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New medicine and new biology

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Medicine, as we all know, is one of the branches of biology. It is applied biology, like agriculture, because it has a clear goal and is not practised for curiosity alone. We also know that in biology there has been an unprecedented upheaval during the past three decades, amounting practically to a revolution in outlook. Has it influenced medicine? That is the question.

The revolution in biology can very loosely be called molecular biology, but it now goes far beyond the function and structure of macromolecules. Though it had roots in earlier research in Britain, and particularly Garrod's first accounts of the inherited disorders of metabolism and Griffith's studies on pneumococci, the beginning of the new era may be marked by the discovery in the USA of the chemical nature of heredity from the experiments of Avery, McCleod, and MacCartney on pneumococcal transformation and those of Hershey and Chase on bacterial viruses. This was followed by the great Cambridge and London period of the early 1950s, when were found the three-dimensional structure of DNA and protein and their basis in a linear sequence, which is the language of genetic information. Biology was then set for the great surges of discovery in the subsequent decades, which still continue. The advances may now be identified more broadly as cellular biology, because so many of the new and exciting findings have concerned the role of molecules in intact living cells, not least the cells of the nervous system and cancer cells. Indeed, the expansion of biological knowledge has been greatest in this interpretation of biological phenomena at the cellular and subcellular levels. Similar solutions to the complexities of tissue, organ, or whole animal and plant have still to come.

The advances have depended firstly on ruthless reductionism and on the determination of the scientists concerned to concentrate on the simplest models—namely, viruses, bacteria, and only isolated cells from complex organisms such as mice and man. Secondly, the advances have depended on new technologies and instruments, and would have been impossible

without, for example, isotopes and computers. But of central, indeed crucial, importance has been a special set of technologies concerned with purification, which began with the ultracentrifuge and chromatography, and then the columns and gels. These allow the separation of pure populations of single species of molecules, and even of cells, from complex and largely uninterpretable mixtures previously available. Latterly this concern with purity has led to the technique of molecular cloning. This means taking a single molecule, which is pure by definition but cannot be studied, and arranging for it to copy itself and eventually produce a large population of identical siblings, which may then be analysed with ease. Not only nucleic acids but also proteins may also be prepared by this powerful new technique.

But I am getting into detail too soon. My aim at this stage is simply to emphasise the blooming of biology, and particularly molecular and cellular biology. I now wish to examine the relevance of all this dizzy excitement in practical down-to-earth problems of human disease. So let us consider three inter-related questions: (a) What if any is the impact of the new biology in the prevention and cure of disease as seen by the clinician? (b) To what extent should private or public funds, earmarked for medical research, be allocated to general biology? (c) Should up-to-date knowledge of the new biology be included in medical education, particularly at the more specialised postgraduate level?

The new biology

Before examining these questions let me pick out some of the highlights from knowledge acquired in the past decade or two. I will confine myself to animal as opposed to plant biology, though this division has become increasingly irrelevant. It is a personal and idiosyncratic list, no doubt influenced in some cases by my contact with the scientists concerned, though I shall hardly mention any by name. You must forgive me if I miss your favourites.

MOLECULAR GENETICS

It is well known that hereditary information is encoded in DNA as a three-base coding system. This code specifies the amino-acid sequence of an enzyme or other protein, and was

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deciphered not many years after the structure of DNA itself. But, even though some protein sequences were then identified, it was another 20 years before Sanger followed up his original sequencing of protein by devising a method for determination of the order of the nucleotides in DNA, thus allowing direct reading of all the coded information. Soon afterwards he and his colleagues reported the full sequence—that is, the total genetic information—of the chromosome of small organism, a virus. Since then other virus chromosomes and individual genes from higher organisms have been sequenced. It is often easier now to determine the structure of a protein from the nucleotide sequence of the gene that specified it. At present biochemists are hard at work trying to create genes by direct synthesis, as well as proteins, by adding the nucleotides or the amino-acids in the right order.

An important related discovery was of special enzymes, which recognise short stretches of nucleotide sequence in DNA and make accurate cuts at a particular and identifiable place. If an intact and known gene lies between the cutting sites it may then be isolated. Even large chromosomes with unknown genetic structure from higher organisms can be cut into many fragments, and these fragments examined for particular genes, and their sequence determined. Methods are therefore at hand now for accurate molecular description of the hereditary apparatus as a whole.

