

Under arithmetic and mathematics, models of surfaces and of crystals are shown; also the calculating machine of the late Charles Babbage, electrical machine for solving equations, and electromagnetic device for solving equations.

It has only been possible to direct attention briefly and imperfectly to the scope of the science exhibit, but this will perhaps serve to give an idea to those interested in science and cause them to visit and examine it in detail. In conclusion, mention should be made of the anthropological exhibit, an interesting feature being that a small space has been set aside for the actual taking of measurements, so that certain particulars of those attending the exhibition can be taken and data added to the large collection already obtained.

F. M. P.

THE PROGRESS OF CANCER RESEARCH.

THE annual meeting of the general committee of the Imperial Cancer Research Fund was held at the Royal College of Surgeons on July 20, Mr. A. J. Balfour being in the chair. Sir William Church presented the annual report, and gave an able exposition of its most salient features.

The Duke of Bedford, who has been a strong financial supporter of the fund from its foundation, was elected president. Mr. A. J. Balfour moved a vote of thanks to the members of the various committees, and to Dr. Bashford and his staff. Mr. Balfour's remarks were mainly directed to the layman, and have received such wide publicity in the daily papers that we need not quote them in full, well as they will bear quoting. Mr. Balfour emphasised the progress made since he presided in July, 1903, and directed attention to the caution characterising the statements emanating from the laboratory, urging the need for patience upon the public, the members of which are not always able to comprehend that the slow progress made by scientific methods is the only progress that can legitimately be expected. Mr. Balfour emphasised the fact that heredity has been shown to be not of main importance, meaning thereby, we infer, that the congenital germ-theory of cancer has been discarded for good, in view of the facts elicited by the Imperial Cancer Research Fund on the association of cancer with peculiar irritants in human races practising peculiar customs, and in some animals.

Emphasis may be laid upon this point; in India, draught-cattle are liable to cancer at the root of the left horn, not of the right horn; cancer of the skin of the abdomen is only frequent in the Kashmiris who wear the "Kangri," or charcoal fire-basket; cancer of the floor of the mouth is only frequent in women who chew betel-nut. Surely these peculiar incidences of cancer are not due to a different distribution of congenital germs in the right than in the left horn of cattle, or in the abdominal skin of Kashmiris other than that in other races, any more than is betel-nut cancer due to a peculiar accumulation of congenital germs in the mouths of those women who chew betel-nut. All these forms of cancer could almost certainly be greatly diminished if the parts attacked were not irritated.

Advance in knowledge must yield information regarding other more obscure forms of cancer. Another point emphasised by Mr. Balfour was his belief in the reasonableness of expecting that the cure and prevention of the dissemination of transplanted cancer, as announced in the report, foreshadows similar achievements for original cancer, although perhaps so much may not be attained in his lifetime.

The other business was purely formal.

The report itself states that King George has consented to become Patron of the Imperial Cancer Research Fund in succession to His late Majesty King Edward VII., who was so largely responsible for its inception, as well as for inciting the modern crusade against cancer, and who in July, 1901, when opening the congress on tuberculosis, stated:—"There is still one other terrible disease which has, up till now, baffled the scientific and medical men of the world, and that is cancer. God grant that before long you may be able to find a cure or to check its course, and I think that to him who makes the discovery a statue should be erected in all the capitals of the world."

The appeal which the investigations of the Imperial

Cancer Research Fund make to students throughout the world is exemplified by the number of foreign voluntary workers attracted to its laboratories. They have flocked to them from Germany, Italy, Belgium, Norway, Austria-Hungary, Roumania, the United States, Holland, and Japan, and many now hold independent appointments abroad. Thus the British national investigations on cancer may be said to have fulfilled their immediate purpose in that the English school of cancer research commands world-wide confidence, which we hope will be confirmed and extended by the director's necessarily technical report, from which we give below extracts of a few important passages. The report makes no pretence to appeal to the man in the street who wishes to know if the cause, the cure, or the means of preventing cancer have been discovered. Nevertheless, to all with "inside" knowledge, the progress made by the indirect method of attack—by the intelligent sapping and mining of hitherto unassailable citadels—must appear full of encouragement for the future.

