypt is not only the oldest in the world, but is the ultimate source from which all other civilizations have originated. 'It is now a finally established fact', wrote H. Breasted in 1926, 'that civilization first arose in Egypt, followed a few centuries later by Babylonia.' It is fortunate that it is precisely this most ancient of civilizations that has bequeathed to us the most complete series of records of man's life and doings, from the dawn of history, *circa* 7000 B.C., to dates well within the Christian Era. Our information is derived from two main sources, from actual human remains preserved by sand-burial or mummification, and from papyri and other written records. From the medical point of view it will, perhaps, be more convenient to deal in the first instance with the anatomical remains, and of these we may suitably begin with the material discovered in an ancient cemetery in Nubia during the excavations on the site which was subsequently to serve as a reservoir in connexion with the Aswan dam. These finds were, in 1910, made the subject of a report by Elliot Smith and Wood Jones. Some thousands of bodies were disinterred, of which about six thousand were submitted to expert examination, and form the basis of the report. In point of date they varied from predynastic times[1] until the earlier centuries of our present era. The desiccating effect of the sand in which these bodies were buried had been so efficient in securing their preservation, that in many cases the soft parts were sufficiently well preserved for pathological conditions to be made out. Thus, pleural adhesions and adhesions in the site of an old appendicitis were sometimes obvious, while lung tissue was found in such a condition as to admit of microscopic sections being made and prepared for the demonstration and differentiation of bacteria. It was of interest to note that very few bodies of young persons were found as compared with the present-day death rates; indeed, if the findings in the Nubian cemeteries can be taken as representing a true index of mortality, then the death rate among the young was less than a fifth of what it is to-day. Of malignant disease, tuberculosis or rickets, there is no evidence. One set of diseases was, however, exceedingly common, so much so indeed, that, in the words of the authors of the report, 'the various pathological changes in bones and joints which are grouped collectively under the title of "rheumatoid arthritis", are so common in the bodies of all periods, that it is true to say that "rheumatoid arthritis" is par excellence *the* disease of the ancient Egyptian and Nubian'. The

[1] The date, *circ.* 3400 B.C., is probably about the date of Mena, the first king of the first Egyptian Dynasty. The term predynastic refers to persons and events previous to that date.

farther back one goes, the more prevalent does this disorder—or perhaps we should rather say this collection of disorders—become. It was indeed stated that the predynastic Nubian scarcely ever grew to adult age without some manifestations of its presence. In no case among the predynastic Nubians was it found before bone formation was complete. It may be added that it is a disease which is prevalent among the fellahin at the present time and it is thought that their daily work in connexion with irrigation, fishing, the repeated carriage of water pots from the river and the general condition of dampness which their occupations produce, have been, and are largely responsible for the rheumatoid arthritis.

As regards anatomical evidence for the existence of malignant disease, the Nubian remains did not show any trace of it, but Elliot Smith records several instances of osteo-sarcoma,[1] three of which were found in a cemetery containing remains of the fifth dynasty. In addition to these, two other cases of cancer were recognized; the first being a growth in the throat which had invaded the base of the skull, and the other a case of carcinoma of the rectum. Both were more than twenty centuries later than the pyramid age. A few instances of vesical and biliary calculi were also recorded; one of the former was found in a boy of the predynastic age and was reported upon by Shattock, while gallstones were found in the mummy of a priestess of

[1] A form of bone cancer.

Ammon, who died at Thebes about 1000 B.C. From the evidence of anatomical remains it would therefore seem that cancer was rare, but it will be seen presently that it was sufficiently common to receive mention in the medical papyri.

We now proceed to a brief consideration of the written medical and surgical record of ancient Egypt. From the earliest times the Egyptians claimed the possession of profound and secret knowledge. This claim seems to have been freely conceded by other nations and was probably allowed without question, at least until the deciphering of their hieroglyphic system by Champollion in the earlier part of the nineteenth century. For centuries these weird symbols remained mysterious, inscrutable, preserving their secret and by the very fact that they were utterly incomprehensible, enhancing the idea that they guarded knowledge which, were it attainable, would be a kind of intellectual revelation of long-lost secrets and profound vision. There are in the Bible several passages which might reasonably be interpreted as meaning that the 'Wisdom of the Egyptians'—a phrase which has become almost proverbial—embraced the whole of attainable learning. Indeed, it is not unfair to say that from the Old Testament to the modern novelist reference has been made to Egyptian mysteries and Egyptian learning as if they really fulfilled the claims originally put forward. It is regrettable, but true, that the claims are entirely unfulfilled, at any rate in the modern sense. Historical results of the highest value have been obtained from the sculptured records of the Pharaohs, but the great majority of the papyri are not only religious texts but are indeed variants on one particular species of literature known to us comprehensively as 'The Book of the Dead'. The Egyptians themselves claimed to possess forty-two books which contained the whole sum of human knowledge. Clement tells us that of these forty-two books, thirty dealt with philosophy and general knowledge, while the last six were devoted to the healing art.

Undoubtedly medicine, as an art, was held in the greatest esteem among the Egyptians. Its special tutelary deity, Imhotep, the Asklepios of the Egyptian Pantheon, was in actual life a high official of the third dynasty, combining the heterogeneous offices of Grand Vizier, architect, priest, sage, scribe, astronomer, magician and physician to the Pharaoh. Although possessed of a perfectly reputable pair of historically recorded human parents, subsequent legend declared him to be the offspring of the god Ptah. Deification of those who had been supposed to have conferred benefits on mankind is no unusual phenomenon in ancient history.

We learn from Herodotus that in his time specialization in medicine was carried to such an extent that each physician confined himself to the treatment of the disease of one part of the body, and incidentally, that the whole country swarmed with these medical specialists. It is characteristic of the extreme conservatism of the people, that innovations in treatment were by no means encouraged, and were only adopted at the practitioner's own risk.

Turning now to the written evidence of ancient Egyptian medicine and surgery, a few medical texts have been recovered of which the oldest is the famous papyrus Ebers. It has the further distinction of being the oldest complete book hitherto discovered either upon medicine or any other subject. This work was discovered in 1872 by the German egyptologist, Georg Ebers. There are at present five main sources of information; the approximate dates of the existing copies of these papyri, their present location, and the number of recipes for treatment and diagnosis which each contains may be seen in Table XVI.