But, as I have pointed out, an isolated molecule cannot be analysed, especially if it is a minor component in a mixture, and many of these successes rest on another series of discoveries entailing cloning. For this, small fragments comprising stretches of DNA from one organism may be propagated by stitching the fragments into a plasmid, which is a special part of the naturally replicating DNA of another organism, such as a small rapidly dividing bacterium, typically *Escherichia coli*. In this way a single gene—for insulin, for example—can be amplified to a huge degree, and, by including the right additional sequences, which act as reading controls, it may even produce insulin itself in the bacterium.

A basic dogma in genetics that we learnt as medical students was that one gene—that is, one continuous stretch of DNA—contains the information for one protein, and DNA, RNA, and protein are colinear. But as a result of the detailed analysis of DNA we now know better. The information for a single protein may be encoded in widely separated stretches of DNA. That means that the gene is split and the necessary final sequence of information for the protein is produced by editing—by excising segments and restitching the original RNA transcript copied from the DNA. This in turn means that the same original sequence of DNA can, by different editing of the transcript, give a variety of alternative proteins. It is precisely this which seems to happen in the synthesis of immunoglobulins, for example, thereby explaining the huge repertoire of antibody specificity.

Some small viruses have so little DNA that they could code directly only for one or two normal-sized proteins, but by different modifications of the same sequence of information a whole range of protein species are derived from a single old-style gene.

Now that a full specification of the hereditary material in small organisms is available the importance of the previously mysterious non-coding sequences, which do not specify the amino-acid sequences in proteins, may be investigated. It seems that, apart from the familiar punctuations, some regions are enzyme recognition sites, perhaps through secondary folding. Indeed, a new field of research has now emerged that is concerned with the linguistic rules of genetics.

SOMATIC CELL GENETICS

The discovery of cell fusion and construction of hybrid cells with two sets of chromosomes, some of which are then eliminated at random, together with the detailed identification

of the individual chromosomes, has provided rapid advances in the cellular as opposed to molecular aspect of genetics. These techniques, originally pioneered in Oxford, have allowed the rapid allocation of a wide range of genes to individual chromosomes and, notably, the demonstration that neoplastic changes are often recessive. Now, individual chromosomes can be isolated and transferred alone from one cell to another, pointing the way to the eventual relief of genetic defects. Before long, molecular and cellular approaches will undoubtedly be merged in the study of gene expression in differentiation and development.

Another quite new approach to development and differentiation comes from new techniques also developed in Oxford, and simultaneously in Philadelphia, for dissecting and reconstructing very early embryos comprising only a few score cells. Cells from two early embryos can now be fused, giving animals with four instead of two parents, and made up of a mosaic of genetically different cells whose interaction can be examined in vivo. Most dramatic is the discovery that certain cancer cells can be introduced into embryos and seemingly cured, because the progeny of the cancer cells can later be found to be functioning normally as constituents of a variety of healthy tissues, even in later adult life. Recently it has even been possible to insert genes from other species into mice by introducing such genes into mouse tumour cells by cell fusion, then incorporating the resulting hybrids into normal mice via the early embryo.

MOBILE CELL SYSTEMS

Though previously defined on detailed morphological grounds by pathologists and haematologists, the interrelationship of the great variety of mobile cell systems of the body has been explained only in recent years, through the development of cell culture techniques and the discovery of precise sets of markers, especially surface protein markers for distinguishing morphologically similar cell types. This is one facet of the marvellous unravelling of the immune system in the past 20 years, to which I can do no more than draw attention. It has enabled cell biologists to understand much of the step-by-step differentiation from primitive stem cells to their functional end products, be they erythrocytes, neutrophils, or different classes of lymphocytes. These last are known to include clonal sets derived from single cells responsive to single antigenic stimuli, and one of the most potent recent advances was the discovery by Kohler and Milstein in Cambridge of a method of propagating the descendants of one of these single cells producing a single species of antibody. It was done by fusion with a tumour derivative of a similar cell, a myeloma. All the descendants of the resulting hybrid yield a single species of antibody globulin, specific for a single antigen. I shall return to this monoclonal antibody technique because it is likely to have more impact in medical science in the near future than most other discoveries.