Cancer in Vertebrates.

Much additional information has been obtained on the occurrence of cancer in lower vertebrates. It is gratifying to record that the systematic investigation of cancer in the animal kingdom has found numerous adherents both at home and abroad. Particular attention has been devoted to the incidence of the disease in cattle and in mice. While in mice the phenomena are presented in miniature even in their most advanced stages, in cattle they are demonstrated on a magnified scale as compared with man, although the universal minuteness of the early stages is independent of the size of the animal. In the course of the past six months, ninety cases of malignant new growths in cattle were obtained from a single abattoir. The histological types comprise the majority of the forms met with in man.

Breeding Experiments bearing on Heredity and Contagion.

The advantages of using short-lived animals for studying the possible influence of heredity were pointed out in 1903. The breeding experiments which have been in progress for five years have yielded a material of nearly 2000 animals of known age and ancestry. Of these, 700 females attained the age of six months or more. In them, seventy-five cases of cancer of the mamma have appeared spontaneously. This material is very complete as regards diagnosis of the disease, age, pedigree, and other important data, and it is now sufficiently large to permit of the most exact analysis of the influence of ancestral constitution on the liability of mice to spontaneous cancer of the breast. Analysed so as to bring out the liability to cancer according as the young were born before or after it appeared in the mother, the figures show a higher incidence in those born before the mother developed the disease. Since the conditions necessary for contagion were present, the opposite result would have been obtained had any analogy existed between cancer and the recognised infective diseases.

Constancy and Variability of Tumour Cells.

Tumours growing in a living animal can be protected from all outside influences, and, when propagated in large numbers of young mice of the same strain, the conditions are as constant as it is possible to provide. In these circumstances, it would not be surprising, on the one hand, if tumours showed little or no departure from the features they exhibited at the outset of propagation; on the other hand, it would not have been surprising if tumours widely different in character had tended all to approximate to a common type, in response to the unvarying nature of their environment. What has actually come out is both interesting and instructive, in that it shows that the tumour cells possess a relative constancy in their general biological properties, but, at the same time, exhibit an inherent tendency to vary in spite of the constancy of the environment, and therefore apparently for reasons independent of it. Each tumour preserves its individual features, and if there be variation, then the variations likewise are individual. The constancy may be very perfect, so that strains of the same tumour propagated separately for three and four years remain indistinguishable in all their properties. On the other hand, the variations arising may be

so great and of such constancy that strains propagated separately from the same mother-material would not be suspected to have any relation to one another if submitted to one ignorant of their life-history.

In former years we have pointed out that an increase in the rate of growth, or in the percentage of successful inoculations, does not necessarily imply a fundamental biological alteration finding expression in an accelerated rate of proliferation of the tumour cells, but may be explained by the selection of particular cells adapted to the conditions of growth, and, consequently, the survival and proliferation of a larger number of such cells. That is to say, these two phenomena may be explained by an increase in the dose of the cells able to grow. The evidence for the acquirement of new properties by tumour cells is very much stronger when one observes the occurrence of morphological alterations which become of relative constancy, such as the disappearance—or latency—of their typical characteristics in the case of squamous-celled carcinoma, the disappearance of acinous structure in the case of glandular carcinoma, the derivation from cubical epithelium of epithelial cells which, if their previous history had not been known, could not have been distinguished from those of a spindle-celled sarcoma. In other cases, the change is made manifest by the alterations taking place in the supporting connective tissue and blood-vessels, so that tumours which at one time exhibited dilated blood-vessels lose this character. Biological alterations occur without evident morphological expression, e.g. some tumours at the commencement of propagation, after an initial exuberant growth, disappear in a large proportion of cases, whereas after the propagation is prolonged, a large percentage of the implantations grow progressively. The opposite phenomenon may also be observed, and tumour strains which grew progressively at the outset of propagation may later be found very liable to disappearance. A tumour which grows well only by the implantation of intact grafts, i.e. if the tissue structure is preserved, can be adapted to transplantation as a cell emulsion, and again brought back to its original condition.