TABLE XVI

	Name	*Location*	*Date*	*Recipes*	*Diagnosis*
1	Papyrus Ebers	Leipzig	Early 16th Cent. B.C.	877	47
2	Berlin Medical Papyrus	State Museum at Berlin (No. 3038)	16th Cent. B.C.	260	2
3	London Medical Papyrus	British Museum (No. 10059)	16th Cent. B.C.	264	0
4	Papyrus Hearst.	University of California	11th Cent. B.C.	63	1
5	Edwin Smith Papyrus		17th Cent. B.C.		

In addition to these there are fragments of three other medical documents dating sometime about

200 B.C., and later Warren Dawson described a Coptic papyrus of the ninth century in the Christian Era. This has been of use in helping to elucidate some of the obscurities in the older papyri, such as the identification of the drugs used in the various prescriptions.

In weighing up the records that have been preserved to us, it is natural to inquire whether there is any evidence of profound medical knowledge. The answer is brief; there is absolutely none, and medicine, as distinct from surgery, was entirely a system of magic. Disease, apart from injury, was regarded entirely as the work of demons, and it was to their expulsion that the whole practice of 'medicine' was directed. In the case of surgical injuries due to obvious causes, the matter was different; there was no need to invoke the supernatural when the cause of the trouble was manifest, and in this respect the Edwin Smith papyrus differs from all the others we have mentioned, since it is definitely a surgical treatise dealing with the treatment of mechanical injuries upon more or less rational lines. According to Wiedemann, the body was divided into thirty-six parts, each presided over by a certain demon. These demons were identified with the thirty-six divisions of the Egyptian Zodiac. In addition to the possible failure of these to carry out their functions, there was always the possibility of the entrance of adverse demons from without, so that in disease it was necessary to recall the tutelary deity to a sense of his duties and to remove the offender, whether by inducing him to depart or by forcibly expelling him. Not only were magical incantations used, but potions of animal, vegetable and other ingredients were administered. In their efficient preparation it was necessary that magical formulae should be repeated over them during the course of preparation. More important from our point of view is the fact that these potions sometimes did contain some ingredient or ingredients of greater or less therapeutic value. Those found to be of use would necessarily tend to be repeated, and one of the ancient medical owners of the Ebers' papyrus has indicated his approval of certain recipes by noting 'good' in the margin. If one such mixture was found to be 'good', it was doubtless considered that a combination of two would be better and of three best. Hence arose the complicated mixtures which survived in the pharmacopoeias until late in the eighteenth century.

For Anglo-Saxon times the earliest medical references are to be found in the works of the Venerable Bede (673–735), and from these it is clear that a definite class of medical practitioners existed, but whether they were clerics or laymen is not certain. Of a later date (*c.* 900–950) is the manuscript known as the Leechbook of Bald, from the name of its owner, for whom it was written, compiled, or copied by one Cild. It contains a reference to two medical practitioners Dun and Oxa, and the contents are largely based upon an extensive popular pharmacopoeia, while the influence of Greek and Latin writers can also be seen.

In the treatment of cancer, this, our oldest native medical book, gives three prescriptions. Firstly, a mixture of goat's gall and honey may be applied; or secondly, a fresh hound's head, burnt to ashes and powdered is to be put upon the sore, while if the disease will not yield even to this, recourse may be had to yet a third, in which the 'leech' is directed to take human excrement, dry it thoroughly, pound it to dust and then apply it. The prescription concludes by saying, 'If with this thou art not able to cure him, thou mayest never do it by any means.'

A charm which would be applicable to a malignant growth, since it is 'against a strange (i.e. unnatural) swelling', runs as follows: 'Sing upon thy leech (i.e. third) finger a paternoster and draw a line about the sore and say, "*Fuge diabolus, Christus te sequitur; quando natus est Christus fugit dolor*" and afterwards say another paternoster and "*fuge diabolus*".'

Here it is evident that an evil spirit was regarded as the source of the trouble. Charms of different sorts with forms of prayer to be recited over the various medicines and applications were quite a feature of early English surgery. It should be mentioned that the ecclesiastical authorities did not always approve of these practices, indeed one, St Eligius or Eloy, Bishop of Noyon in the seventh century, pronounced against them in the very strongest terms.

There is one remarkably interesting feature about this Leechbook of Bald, namely, that it was written in the vernacular, and Anglo-Saxon translations of other works such as the Herbarium Apuleii Platonici are also known. There are some Latin hexameters at the end of the second part of the Leechbook wherein Bald states that he is the owner and Cild the writer of the book. From their very personal character, the inference is that the book was not written in Anglo-Saxon because Bald did not know Latin. Taken with other Anglo-Saxon manuscripts on more or less allied subjects, which are professedly translations, it rather seems to suggest a native school of medicine.

There is no evidence and, indeed, no probability that the Norman Conquest introduced anything new or valuable into our Saxon surgery. For reasons that we shall consider later, surgery generally from the eleventh century until the time of Elizabeth was very much on the down-grade, and was indeed mostly in the hands of very disreputable quacks. There were, however, some notable exceptions such as John of Arderne who was of knightly family ; he served abroad during the Hundred Years War, and was the associate of the princes and nobles upon whom he attended.

The Saxon traditions of surgery continued to have a very strong influence in this country, as may be seen in the writings of John of Arderne and others. These traditions lay more especially in the extensive use of herbal remedies and of spells and charms. It is but fair to conclude that they were regarded rather as 'placebo' measures than as efficient methods of treatment. Side by side with these, there can be traced the influence of the schools of Salerno and Montpellier. In the continental schools, owing to Arab influence, the use of the knife was largely displaced by that of the red-hot cautery, although the Italian surgeon Guglielmo Salicetti (1201–77) advocated the knife in preference; his pupil, Lanfranchi, differentiated between cancer and simple overgrowth of the female breast, but unlike his master was an advocate of the cautery. Guy de Chauliac (1300–70) recommended the excision of cancer in its early stages but used the cautery in fungous varieties.

John of Gaddesden (*c.* 1280–1361), an English court physician, the first of whom we have any record, refers to the treatment of cancer in his *Rosa Medicinae*, as he himself calls his book, though it is commonly known as the *Rosa Anglica.* This book was compiled in the year 1314, and need not detain us beyond noticing the fact that in the treatment of cancer he recommended the use of a cautery of gold.