MEMBRANES AND HORMONES

Though the lipid bilayer structure of cell membranes has been accepted for many years, and the specialised membranes of nerve cells extensively characterised, only in the past decade have functional units in cell membranes in general been identified, and quite new ideas emerged about their operation. Some of this began in London with the finding that molecules visualised by immunofluorescence, which bound to the cell surface, did not remain stationary, but moved around and sometimes clustered together. We now know that this is because the cell surface bilayer is a two-dimensional fluid, like a thin layer of oil on water with functional protein units, such as transport sites, hormone receptors, antigenic determinants, etc, which float around, some more, some less mobile. This variation in mobility now seems to be due to anchorage of the membrane proteins, some of which extend right through the lipid layer, to

muscle-like microtubules and microfilaments beneath the inner face of the membrane, and which may exert control over membrane protein movement.

Of great importance is the recent finding that the action of a hormone, such as insulin, which binds to a receptor floating in the membrane layer depends on aggregation or clustering of more than one insulin receptor to form a complex. It has recently been shown that the action of insulin can be mimicked by aggregating its receptors with antireceptor antibody. It now seems possible that peptide hormones themselves may have no further role once they have attached to and mobilised the target cell receptors.

The changes in transport efficiency of small molecules are probably controlled similarly by aggregation or disaggregation of membrane sites. It is also believed that some of these membrane receptor complexes can interact with other structures lying in the membrane, such as the enzyme adenylcyclase, leading to the cascade of cyclic AMP-dependent phenomena that are currently attracting so much interest. Perhaps, of all fields of biology, membrane structure and function are likely to progress most rapidly in the coming years.

Many new types of hormone-like control molecules have come to light in recent times. There are, for example, the mitogenic factors found in blood and tissue. The source of these is unknown, but some of them are stored in platelets. For a particular type of cell to start a cycle of division the right combination of these hormones must all bind to their own cell surface receptor. This provides the required signal, a sort of telephone number for that cell type alone, which must surely play an important part in morphogenesis.

Perhaps the biggest surprise has been the discovery of the peptide hormones of the central nervous system, which I have not mentioned so far. The presence of naturally recurring brain cell receptors for plant products, such as opiates, has always been a puzzle. Nevertheless, it has led to the discovery, originally in Aberdeen, of a set of small peptides or opioids that exist naturally in the brain and which can bind to the opiate receptors. These encephalins, and related endorphins, discovered in the USA, are now believed to modulate the pain pathways in the central nervous system. These open a new approach to brain function, not limited to short-range neurotransmission, but via a whole range of oligopeptide hormones as well. Indeed, we must now accept that the brain is an endocrine organ.

You must forgive me for not describing other remarkable discoveries on the central nervous system, such as the new understanding of visual perception from the mapping of circuits in the visual cortex. I emphasise again that I have limited myself to a few personal choices of major advances in biology at the level of molecule and cell.

Impact and relevance

I now turn to medicine and ask the first of the earlier questions. What, if any, is the impact of the new biology on the prevention and cure of disease as seen by the clinician?

I try to keep some contact with my old profession by scrutiny of the leader columns in the *British Medical Journal* and the *Lancet*. So before preparing this talk I examined the leading articles over a nine-month period to see how many dealt with topics that referred directly or indirectly to the advances in molecular and cell biology to which I have referred. Out of 235 leaders, only three were strictly relevant, one on opioids, one on the molecular structure of smooth muscle, and one on viroids, interesting objects, but so far only found in plants. In another 11 mainly clinical subjects I noticed a brief reference to some recent advances in biological science of the type I have mentioned. From this, at least, it does not look as though the new biology has revolutionised medical practice.

But let us look at it another way. What are the major advances in clinical practice during the past decade or so, and how much

do these depend on the advances of molecular and cell biology? On this I am even less qualified to speak, except perhaps in oncology, where advances have been lamentably few. In effect I can give only a layman's view, which would include the following in no special order.

Life support systems—The ability to keep the nearly dead alive is an incredible new development, with problems as well as blessings. But it seems to be based on new, mainly electronic instruments; new drugs, mostly from empirical research; and old, well-established principles of physiology, rather than molecular biology.

New classes of drugs—The discovery of tranquillisers, corticoids, and β -blockers, etc, did not depend on molecular biology, though the last are of interest to cell biologists because of their relation to peptide hormone pathways and cyclic AMP.