Of the twenty-nine tumours of the mamma that have been propagated in the laboratory for more than two years, as many as sixteen have shown departures from the features they exhibited at the outset, these departures affecting the degree and nature of the histological differentiation, the percentage of successful inoculations, the rate of growth of the resulting tumours, the relative proportions of progressively growing tumours and of tumours which undergo spontaneous absorption after transitory growth, the susceptibility of the tumour to method of transplantation, to dose, to race, to age, and to the influence of induced immunity.

Thirteen tumours have shown a relative constancy of their structural and biological characters.

Of the sixteen variable tumours, nine have varied from the primary condition in both respects. Two have shown biological variations without histological change, and five have altered in microscopical characters without noticeable modification of their biological behaviour. On the whole, therefore, histological character is less constant than biological behaviour.

The relative constancy, but still more the variability which the tumour cells exhibit during propagation, throws indirect light of the most suggestive kind upon the nature and the manner of the development of cancer. The variability in a constant environment, during propagation, allows one to infer that corresponding variations may take place while the cells are under the influence of the particular environment provided by the animal in which the tumour developed spontaneously. The environment of the cell will depend on the individuality of the animal, and, with the progress of life, distinctions between one animal and another may become more and more marked. This inference accords with what has been said above on the ease with which auto-transplantation is effected and the difficulty with which transplantation can be effected to another individual, and therefore also with the fact that all cancerous mice do not exhibit an equally suitable soil for tumours in general.

These spontaneous variations of the parenchyma cells of tumours during propagation suggest that we have here a

repetition, in a minor degree, of the cellular processes responsible for the primary transformation of non-cancerous into cancerous tissue; just as cellular changes occurring during propagation may transform within a brief space of time an acinous growth into a solid one, or a slow-growing tumour into one rapidly proliferating, so in the tissues prior to the development of a malignant new growth the responsive proliferation of cells may pass into the progressive, independent proliferation of cancer.

Experimental Sarcoma.

In this connection it may also be well to refer again to the production of sarcoma under experimental conditions from what have been the non-malignant connective tissues of carcinoma. Not the least significant aspect of the origin of sarcoma by the transformation of the stroma of transplantable carcinomata is the rarity of its occurrence. Two only of our strains have exhibited it, and the conclusion seems warranted that in these cases the parenchyma is possessed of peculiar properties. In one of our strains the change occurred only in a small number of animals, and the whole process, from the first indications of sarcomatous changes in the stroma to the substitution of the carcinomatous elements by pure sarcoma, took place slowly, and was only completed after several successive transplantations. In the other strain, the transformation was much more frequent, took place more rapidly, and the disappearance of the carcinomatous element may be complete in one transference. In spite of these differences, the parallelism between the histological pictures in the two strains is extremely close, and leaves no doubt of the essential similarity of the processes involved. The stimulus exerted by the carcinoma cells on the stroma must be different in these two strains from that exemplified by the other transplantable tumours, otherwise every transplantable carcinoma should end in sarcoma, as it has, indeed, been asserted they might do. A fairly long duration of the stimulus exerted by the carcinoma cells without cessation of their proliferation seems to be necessary, and the first steps of the process are always localised in an extremely minute area of what are often large tumours. The parallel to the circumscribed origin of squamous epitheliomata arising in areas subjected to chronic irritation in man (chimney-sweeps' cancer, paraffin cancer, Kangri cancer) does not require to be insisted on further, since it has been emphasised in previous years.

Immunisation.