With Master John Arderne (1307–1400), the first English surgeon who has left us any writings, we enter upon the study of accurately recorded case-histories, some of which deal with the subject of cancer. That he was held in high esteem by his contemporaries is shown by the large number of MSS. of his works which have survived; some of them are in the original Latin while others are English translations.

To the fifteenth century belong some medical treatises which have been edited by Henslow. They are written in English and contain recipes for many ills including 'cankers'. The term must not be taken as synonymous with cancer, although the latter would be included in the class of lesions the term is used to designate. Thus a plaster for a canker consists of a mixture of the leaves of 'spearwort',[1] black nightshade and salad burnet pounded and mixed with honey. A second prescription directs that a powder made by burning together sulphur, lead and 'arnement'[2] should be applied to the ulcerated surface which must first be washed with the urine of a male child. A third recommends that dead flesh be 'carved away' with a sharp razor, after which the part is to be washed with the patient's own urine and then dressed with a mixture of rye flour, powdered glass and honey. If it is desired to 'slay the canker', 'take a roky's egge and put it in a new pot of erthe and brenne it all to powder'; the powder so made will 'slay' it. Another powder made of burnt hen's egg could be used but it was necessary to cover with a plaster of ox-dung as well, though the extra trouble is apparently worth taking as it 'relieves wonderfully'. One prescription, for 'dwale', is interesting, since it was used to produce insensibility during surgical operations. The heading of the recipe is certainly blunt and outspoken. *For to maken a drynke that men calle dwale to make a man slepen whiles men kerue* (i.e. carve)

[1] *Ranunculus flammula, Solanum nigrum* and *Poteria sanguisorba* respectively.

[2] Arnement—the black powder used for making ink. (Lat. *atramentum*.) Compare pharmacopoeia of Ebers papyrus.

hym. There is a slight modification in the formula according as the draught is intended for a man or a woman. If for a man, the bile of a male pig, if for a woman, that of a sow is to be taken. To this are to be added three spoonfuls of the juice expressed from the following plants: hemlock, bryony, lettuce, poppy, henbane, and three spoonfuls of vinegar. The mixture is to be heated to boiling in a well-stoppered glass vessel. Three spoonfuls of the mixture are to be put into a pottle of good wine or ale and well mixed.

The patient is then to be put near a good fire, and to drink so much as will make him sleep. As a pottle contains four pints, the patient might reasonably become drowsy when placed near a good fire. How deep was the anaesthesia produced would, of course, depend upon the quantity consumed. When the carving was over, consciousness was to be restored by washing the temples and cheeks with vinegar and salt. The use of this method of producing insensibility was discontinued later, whether on account of its danger or inefficiency we do not know ; very probably both.

In 1131 the Council of Rheims denounced the monks and regular clergy who 'despised the rules of the Blessed Benedict and Augustine' and who practised law or medicine for gain. By the same authority bishops, abbots and priors who connived at the custom were to be degraded. The Lateran Council (1139) repeated the enactment almost in the same words, it was re-stated by the Council of Montpellier (1162) and in 1163 came the pronouncement of the Council of Tours—'*ecclesia abborret a sanguine*'. The Lateran Council of 1215 expressly forbade subdeacons, deacons and priests to practise any surgery which involved cutting or burning. Since at this period the elementary arts of reading and writing, to say nothing of any more advanced studies, were almost exclusively a clerical monopoly, the effect of such legislation upon the healing art is only too plain. It was doubtless convenient to those in authority that there should be exceptions, so we find that Theodoric, in addition to being a bishop, was surgeon to Innocent IV, while the famous medieval surgeon, Guy de Chauliac, held the post of commensal chaplain as well as physician to Clement VI, Innocent V and Urban V. Medicine did not lie under quite the same ban as surgery, since it was considered that it could be learned from books without any practical experience whatsoever. Since, however, ailments and accidents requiring surgical treatment have a habit of existing in spite of legislative enactments, some kind of surgeon was an obvious necessity. The result was as might have been anticipated—the rise of an army of quacks and impostors. The barbers, having been accustomed to help the clerics with their operations, at first formed the most respectable class of surgical practitioners. The times of the Normans and Plantagenets and their successors were essentially times of fighting, and more or less competent surgeons were a necessary part of the retinue of those princes and nobles who took the field, consequently the military surgeons became the aristocracy of the profession. When they were first formed we do not know, but two gilds were existing side by side from an early period. These were the Gild of Barbers and the Company or Fellowship of Surgeons. This is not the place for a history of surgery in London —those who are interested will find the information they want in D'Arcy Power's admirable and interesting papers on the subject.[1] Both classes, however, endeavoured to raise the professional status of their members, and to ensure some degree of competence by examinations. The London Fellowship of Surgeons was a very small and select body; it probably never had more than twenty members and sometimes the number dwindled to about a dozen. On passing the suitable examination the title of Master in Surgery and Anatomy was conferred, and D'Arcy Power quotes the case of Robert Anson who was examined and approved on 8 August 1497, the licence stating, among other things, that the said Robert was 'found able and discreet to occupy and use the practice of Surgery as well about new wounds as cancers, fistulae, ulcers and many other diseases'.

The Company of Barber-Surgeons was founded in 1540, and it was during the years immediately preceding and following that date that surgery reached its lowest ebb in England. Two pieces of almost incredibly stupid legislation must have largely assisted this degradation.

[1] *Selected Writings, 1877–1930.* Oxford Clarendon Press. 1931.

