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THE LATEST RESULTS OF EXPERIMENTAL CANCER RESEARCH AND THEIR IMPORTANCE ON THEORIES OF CARCINOGENESIS

by

Dr. Hans Bettinger.

Professor of Pathology, Military Medical College, Canton.

Experimental cancer research made its real start in 1913, when Fibiger achieved for the first time the production of cancer experimentally. It was not that there had been no cancer research before that year, but earlier work was restricted mainly to the inoculation of accidentally found tumours from one animal into another. Naturally, conditions were studied under which these inoculations were more or less successful, the manner of growing and spreading of these tumours were studied, but investigation of the causes of the tumours was hindered by the idea prevailing at that time, about the tumourgenesis. The work was directed mainly to bringing forward proof for these theories. Investigators inoculated embryonic material in order to get support for Cohnheim's theory, but these inoculations did not give rise to carcinoma or sarcoma, but only to teratoma-like tumours. Other experiments, based on Virchow's irritation-theory sought to produce cancer by external application of various means (Scarlet dye) but conclusive results were not gained. Further, influenced by the discoveries that bacteriologists had made, the main line of research work was to try to discover the parasite which might produce cancer in the same way as tubercle bacillus produced tuberculosis. Reviewing such work we can say that the majority of these experiments must have failed because they were based on wrong premises. Fibiger's great discovery was really an accidental one. Working on other lines he had casually found cancer in the stomach of rats and in the cancer parasites, the later so-called Spiroptera neoplastica. He did not succeed in producing cancer by feeding these parasites to other rats until he had first fed the parasites to cockroaches which he found to be the intermediary hosts of these parasites. His discovery seemed at first

to confirm the parasitic theory and had the tendency to lead the research work in a wrong direction. But as these tumours were studied more exactly, it was found that the metastases never contained any parasites and were therefore not caused by them, and so spiroptera cancer became eventually an argument against the parasitic theory; for it was seen more and more clearly that there were fundamental differences between inflammations caused by parasites and tumours, and that the cancer problem was a problem of growth and not of infection. Once the search for the one cause of cancer was abandoned, the search for all the various possible causes of cancer could begin. The liberation from this prevailing theory gave a great impetus to experimental cancer research work and we can see that it developed fruitfully in three different ways. The first way followed the former experiments: the well-known animal tumours were now used for a very exact investigation of the qualities of the tumour-cells and as a test object for the ever and again proclaimed cancer remedies. The second way tried mainly to discover the intrinsic factors, especially by heredity experiments on a large scale. The third way was the study of the extrinsic factors, and in this way the most surprising results were deduced.

EXPERIMENTS ON ANIMAL TUMOURS.

Up to the last few years there were only four tumours which gave consistent results, the two mouse carcinomata of Ehrlich, the rat carcinoma of Walker and the rabbit carcinoma of Brown-Pearce;—we will disregard the Rous chicken sarcoma because its position in the system of neoplasms is not yet fully clarified—. A number of other carcinomata and sarcomata was also known, about twenty in all, but their transplantation did not give results equal to the tumours mentioned above. Each investigator who intended to start with such work, had to face the great difficulty of getting proper material. Since then, it has been possible to get about seventy-five tumours which can be transplanted without special difficulties. That, in itself, is great progress. We have now at our disposal sufficient and well-fitted material for all purposes. What are the problems suited to be investigated by these means?

It has been much emphasised that these tumours are relatively benign, not in anyway comparable to human cancers. That may be true, in so far as the infiltrative growth and the production of metastases is considered. But usually it is not possible to cure these cancers, even by application of means which would by their quality or quantity not be applicable in man. Therefore, those who say that one who succeeds in curing these animal cancers will be able to cure the majority of human cancers are right. And so the animal cancers are an excellent test object for all our therapeutic efforts. Some noticeable results have been gained in this way. It is possible, for example, to produce

immunity or at least high resistance against the inoculation of such tumours by cell-free tumour filtrates or various organ extracts. Furthermore, it is possible by biological, physical, or chemical means to slow down the growth of such tumours or bring them to a standstill. Only in a very small number of cases has a real cure of these tumours been achieved. The value of these experiments is that we have here exact possibilities of comparison, because we know for each race of animal and each kind of tumour the percentage of positive inoculations and the average length of time the animals survive. I will not enter into the details of the results of these experiments, for, interesting as they may be, they were gained by means not applicable in the same way to man.

Another point especially suited for studying in these animal tumours is the biological behaviour and the metabolism of the tumour cells. I mentioned above the high resistance of the tumour cells. It is astonishing what can be done with them. Ehrlich kept tumour fragments for two years at —8°C. on ice and afterwards got positive inoculations. Roessle froze them for three minutes in fluid air at —195.7°C. without killing them. Radiated by x-rays they endure more than 100 times as much as normal cells.