Successful cancer chemotherapy—The cure of a few rare cancers, such as Hodgkin's disease, acute lymphatic leukaemia, and chorioncarcinoma, by chemotherapy and radiotherapy cannot be claimed by basic biologists. The drugs were nearly all discovered for other purposes, and the successes have been due to patient and methodical clinical trials rather than knowledge of the abnormalities of cancer cells.

Scanners and ultrasound—These have depended on advances in instrumentation, especially computers, and are based on transistors, semiconductors, and in turn basic physics, especially the solid state physics started in Cambridge in the early 1930s.

Smallpox—The elimination of smallpox, probably from the whole globe, should be regarded as one of the greatest of the recent medical triumphs, even though it is not so obvious in Britain. It has been due to old principles in microbiology and immunology, and a newish invention by politicians—namely, the World Health Organisation.

Lung cancer—This remains one of the commonest fatal diseases. But we now know how to avoid it, and this should surely be regarded as a major achievement—even though our advice is not heeded. But once again the discovery is not the result of the new developments in biology.

Transplantation—Thirty years ago it would have been difficult to predict the large number of people with transplanted organs, leading even to Olympic games for transplant patients. But this new branch of medicine has been possible only with matching systems that are based on a new knowledge of transplantation antigens—that is, in man, the HLA system. This new knowledge is very much at the centre of research on membrane structure and molecular genetics.

These are all major achievements, only the last of which really depends on advances in basic biology during the past three decades. But there are other less dramatic areas of advance which come about directly from molecular and cellular biology.

The haemoglobinopathies, for example, benefit from new understanding that stems directly from discovery of the structure of the haemoglobins and their genes, and the processing of the relevant information in the cell. In another group of diseases, the muscular dystrophies, particularly myasthenia gravis, an entirely new view of the aetiology comes from knowledge of muscle cell membranes, the operation of the transmitters and receptors and of the immune system. Prenatal diagnosis of hereditary disorders by amniocentesis is possible only because of new techniques and understanding of chromosomes and gene products. Finally, in preventive medicine the new methods of screening for mutagenic carcinogens in the environment come from advances in bacteriophage genetics and DNA repair systems.

So far, then, we should conclude that the advances in biology have had a few successful rewards in practical medicine, but that the impact is really quite small.

TIME FACTOR

We forget the time factor, however. It took, after all, 100 years from the original discovery of micro-organisms as the cause of

infectious disease by Pasteur and his followers to the major successes, such as antibiotics and successful vaccination against a wide variety of infectious agents. Can we predict some practical advances from molecular biology in a similar or, we hope, shorter time span? Let me at least attempt a bit of guess-work.

Taking first the next decade—that is, the short term—there are two obvious examples. Firstly, gene cloning could allow large-scale production of useful biological products. Growth hormone and insulin have already been produced, and commercial synthesis of a wide range of peptide hormones should follow within the next five years. Synthesis of interferon is more difficult but has been claimed in recent months. Pure virus vaccines from cloned viral gene products have also been synthesised from an influenza virus and hepatitis B virus. Commercial development will not be long.

Secondly, the monospecific antibody globulin technique, and the new knowledge of antibody structure, should within the next few years give precise new diagnostic aids based on exact detection of individual proteins, which will revolutionise the diagnosis of many diseases, including cancer. It may lead to a reappearance of an old method of prevention and treatment—namely, passive immunisation—since a single pure species of immunoglobulin in high concentration could be used instead of a minor component in a complex mixture, as in the old antisera. In addition it gives renewed hope of directing cytotoxic drugs specifically to target cells, such as cancer cells.

Possible advances

Let us now turn the crystal ball to the distant and the more cloudy future, and to advances that are possible even probable, but only after several decades. Thus they may only be of benefit to our grandchildren or great-grandchildren.

Firstly, the fuller understanding of immunity and the HLA system may eventually allow transplantation to become commonplace. This will be increasingly important even in the nearer future, not for whole organ transplant but for replacement of defective stem cells in aplasias and other haematological disorders. Secondly, research on hormone and transmitter molecules in the brain may lead to new drugs that have a profound effect on pain and perhaps on behaviour, though I should think that the alleviation of mental disturbance by any sort of rational approach is still beyond our horizon.