In 1511 the licensing of surgeons was allocated, in London, to the Bishop and the Dean of St. Pauls, and in the provinces to the Bishops and their Vicars General. The act seems to have been unpopular and was, therefore, superseded by one still more absurd by which it was made 'lawful to any person being the King's subject, having knowledge or experience of the nature of herbs, etc., to minister in and to any outward sore or wound according to their cunning'. The result was, as will be seen later, to encourage the very scum of mankind to the practice of surgery. Theoretically the incorporation of the Barber-Surgeons in 1540 superseded this, but empirics flourished and the bishops continued to license until 1715, when the Bishop of London vainly endeavoured to enforce his claims. The effect of this army of incompetent rascals upon the unfortunate sufferers from incurable disease, such as cancer then was, must have been deplorable. We shall see later what they had to suffer at the hands of competent surgeons whose operative services were rendered unwillingly as they themselves thought that they could be attended by but little success. The quack had no such scruples and indeed traded on attempting to cure diseases which those competent to judge had pronounced incurable. In Elizabethan days a strong effort was made to resuscitate surgery, and some eminent surgical writers of that time have left accounts of the types of rascal who set up for being surgeons. William Clowes refers to them as:

'this beastly brood following: which do forsake their honest trades whereunto God hath called them, and do daily rush into physic and surgery. And some of them be Painters, some Glaziers, some Tailors, some Weavers, some Joiners, some Cutlers, some Cooks, some Bakers, and some Chandlers. Yea, nowadays it is apparent to see how Tinkers, Tooth-drawers, Pedlars, Ostlers, Carters, Porters, Horse-gelders and Horse-leeches, Idiots, Apple-squires, Broom-men, Bawds, Witches, Conjurers, Soothsayers and Sow-gelders, Rogues, Rat-catchers, Runagates and Proctors of Spittle-houses with such other like rotten and stinking weeds which do in town and country, without order, honesty or skill, daily abuse both physic and surgery, having no more perseverence, reason or knowledge in this art than hath a goose, but a certain blind practice without wisdom or judgement, and most commonly useth one remedy for all diseases and one way of curing to all persons both old and young, men, women and children, which is as possible to be performed or to be true as for a shoemaker with one last to make a shoe to fit for every man's foot and this is one principal cause that so many perish.'

Comment such as this affords strong, if not precisely eloquent, testimony to the probable fate of such poor creatures as might fall into the hands of this 'rabblement'. The opinions of three most eminent surgeons of their time, Gale, Clowes and Halle, are unanimous as to the character and professional attainments of these quacks. It is especially the victim of some intractable or incurable disease that relies upon the fulsome promises of the quack fraternity, and of all such maladies, cancer has always been that for which they professed to give certain cure or relief. We have already seen and shall see again later that the best type of surgeon was averse to operation for cancer, preferring to relieve symptoms rather than to subject the sufferer to useless pain ; the quack was devoid not only of skill but of compassion, anxious only for gain and utterly unscrupulous as to the means he employed in acquiring it. In addition to irregular practitioners not only entirely without any medical qualifications, but in some cases unable to read or write, there was also a numerous class holding the bishop's licence. These come into more prominence in the seventeenth century, when they developed a 'literature' of their own, and carried on a paper war among themselves in which, as might be expected, personalities not of the most refined kind were freely exchanged.

It seems extremely probable to us that the activities of these gentry had a vast deal to do with the horror of cancer as it exists even down to the present time. Those of the legitimate surgeons were ghastly enough, as may be gathered from their own writings. But there was the marked difference that we have already noted —unwillingness to operate unless at the sufferer's urgent entreaty when there was no prospect of more or less permanent relief.

Richard Wiseman (1622-76) described his surgical efforts to relieve cancer and concludes:

> These unsuccessful attempts may render us extream cruel to those who feel not the misery these poor creatures suffer with Cancers in their Mouths.

It is clear from the remarks of Wiseman that he was no advocate of operation when he thought there was little or no hope of cure. On the question of cancer in general he writes as follows:

If the Cancer be but in some particular part, as the Tongue, Gum, etc., though the Patients have no certain hopes of being cured by knife or fire, yet they generally put it to trial sooner or later. How much more then shall these poor creatures who have Cancers overspreading their Mouth, eating and gnawing the Flesh, Nerves and Bones? Who besides the danger they are in every minute of being choaked with a fierce Catarrh, do suffer hunger and thirst; and if they can swallow Broth, Caudle or Drink, yet it is with an unsavoury tast, by reason of its passing through such sore corrupt Parts, from which putrefaction their Stomach nauseates its Sustenance, and their Spirits are infected with the stink, whence Fainting frequently happens; Sleep is a stranger to their eyes, their Slumbers are very troublesome, and Death is onely their desire At such a time as this it is not to be wondered if they try a doubtfull Remedy, though painfull.

What I have attempted of this kind hath been at the earnest request of the Patients and their Friends, and by the Authority of a consultation of eminent Physicians and Chirurgeons. *That the Cure succeeded not, must be imputed to the greatness of the Disease and may teach others how dangerous it is to neglect the consulting the experienced Chirurgeon while the disease is recent, and easie to be eradicated.*

It may be of interest to record that the first definite notice of cancer of the tongue is in English and is contained in the *Chirurgicall Lectures of Tumours and*

Ulcers, by Doctor Alexander Head. The book is dated 1635, and contains the substance of lectures before the United Company of Barber Surgeons in the three previous years.

From the middle of the seventeenth century onwards cancer of the tongue was a well-known disease in England, as can be seen in the works of Wiseman. It seems, nevertheless, to have been rare in Germany since Paul de Sorbait, in publishing the record of a case in 1672, observed that

> we saw an ulcer degenerating into cancer in the case of the noble Baron Vertemali, which caused such a haemorrhage from destruction of the sublingual arteries that the patient was suffocated. He recognized with great penitence that the cause of his cancer was a divine punishment because he had often abused the clergy.

From the last statement it would appear that the disease was, to say the least, exceedingly uncommon, otherwise such a remarkable cause would hardly have been assigned to it.

The rarity of the condition in Germany is borne out by a subsequent observer, Bonetas (1620-89), who, writing upon diseases of the tongue in 1685, again quotes this case. Whether he was struck with the beauty of the moral lesson or was unable to find another case to record is, however, not quite clear. The Baron Vertemali was apparently in the habit of swearing at everybody, but his choicest specimens of invective were reserved for the clergy and members of religious communities. On one occasion, having expressed himself with his usual freedom towards a certain 'holy brother of good repute', the latter said to him, 'Your foul tongue has long deserved that punishment from an offended God, which it will shortly receive!' A few days afterwards a small swelling appeared on the side of the tongue, increased rapidly in size, and terminated as already described.

D'Arcy Power is of the opinion that cancer of the tongue has always existed, but that during the classical and medieval periods it was so rare as hardly to merit attention in ordinary surgical writings.