It is now possible, under given experimental conditions, to prevent a secondary transplantation, i.e. artificial metastasis, taking place for certain tumour-strains. This result has been obtained by inserting between the primary and secondary transplantations an inoculation of a very rapidly growing tumour showing only transitory growth, as the following sample experiment shows. Of twelve mice, already bearing progressively growing tumours and treated in the manner described, the secondary inoculation was successful in three only, and then the tumours were very much smaller than in the control consisting of thirteen mice, of which ten developed new progressively growing tumours on secondary inoculation. A similar result can be obtained by the implantation of tumours growing much more slowly and liable to spontaneous absorption, as well as by an inoculation of normal mouse-tissue. By similar methods the growth of the primary transplanted tumour may be greatly hindered, can be brought to a standstill and the animal cured, in circumstances under which the disease would certainly have progressed, and where the possibility of the occurrence of spontaneous cure can almost certainly be excluded. Thus the control of *transplanted* cancer has been brought within the region of probability.

These achievements must not be confounded with successful vaccination against spontaneous cancer arising, or against infectious disease. Animals perfectly protected against the repeated inoculation of cancer may develop tumours of their own—an observation often confirmed. Still more emphatically do we warn against applying to the human subject the methods which, after long perseverance, have enabled us to arrest the growth, and even to cure, animals of transplanted tumours that were well

established, and also to render animals resistant to a secondary inoculation, *i.e.* to dissemination and metastasis formation.

The immunity reactions to transplanted cancer are throughout clearer and more easily studied than are those of spontaneous cancer. The problems presented by spontaneous tumours are more delicate and elusive. The methods effectual in normal animals against primary inoculation with transplantable tumour, which, as mentioned above, also arrest the growth of growing transplanted tumours and prevent successful re-inoculation in suitable circumstances, have been without action on the continued growth of the twenty-five spontaneous tumours on which they have been tested, have failed to prevent recurrence or dissemination, and have not yet prevented a successful re-inoculation of the spontaneously affected animal with its own tumour. The investigations must go on until a higher degree of resistance can be obtained in this way, or it may be that an entirely different method must be sought. The expectation of ultimate success seems a fair inference from the results obtained with transplanted tumours which reproduce all the phenomena of growth and dissemination of spontaneous tumours, and from the rare but undoubted cases in which temporary arrest of growth or total disappearance have occurred in spontaneous tumours.

The prospect is made the more hopeful by the discovery of a method whereby an animal can be immunised by means of one of its own tissues against a primary inoculation of a tumour transplanted from another animal. This, again, is a very different matter from immunising an animal against its own tumour. Nevertheless, it illustrates how much that was previously unsuspected is being revealed, as step by step advances are made into yet unexplored regions. Inquiries into the effects which the several tissues of the body may have, either singly or in combination, in inducing protection are being made.

Chronic Irritation and Cancer.

A practical result arises out of the association of various forms of irritation with the development of cancer in sites where more obscure influences can be excluded, especially from what has been ascertained on the incidence of cancer in native races practising peculiar customs, and on the incidence of cancer in some animals. Experiment has emphasised this relation, and has thrown light upon the mechanism which makes the irritation effective, leading to similar consequences, although the irritants themselves have nothing in common. Recent legislation is thereby justified in the interest of workers employed in circumstances exposing particular parts of the body to chronic irritation of peculiar kinds. In 1903-4 the feasibility of obtaining more accurate information of the incidence of cancer in different occupations was before the Statistical Sub-committee. The progress made since renders such an investigation still more urgent to-day. It must not be supposed, however, that cancer has been proved to be always the result of irritation. The *mediate* influence of irritation has only been defined more closely than ever before.

MANGANESE MINING IN INDIA.¹

THE many uses of manganese in the arts were known long before the metal had itself been recognised. It has been used since prehistoric times as a colouring material, and by primitive Indian smiths as a flux and as an alloy for hardening iron and bronze; and its power as an oxidiser now renders it one of the most important of disinfectants, and a valuable chemical reagent. The metal has an interesting, but uncertain, history; the origin of the name is doubtful, but it appears to have been first used in the sixteenth century as a variant of magnesium, from which it had not been separated; and even after its recognition as a distinct metal by Gahn in 1774, Bergmann still called it magnesium, though the name man-

¹ Memoirs of the Geological Survey of India. Vol. xxxvii. The Manganese-Ore Deposits of India. By L. Leigh Fermor. Part i., Introduction and Mineralogy. Pp. xcvi+231. Part ii., Geology. Pp. 232-405. Part iii., Economics and Mining. Pp. 406-610. (Calcutta: Geological Survey, 1909.) Price 3 rupees each.

gane, derived from *magnésie* by the reversal of two letters, had already been used.