Genetic manipulation of the germ line and of embryos—for example, by addition of cells with artificially modified chromosomes to complement a hereditary defect—may also be predicted in the long term, and we know that it arouses considerable social fears. Cloning of individuals is theoretically possible now but is unlikely to interest geneticists or doctors, as we like to think of ourselves.

And finally we come to the prospects for alleviating cancer. Unfortunately the more progress we make at the molecular level in cell and gene regulation in normal cells, the more subtle and complex do we find the nature of the cancerous change. Nevertheless, there is now a growing confidence that this gradual unravelling is unescapably the right approach and that in time, with much patience and distant vision, the problem of cancer can and will be solved.

So the answer to our first question on the impact of the new biology on the prevention and cure of disease is this: very little, but—as Eliza Doolittle warned Professor Higgins—“just you wait.”

The other questions may now be answered more briefly.

Medical research in Britain is funded from public sources, private charities, and pharmaceutical and other companies. To some extent most of it is earmarked for the alleviation of disease. To what extent should this money be used to pay for basic biology, the understanding of living systems, which might have an impact on medicine in five or 50 years, or perhaps no impact at all?

Because of successes in applied, mission-orientated research, particularly in the space and weapon programmes, there has been increasing pressure in the past decade for much more relevance and closer control in the medical research programmes funded by governments. When working as research director of a major cancer charity this problem exercised me a great deal, since our funds depended on donors who, unlike the anonymous taxpayer, were asking for their contributions to be used for a very specific goal.

Clearly, there are many immediate and expensive problems in application and development of existing knowledge that deserve a large slice of any medical research budget. So why should any money at all be set aside for research that is carried out to satisfy intellectual curiosity and the urge to understand mechanisms rather than solve problems? Such research would not be needed if the pool of accumulated basic knowledge was sufficient, and energetic application was all that was needed to alleviate human suffering from disease. But we all know that that is not the case. In the major afflictions—heart disease, cancer, and mental disease—we are almost totally ignorant of the underlying mechanisms, and we have no way of telling which of the many possible approaches will be successful. The solutions will lie in discoveries to be made in the future, which by definition are unknowable now. Such discoveries can be made only by those who can follow their inquiries freely wherever they may lead.

The evidence of this comes from history. You may know of the extensive investigation by Comroe and Dripps, who with the aid of numerous colleagues identified the series of key discoveries essential for ten practical advances in cardiac and pulmonary disease, ranging from open heart surgery to treatment of tuberculosis. Their extensive analysis showed that 41% of the discoveries essential for the later clinical advances arose from research carried out without any motive at all directed to practical clinical applications. Over 60%, indeed, was really basic research in the sense that it was concerned with mechanisms and not with application.

Even when seeking one goal another may be reached. Let me here give a personal example. When beginning cancer research for the MRC in 1959, McPherson and I isolated a certain line of cells for neoplastic transformation studies. It turned out that this cell was also ideal for growing foot and mouth disease virus for vaccine, and thanks to British veterinary virologists at Pirbright it is now the main source of the world's vaccine supply. Therefore our small effort contributed indirectly to human life not by helping patients with cancer, as dictated originally by our funds, but by increasing meat supply and reducing starvation.

So even though application and development of current knowledge are essential, we must conclude that major advances in the great diseases will come from untargeted, untidy research carried out for its own sake, and someone has to pay for it. Surely the funds earmarked for medical research should contribute their share. Fortunately I am glad to say the Medical Research Council have always accepted this view, and much of the molecular biology to which I have referred stems from Sir Harold Himsworth's staunch adherence to this principle.

Medical education and biology

Finally, I come to my last question, which is aimed, I admit, partly at the British Postgraduate Medical Federation. To what extent should a knowledge of modern biology be included in medical education, particularly at the postgraduate level?

It is an important question with some degree of urgency. This is because the biological sciences on the one hand and medical practice on the other are becoming increasingly complicated, and the output of information so large that polarisation is becoming more and more apparent. For example, it is particularly noticeable in cancer research, where, with some

notable exceptions, clinicians and, let us say, molecular oncologists are becoming more and more distant from one another, and with little common language. But surely two cultures are the last thing we want in biomedical sciences.

There are a few branches of medicine, some the concern of your own institutes, where specialised knowledge of some aspects of cellular and molecular biology will automatically be a part of the trade; obviously, for example, in cancer research, also in neurology and in paediatrics, where a knowledge of genetics will be needed, or in other specialties where immunity is important. But we must admit that for most specialised branches of medicine a knowledge of recent advances in biology is not of paramount importance. The nucleotide sequence of a cancer gene, for example, will not at present help anyone to help or treat a patient with cancer.