Among the miscellaneous 'remedies' used for cancer may be mentioned the application of a live toad bound over the diseased part and left *in situ* for twenty-four hours. The origin of the practice is not known. Haddow suggests that its wrinkled and warty-looking skin was perhaps thought to resemble certain stages of cancerous growth in appearance, in which case its use would be an obvious application of the 'doctrine of signatures' which had such a vogue in the Middle Ages. On the other hand, there may have been some idea of a connexion between the acrid secretion of the toad's skin and the consequent destruction of the cancer by corrosion. An eighteenth-century record of this method of treatment states that the animal was kept in a linen bag, with the head exposed and applied to the diseased part. Probably the 'cure' is still in use in various more or less out-of-the-way places. Sambon, when in the

Trentino in 1904, was told that lizards were minced and eaten raw by cancer patients, as well as applied to ulcerated tumours.

Ambroise Pare (1510–90) recommended the use of leeches for mitigating the pain in ulcerated growths and attributed their effect to removing some part of the 'malign tumour'. Another anodyne was the application of live kittens, puppies, fowls or pigeons split lengthwise, and changed as soon as they became evil. Sambon recorded the case of a quack in Holland who employed a puppy for the purpose in 1925 and was very inadequately punished by the infliction of a fine for his disgusting cruelty. But Ambroise Pare is to be credited with the first advance in the treatment of cancer that we have been able to find, namely, the designing of a pessary to carry off the discharge in uterine cancer, while he also employed lead plates smeared with mercury as local applications and made liberal use of lead salts in the various lotions, fomentations and ointments which he prescribed in the treatment of cancer. These were commonly mixed with different vegetable juices extracted from the nightshade, henbane, pomegranate and lettuce, together with the oil of roses. In accordance with the 'doctrine of signatures', he also had recourse to the ancient remedy of pounded crabs.

The year 1754 brought an official notice of a cancer cure published by the government of Virginia:

A *Receipt* for curing *Cancers*; made public in pursuance of a Resolution of the General Assembly of the Province of

Virginia, after having appointed a Committee to make Trial of its Effects, and receiving the report of its Success.

The recipe is as follows: Take a peck of garden sorrel, rather more than half as much celandine; pound them in a mortar ;and squeeze out the juice through a cloth into a pewter basin. Next, take a large handful of the inner bark of the perlimon from the south side of the tree, pound it up, add a little spring water and let it stand for an hour, squeeze the juice through a cloth and mix it with the contents of the pewter basin. Then heat an iron pestle very hot, and 'with it run in four ounces of alum to the above mixture', mix all thoroughly, and place in the sun to dry it. The best time for making it is at the end of May or the beginning of June. The method of application is not given.

There are two or three points of interest here; the pewter basin, the cutting of the perlimon bark from the south side, and the time of preparation at the end of May or the beginning of June. The pewter basin indicates the use of lead in the remedy; the references to the south side of the tree and the times of collecting the ingredients point to some old astrological superstition.

In 1789 we have some remarks on more scientific lines extracted from the *London Medical Journal* (Vol. X, Part 1). The note is headed: 'A Case of Cancer of the Breast, with remarks. Communicated in a letter to Dr Simmons by Mr T. Hughes, Surgeon at Stroud Water in Gloucestershire.' It is pointed out that statistical treatment of the records of different forms of treatment is essential, but that any one surgeon's collection of cases is insufficient for the purpose; the criticism is also made that people are too fond of reporting successful cases to the exclusion of failures, and that claims of success are made far too soon after treatment. Mr Hughes's criticism is as true in 1949 as it was in 1789. He then proceeds to give an analysis of rather over 200 cancer cases under his own treatment.

The year 1802 saw the publication of a remedy which was certainly brief and to the point:

> For a cancer. The corns and parings from the feet of a stone-horse[1] dryed in an oven, then beat to a powder, and as much as will lie upon a sixpence taken night and morning in a glass of white wine.

Three years later William Thomas, M.R.C.S., made an attempt 'to induce the unfortunate sufferers who daily shrink from the knife to yield to the application of arsenic'. Editorial comment is that the intention is laudable, and that Mr Thomas seems perfectly master of his subject. Another medical practitioner, Samuel Young, M.R.C.P., published in the same year (1805) *An Enquiry into the Nature and Action of Cancer; with a view to the establishment of a regular mode of curing that Disease by natural Separation.*

We may fitly close our list with the notice of a treatment advocated by William Lambe, M.D., who regarded

[1] A stone-horse—a horse that has not been castrated.

the disease as caused by eating animal food and drinking impure water. The obvious preventive and remedy were to exist on a strictly vegetable diet and to drink nothing but distilled water. This was in 1812, and it would be interesting to know how many people took the advice, particularly as a preventive. The Regency does not strike one as a period in which such a remarkably Spartan diet would have a large following, especially from the preventive point of view. The historical narrative ends here.

From 1812–1949 is a period which we may look upon in medicine and in the study of disease (pathology) as having in a sense obliterated the past, not in the sense of destruction but rather of effacement. Let the veil be drawn over the years in which the treatment of cancer was carried on with no supporting study of the cause and nature of the disease. Many of the physicians before 1800 were undoubtedly men of great ability but they lacked the kind of support which science was to give them in the next century and a half. Nothing could exemplify better the mutual aid of the sciences than the sort of technical aid given to medicine by virtue of the great awakening that now occurred in the fields of physical and chemical science. The microscope was not at that time a new invention but its use in medicine was waiting for two essential features of technique which were to make it an instrument of supreme importance. One was the means of preparing specimens, or 'sections' as they are called, and the other was the differential staining of these sections. Before the year 1846 all that could be done in the microscopic viewing of the soft tissues (including cancer tissues) of the body was to tease out as small a piece as could be handled and then attempt to transmit enough light so that one could see through it ; but little was gained by such attempts.

CHAPTER XIV

CANCER IN THE FUTURE

Having traced, however imperfectly, the general outlook upon cancer down the ages, it is inevitable that one questions: what of the future? Is there any reason for a fatalistic outlook, that this disease will always present itself as one in which the cause or causes will never be resolved and its cure never realized?

It is axiomatic that people do not attempt to solve problems which they consider insoluble; so we may be quite sure that those engaged in seeking the cause and cure of cancer share no such general fatalistic outlook. This being so, we may inquire how far they have a warrant for a reasonably hopeful attitude towards this problem, and an answer is found among three significant facts which will come readily to the mind of the reader as he thinks of this brief record of the past.