Manganese is one of the most widely distributed of the metals. According to Mr. F. W. Clark it forms one-thousandth of the earth's crust, and is the fifteenth of the elements in quantitative importance. Mr. Fermor, accepting the number of mineral species as 1000, reports that no fewer than 130 to 140 of them contain manganese as an essential constituent. The manganese minerals are especially conspicuous, as they are mostly found in decomposed rocks upon the earth's surface; and as manganese salts are easily dissolved, the metal is a common constituent in the ash and latex of plants, and is found in the blood and tissues of many animals. According to Penrose, the proportion of manganese to iron in the human body is said to be as 1 to 20.

The increased use of manganese as an alloy has led to a more active search for its ores, with the result that the once important manganese mines of the south of England have been closed owing to the discovery of much larger supplies abroad. The manganese mines of India, according to native traditions, supplied ores to the Phœnicians, and the local smiths faced their anvils and hammers with manganese steel, which they knew as *kheri*. It was not, however, until 1802 that India began to produce manganese ores for export, with the small contribution of 685 tons. The ores are abundant in India, especially in the Central Provinces and in the States of Hyderabad and Mysore, and as the deposits are on the surface, and can be worked by shallow quarries, the Indian output increased rapidly until, for the years 1890-1906, it was second only to that of Russia. In 1906, and possibly some later years, India has taken the front place as a producer of manganese ores. The other countries in order of yield are Brazil, Spain, Turkey, Chile, France, Greece, the United States, and Japan, while large quantities of manganese iron ores are raised in the United States, Germany, and Greece.

The manganese ores of India have frequent but short references in geological literature, but little was known certainly about them until after the discovery of their economic importance. They have now been carefully investigated by Mr. L. Leigh Fermor, of the Geological Survey of India, and he has issued the result of his studies in a monograph that forms a most important addition to the geology and mineralogy of manganese. The Indian mines have added several new species of manganese minerals, amongst which the most important are *hollandite*, the crystalline form of *psilomelane*, and two new species characterised by their striking pleochroism—*juddite*, a manganese pyroxene, and *blanfordite*, the corresponding amphibole. Mr. Fermor also introduces new names for two manganese garnets, *grandite*, an abbreviation for *grossular-andradite*, and *spandite*, for *spessart-andradite*. Commercially, the most important of the Indian species are *braunite* and *pyrolusite*, which together produce 90 per cent. of the output.

Mr. Fermor's memoir includes a detailed account of the manganese minerals. The chemical composition of the various species is re-considered, and the complexity of many of them is shown by the elaborate general formulæ, by which alone they can be adequately represented.

The Indian manganese ores are mainly found in the pre-Cambrian rocks, though some interesting deposits of secondary economic importance occur in the laterites. The chief ores are associated with a varied series of igneous rocks, which Mr. Fermor groups as the *kodurite* series. They range from acid to ultra-basic varieties, all characterised by being rich in manganese and manganese minerals. Mr. Fermor describes in detail the petrography of this interesting rock series. The *kodurites* are apparently intrusive—though the evidence for this fact is described as incomplete—into two series of Archean gneisses. The first series consists of calcareous gneisses and the second of the metamorphic gneisses, which have been described by Mr. J. T. Walker as the *kondalite* series.

As usual with manganese deposits, the Indian mines are still shallow, and the deposits are probably very limited in depth; for they have been formed by chemical processes that only take place near the surface. They are generally due to the replacement of rocks by solutions containing manganese. Mr. Fermor reports that many of the deposits