So when there is so much to learn to maintain a high professional standard why bother about basic biology? For a large proportion of clinicians we must admit that it will make very little difference. But the leaders of the profession, and especially the teachers, will be in serious trouble if they fail to acquire a knowledge of the new concepts in the basic sciences. In ten or 20 years' time medicine will be vastly different, not just because of computers and robots. Then it probably will be necessary to

know about terminal amino-acid sequences and stop codons and such like, because, who knows, you may need to write these into your prescriptions. And make no mistake, the young medical student coming through in these future years will have all this at his fingertips. Being ignorant of the new biology then would be like managing the treatment of an infectious disease without knowledge that bacteria and viruses exist. Moreover, the leaders of the profession, many of whom I hope will still emerge from the network of the Postgraduate Medical Federation, should be in important positions for influencing decisions on strategy and tactics in future medicine and medical research. In such influential positions a wide and up-to-date view of the scientific basis of medicine is required.

It is for this reason that I have always so much admired the Federation's series on the scientific basis of medicine. Looking back on this series over the years one sees now that it has covered much of the exciting new biology that I have been discussing and which is going to change our lives. Whatever the future holds for postgraduate education in medicine I hope that this type of education for doctors will be expanded and developed further. Meanwhile the series shows the vision and wisdom of the leaders in the federation. It is no accident that it began under Sir Francis Fraser, and it is a fitting tribute on which to close.

SHORT REPORTS

Beware the bay leaf

Two cases of unusual foreign body ingestion requiring endoscopic removal are presented.

Case reports

Case 1—A 77-year-old man with a history of pharyngeal pouch for several years suffered symptoms of fullness and persistent aching in the region of the pouch after eating the Moroccan dish tarjin. The pouch failed to empty, and two months later at endoscopy under general anaesthesia a bay leaf was removed. There was mild inflammation of the mucosa.

Case 2—A 61-year-old man was eating pâté and felt something stick in his throat. He thought this was metallic but no radio-opaque foreign body was seen on plain x-ray film. At endoscopy under general anaesthesia a bay leaf was found stuck in the hypopharynx.

Comment

The bay laurel (*Laurus nobilis*) is an evergreen shrub whose leaves were used in classical times to make wreaths for crowning the victorious. The leaves are 5-10 cm long with a wavy edge (figure), which may explain their tendency to adhere to the mucosa of the pharynx.

Leaves of the bay tree.

Bay leaves are commonly used as flavouring for puddings, stews, and other dishes. Tarjin, a popular Moroccan dish, is a stew that simmers all day over a very slow heat, the ingredients being left much to the cook's imagination. There is a meat constituent and a concentrated stock which contains plenty of butter, oil, and herbs, in which bay leaves usually abound. It should be served in a vessel of glazed earthenware.

In the first case a bay leaf remained unchanged for a long period within a pharyngeal pouch and caused mild symptoms of inflammation. The patient was reluctant to undergo operation, and so the foreign body was removed by endoscopy. Endoscopy also showed that there had been no malignant change in the mucosal lining. As the patient intended to return to Morocco he was advised to eat tarjin in the traditional manner, using fingers to dip the meat in the soup, and so avoiding further bay-leaf ingestion.

Conquerors have been crowned with laurel, perhaps leaving the vanquished to console themselves with soup flavoured with bay. Without care they may have not seen the end of their troubles.

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Outbreak of botulism in Kenya after ingestion of white ants

Six cases of botulism, five of them fatal, occurred in Kenya in October 1979. The contaminated food was a collection of termites (order *Isoptera*), commonly known as white ants. These are considered a delicacy by several tribes in Kenya. They are collected as they emerge, en masse, from the soil to make their nuptial flights when suitable conditions of humidity and temperature prevail. They are rich in protein and fat and have been considered as an exploitable food source. All patients (five from the Luhya tribe, and one Luo) ate the white ants, either raw or fried, at a meal in Nairobi three days after they had been collected in Kakamega, 400 kilometres from Nairobi. Some of the ants had been eaten fresh by about 12 people in Kakamega, none of whom fell ill. The remaining ants were transported to Nairobi by one