A century ago the disease was one in which the one sole hope of relief was operation at an *early* stage of the disease; further, it was a disease of which even the most elementary microscopical knowledge had hardly been gleaned. It was not, indeed, until the year 1846 that the first specimen of a malignant growth was examined microscopically. Thirdly, the public outlook was one of fear and all that such an attitude towards an ailment entails ; fear leads to concealment, an act for which a terrible penalty can be exacted.

The century has certainly brought great changes in each of these categories ; the last fifty years have brought one entirely new treatment to bear upon the disease, with the result that just as many sufferers from cancer in this country get radiological as surgical treatment, possibly more.

Further, the advances in pathology have been immense, for not only is there an elaborate knowledge of the whole pattern of malignant growths as seen under the microscope, but also an impressive mass of information upon the behaviour of these growths in the human body which, gleaned by clinicians and pathologists, is of supreme importance in weighing the evidence presented by any single patient.

Finally, the public outlook has changed, in the sense that fear does not dominate outlook or control action to anything like the extent it did a century ago. This is far from saying that the fear has gone out of cancer; far from it indeed, and there must always be thoughtful apprehension of a disease with such characteristics as this one. Nevertheless there is a changed outlook and it is largely due to the plain fact that more is now done for the patient than ever before.

The outlook on these three main scores then is an improved one ; how much more can we expect in the coming years? There is no time limit in such a term as the 'coming years', but general use will give it the meaning 'in our time'; in time to meet the needs of those about us.

A few essentials for further advances in treatment would appear to be:

1. A greater readiness on the part of people to seek medical advice when they are aware of something 'not normal'.
2. Greater facilities for hospital diagnosis and treatment, especially in the rural areas.
3. Further encouragement of experimental research by means of:
   (a) Better laboratory facilities at many of the large treatment centres.
   (b) Greater inducement to research men outside the purely medical sciences to participate in this work.
   (c) An increase in the number of Travelling Fellowships for Cancer Research.

Economic restrictions are a heavy handicap to a man who ardently wishes to extend his outlook on this subject. He can know very little about the methods employed in a foreign laboratory by reading the reports which issue from them, in fact he can only know and appreciate them to the full by working among those who have practised and perfected them. There is a surprising degree of agreement about this among those who have been fortunate enough to study and work under some chief who brings a different perspective to bear upon problems of mutual interest.

There is now a considerably greater number of research men and women engaged in the task than twenty-five years ago. Turning to the *Annual Report* (1947) of The British Empire Cancer Campaign, we find that there are ten Research Centres (Clinical and Experimental) of considerable size, nine other smaller ones and nine other qualified people attached to laboratories which are not especially devoted to cancer, receiving Grants-in-Aid from the Campaign. The total number of these qualified people (with medical and scientific degrees) amounts to approximately 160, and if we take into account those who do not figure in this official list, the number might well be 300. It is not a very large number, but the work they carry out can probably be represented as being on the whole well supported in the way of facilities, equipment, access to literature and so on.

It is certainly not a large number when we think of the scale on which cancer is unfortunately operating. There is no need at this stage to repeat mortality figures which will have given the reader some idea of the menace among us. He may well ask whether a big increase, say a three- or four-fold increase in this personnel total of 300 would give a proportionate increase in results. The answer must surely be that cancer results do not come in this fashion. It is the man or the woman who makes the discovery and it is, therefore, self-evident that it is to the individual that we must look for the final attainment. And how are these essential people to be secured for a task which has defeated so many? There seems to be no positive way of doing it, because the impulse to study cancer must arise in the man or woman. Encouragement may do a lot, in the sense of reassurance that time, perhaps the greater part of a lifetime, can so be spent with the degree of satisfaction that comes from any serious attempt at a problem, rather than by persuasion to enter the field of cancer investigation.

With the growth of what are usually known as controls in our lives, it is not to be wondered at there is occasionally some apprehension that they will perhaps invade territory which has, up to the present, been so refreshingly free of them. Research people are engaged upon those parts of this problem which not only interest them, but engage them to the limit. Further, it is a fact that the various bodies (Chapter X) which dispose of supporting funds do so with an absolute minimum of anything that can be called interference. May such a spirit continue as long as the problem of malignant disease remains unsolved.

Compared with that of fifty years ago the position regarding cancer is more favourable from at least three aspects. Far more is known by physicians, surgeons and pathologists about the disease; secondly, improved methods of diagnosis and treatment are now in operation and, finally, more people are engaged in laboratory investigations into the cause and cure of the disease.

Of no other disease than cancer can it be said, 'Here is an agent that can produce the disease, here is another and another . . . yet we do not know the cause of the disease.' Yet this is exactly what can be said about cancer.

In the course of these pages no less than ten different agents are mentioned as being able to cause cancer in man, yet not one of them can be called 'the Cause of Cancer'. We can actually *make* substances which can produce cancer. E. L. Kennaway and his associates (Mayneord, Hieger, Cook and Hewett) have developed such work on a very considerable scale in preparing what are called polycyclic hydrocarbons. Other classes of cancer-producing substances have been prepared by Yoshida and by Lacassagne; there are now several hundred pure chemical compounds of known composition which are capable of producing cancer in animals; yet here again none of them is to be looked upon as 'the Cause of Cancer'. Many red herrings are indeed drawn across the path down which the seeker is travelling.

It may be, however, that all of these agents have some power in common, the study of which may give a valuable lead in the search for *the* cause. That is why experimental research into the mode of action of cancer-producing agents is so well worth while. When they are applied to living tissues these agents all appear to do some one thing which sets going a process in the cells leading to abnormality; but it is a definite and unusual kind of abnormality because it persists from one generation to another of the damaged normal cells.

So we may say, regarding the cause of cancer, that the issue is gradually being narrowed down. Although many more cancer-producing agents may be discovered, the essential cause must not be looked for amongst them, but it will be found as a 'resulting process'. It is probable that all cancer-producing agents set up some unique process when they are applied to human or other animal tissues, but we do not yet know what this process is.

Surgery by itself has probably reached the stage at which we must not expect any *great* advance in method as regards cancer treatment, but there is a field of great utility when surgery is used in conjunction with X-rays or Radium, and this method of combined treatment has certainly not reached its zenith. In radiotherapy itself, the advances are likely to continue for some years because not only are new technical advances continually being made, but they can well take on a wider scope when we know more about the biological actions throughout the body, brought about by exposure to X-rays and Radium. Not only so, for the advances by physicists and electrical engineers have brought new machines into existence which produce radiations of a character different from X-rays. In the machine known as the cyclotron, for instance, high-speed particles are produced in quantity so that a stream of them can be directed on to the body which they penetrate to much the same degree as a penetrating beam of X-rays. Already there are indications of important differences in the effects produced upon the tissues by these high-speed particles and by X-rays. There is obviously much ground to be covered before we can say that the treatment of cancer by means of rays has reached its limit of usefulness. Nevertheless, in any prospective view of cancer treatment, one cannot help inclining to the view that the ultimate hope is for some form of generalized and not localized treatment. When Ehrlich discovered the drug salvarsan in 1910 he also named it 606 as this represented the number of attempts he had made at producing a drug which would kill the spirochaete of syphilis without appreciable harm to the patient.

Dr Frank Adair recently stated that over 600 chemotherapeutic substances had been tested in the clinics of the U.S.A. in attempts at the relief of cancer. Success in so far as a cure for cancer is concerned has not yet come, yet even though those who know most about the subject are not generally the most sanguine of prophets, there is now a better founded and more sustained hope that the day will come when cancer can be cured.

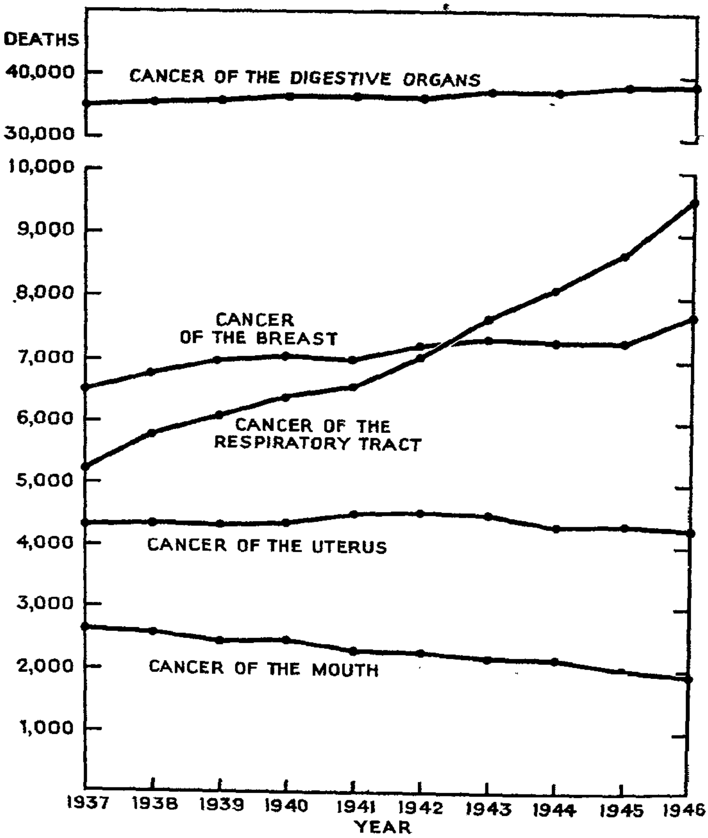
One hundred years ago pathologists began an epoch in knowledge of the structural character of malignant disease ; another epoch was started just over fifty years ago when radiological diagnosis and treatment were first undertaken. It is not an undue venture to suggest that the next twenty-five years will see just as great advances in both diagnosis and treatment. Disappointment, repeated a hundredfold, cannot succeed in shaking conviction that a cure for cancer can be found.

APPENDIX I

The following information is taken from the Registrar-General's *Statistical Review of England and Wales* for the year 1946 (New Annual Series, No. 26). A selection has been made from the total deaths from cancer for that year, with respect to various organs of the body, and readers may gauge their relative importance in numbers by remembering that the total deaths from malignant disease in 1946 were 75,407.

Parts of the body	*Deaths from cancer*		*Total*
Digestive organs	M.	20,362	
	F.	18,289	
			38,651
Respiratory organs	M.	7,686	
	F.	1,821	
			9,507
Breast	M.	69	
	F.	7,711	
			7,780
Womb	F.	4,287	
			4,287
Male genital organs	M.	2,944	
			2,944
Urinary organs	M.	1,809	
	F.	1,013	
			2,822
Mouth and throat	M.	1,869	
	F.	527	
			2,396
Skin	M.	534	
	F.	426	
			960
Brain and other parts of the nervous system	M.	457	
	F.	371	
			828

APPENDIX II



	Deaths in 1937	*Deaths in 1946*
Cancer of the Digestive Organs and Peritoneum	35,100	38,600
Cancer of the Breast	6,516	7,711
Cancer of the Respiratory Tract	5,250	9,500
Cancer of the Uterus	4,330	4,287
Cancer of the Mouth (Males)	2,639	1,869

Data are taken from the Registrar-General's *Statistical Review of England and Wales* for the year 1946 (New Annual Series, No. *26*), Tables, Part 1, Medical.

APPENDIX III

PUBLICITY IN CANCER

In the years between the wars, The Middlesex Hospital decided that it could do a useful service to its patients by distributing leaflets containing vital information about various diseases. Three of their leaflets were on the subject of cancer and the statements in them are just as true to-day as they were twenty years ago.

With the consent of the Middlesex Hospital Press, two are reproduced here in the hope that the information contained in them may be spread to an even wider circle.

IS CANCER A CURABLE DISEASE?

It is a common belief that cancer is, in its very nature, incurable. This belief is founded upon the erroneous notion that cancer is a blood disease affecting from its very beginning the whole body. But all research up to the present tends to prove that it begins as a local disease, strictly confined to the part in which it originates. If at this stage the diseased part can be removed, the cancer is cured.

The Medical Society of London recently collected over two hundred cases of one particular variety of cancer in which the patients were alive more than ten years after operation, and there can be no doubt that most of these cases were cures.

In a large majority of patients suffering from the disease, cancer arises in situations in which it can be treated. Fortunately, it is the exception for a growth to start in such a deep-seated part that, when the patient is conscious of something really wrong, the removal of the cancer has already become impossible. Yet it is, unfortunately, true that the cure of cancer is much rarer than it might be. In the past the treatment of cancer was not so well understood as it is to-day, and operations for its removal were painful, dangerous, and often unsuccessful. Great progress has been made in quite recent years by a study of the manner in which cancer spreads, and this has shown that the former methods of operation were in some directions too extensive, in others too limited. The danger of even extensive operations for cancer has been reduced to a minimum. Moreover, in many cases the chief pain caused is the pain of anticipation. The patient is unconscious during the operation, and the healing of the wound is almost painless. In the operation for cancer of the breast, to take one instance, the chances are about 200 to 1 in favour of the patient's recovery, and during convalescence no sensation worse than mild discomfort is experienced. If people realized these facts, they would face cancer operations as calmly as the plucky children of to-day face the discomforts of the throat operations which have done so much to improve the health of the rising generation.

We have not yet answered the oft-repeated question: Why is cancer not more often cured? Sometimes the disease is not recognizable at a stage sufficiently early to allow of successful treatment by Radium, X-ray, electrical diathermy, or the knife. But in the great majority of cases in which cure is not attained, it will be found that the patient, *knowing something was wrong, has nevertheless delayed seeking medical advice.* In a series of cases of cancer it was found, on the average, that the patients had been aware of something definitely wrong for six months before seeking medical advice.

If a householder, knowing his house was on fire, gave the fire an hour's start before giving the alarm, he could not blame the fire brigade for the ruin of his home.

Although this waste of precious time makes a cure in many cases almost impossible, even in these cases a further lease of life can often be secured by proper treatment. Taking breast cancer again as an instance, experience shows that, if the disease is still in an early stage, four out of five patients can be freed from the disease for years, and probably for ever. If, however, the cancer has grown beyond a certain stage, in four cases out of five it will ultimately return.

WHAT SHOULD BE KNOWN ABOUT CANCER: ITS PREVENTION AND TREATMENT

Cancer not an 'incurable disease'

Cancer, *in its earlier stages*, unless occurring in an inaccessible part of the body, is often curable, and is nowadays not infrequently cured by operation, while in certain varieties of the disease good results have been obtained by the use of Radium or of X-rays. In their efforts to cure the disease doctors are terribly handicapped by the reluctance of patients to seek early advice. Often by the time the doctor is consulted the disease is too far advanced for treatment.

Pre-cancerous changes

Cancer is especially liable to arise in parts which are the seat of long-standing irritation leading to chronic inflammation. These chronic inflammatory changes are termed pre-cancerous conditions, and they can sometimes be cured by simple treatment or by a trivial operation.

Pre-cancerous changes may be set up:

(1) By *mechanical irritation*, as by the irritation of the tongue by a jagged tooth, or by a sharp dental plate, or by the rubbing of a mole or birthmark by the collar.

(2) By neglect of cleanliness. Naturally this cause affects chiefly these parts of the body which are difficult to keep clean.

(3) Local infections. In some cases as the result of a want of cleanliness, in other cases quite apart from this, microbes gain a foothold at some point in the tissues of the body. The irritation there set up may become in time a potent cause of cancer.

(4) A particular mention must be made of the microbe of syphilis. This microbe is apt to cause areas of chronic inflammation in various parts of the body, especially the tongue, which many years after the disease has been contracted may become the seat of cancer.

(5) It is dangerous for the public to treat moles and warts by caustics or similar local treatment which may set up irritation and cause cancer later.

Early treatment of pre-cancerous conditions often prevents cancer

It is to the patient's advantage that such conditions as are frequently followed by cancer should be thoroughly dealt with either medically or surgically, and that the 'pre-cancerous' state should not be allowed to pass, owing to neglect, into actual cancerous disease. It is in this sense that we are justified in speaking of the 'prevention of cancer'.

Inefficient cleaning of the mouth or teeth, syphilitic disease of the tongue, or irritation of the side of the tongue by a jagged tooth, may be followed by cancer of the tongue, and so we urge proper treatment of the dirty mouth or the syphilitic disease or the jagged tooth, in order to guard the patient, as far as possible, from the grave danger of cancer of the tongue.

In the same way, long-standing ulcers, whether of the face or of the stomach or of the leg, sometimes become cancerous, and we urge proper treatment of all ulcers in order to avoid this danger.

Similarly, cancer is often found in breasts that have become hard and knotty ; cancer of the womb may follow long continued discharge.

Often the time between the beginning of the 'pre-cancerous' condition and the occurrence of undoubted cancer is fairly long, so that ample time is given for efficient treatment if the patient will only consult a doctor directly something wrong is noticed.

What the public can do for themselves to prevent cancer

What we have to say under this heading may be largely summed up in the word *cleanliness.* It is, for example, very rare to see cancer in a mouth which has been kept clean.

It is not ordinary washing of the skin to which we are referring ; but the regular cleansing of those recesses where the secretions may stagnate and decompose. *Cleanliness of the teeth* is specially important, for if foul secretions from the mouth are swallowed they are likely to lead to digestive troubles, even if more serious consequences do not follow.

Tar and paraffin workers and chimney sweeps should be especially careful about cleanliness, for tar, paraffin and soot are specially irritant to the skin.

Cancer often occurs in persons who have lived regular and healthy lives. No disgrace attaches to the cancer patient, nor is he a source of infection to those around him. It must be recognized, however, that persons who have had syphilis are more likely to suffer from cancer; therefore sexual promiscuity tends to increase cancer. There is no good evidence that cancer attaches to particular houses.

Temperance in eating and drinking, regular exercise and fresh air, are important aids in the maintenance of health, and, therefore, presumably in the prevention of cancer.

The early stages of cancer

Cancer usually begins at one particular spot in the body as a local growth, often to be felt as a lump. In this stage it can in most cases be removed safely and without pain, and with a good prospect of cure.

Why do most patients consult a doctor too late?

How is it that in a disease which excites so much dread it is often the case that the patient consults the doctor too late to be saved? This deplorable fact springs from a misconception, almost universal in the public mind, that cancer cannot exist without pain. To root out this misconception we here state emphatically that *cancer in its earlier stages is painless.* Upon what, then, must a patient rely as an indication for seeking medical advice? There need be little fear of cancer before the age of forty. After this age, the appearance of a lump anywhere, or the presence of a hard patch or any obstinate ulcer, of an abscess or of a discharge of blood or matter from any of the orifices, or of persistent indigestion or constipation, or difficulty in swallowing, *may* possibly indicate the presence of a cancer. If you notice any of these symptoms or any marked decline in health, *do not nurse your dread,* but seek medical advice, which will either relieve you of a groundless fear or give you the best chance of cure.