Furthermore the study of these tumours shows very clearly the cellular nature of tumours. Although the idea that parasites might be transferred with the tumour cell, has become more and more unpopular, it has been in recent years suggested that an ultravisible virus or other agent might be set free from perishing tumour cells and might then induce the cells of the inoculated animal to give rise to cancer. Roessle was able to show by 1,200 transplantations that in studying the very beginning of neoplasms it is clearly to be seen that the surviving cells of the first animal are those which produce the neoplasms in the other animal.

These animal tumours prove, in addition, the specific individuality of the tumour cells. The cell of a definite tumour produces ever and again the same kind of tumours even if one brings it through many animal passages or cultures it for a long time outside the body in tissue culture.

These tumours show clearly the so-called autonomy of tumours relative to the growth in the body of animals, as well as, considering the fact that they transgress a law which is valid for all other tissue or organs of the higher animals, that a transplantation with all active vital functions is possible only autoplastically, but not homioplastically.

It is furthermore an astonishing fact that the cancer cell is practically immortal. Just those cells which destroy the body of their hosts and kill them are able to survive for an unlimited length of time when transplanted from one animal to another or when bred in tissue culture.

Thus we can state with all certainty that with the transition of normal cells into tumour cells fundamental changes must take place in the cells. Warburg was able by studying such tumours in the tissue culture to show such changes in the metabolism of the cancer cell. They are able to live without any oxygen by glycolysis only, and even if they have enough oxygen at their disposal, they oxidise only one-thirteenth of the sugar while twelve-thirteenths is broken down into lactic acid. A major part of these fundamental changes is therefore the regaining of embryonic qualities. And now you will naturally ask what kind of factors may be suited to bring forward such changes of the cell character? Were we able to answer this question thoroughly we should have had solved the problem of neoplasms. Still, Carell made a great step forward in this direction, a step we can only compare with Fibiger's great discovery. He succeeded in transforming in tissue culture not only embryonic cells but also the monocytes of the blood into cancer cells by adding to the culture cell-free tumour filtrates or by radiation with X-rays. These cells showed in the cultures all the qualities of cancer cells and kept these qualities for an indefinite period and in inoculated animals they gave rise to tumours. So the production of cancer in the test tube has succeded.

Before we consider other methods by which artificial production of cancer has been tried, we will first enter into the discussion of the intrinsic factors, because it is hardly possible to state exact dates of the effects of extrinsic factors so long as the intrinsic factors are not known.

HEREDITY.

As the intrinsic factors are mainly dependent on heredity, we have now to ask what we know about cancer heredity in man. And there is only one true answer and that is practically nothing. There are three methods by which we can study cancer heredity. First, the statistical method which has achieved noticeable results relative to the distribution of cancer in the different ages, the geographical spread and the differences in the sexes, but even when we are able to prove that the offspring of cancer patients have more cancer than those of non-cancer patients, we do not gain much from this result.

The second method is the family tree research. Here we have to face many difficulties. It is hardly possible to rely upon diagnoses made a hundred years ago. Cancer may be more frequent in some families without being inherited because the majority of these family members may have been exposed to the same extrinsic factors, and as out of ten men and seven women, one dies of cancer there may occur accidental accumulations in certain families. Furthermore, results of real value occur only in those kinds of tumours which follow the strong one factor scheme of Mendel. Only three of all the various kinds of human tumours do so. They are the *Neuroblastoma retinae*, the *Xeroderma pigmentosum* and the *Polyposis intestini*. All these

three, expecially the first two are rare and uncommon tumours, not the kind we have to deal with every day.

The third method, the twin research, has too little material at its disposal. Only 15 cases of concordant tumours in identical twins (7 males, 8 females) are known. Among these are quite a number of rare and uncommon tumours.

We therefore have to take resource in animal experiments to answer the questions. What influences has heredity in carcinogenesis? For here we are able to control crossing and breeding at our will. Astonishing and interesting results have been achieved in this way. Scientists (Maud Slye and others) succeeded by extreme inbreeding (by continual crossing of brothers and sisters) and strongest selection in breeding of mice races which developed cancer in 100% on the one hand, and on the other hand of such as were absoltely cancer resistant. They bred races which developed not only cancer, but cancer of a definite organ, at a definite time of their lives. Cancers which were usually not transplantable could be inoculated in certain races with success. By crossing such differently susceptible races it could be demonstrated that there are races in which the transmission of the cancer predisposition is only dependent on the mother. When one crosses a male animal of a cancer race with a female one of a cancer-free race, the offspring do not develop cancer and vice versa. This observation cannot be explained by the Mendelian laws according to which at least a part of the daughters of the father of the cancer race should have developed cancer. We have to take for granted that in these cases the protoplasm of the ovum is the carrier of the cancer predisposition.

In the course of such experiments it could be demonstrated that all these cancers were not dependent on only one single Mendelian factor. It could be shown that often 5 or 8, sometimes 10 or 12 such factors have to come together in order to produce cancer without any extrinsic factors. Moreover it resulted that often presence of all these chromosomal factors was not sufficient, that other factors were able to suppress the manifestation of these factors, that all depends on the co-operation of all the hereditary factors, but these experiments showed also, that even in these specially bred races other factors have their influence. Metabolic disturbances, expecially hormonal disturbances, and even extrinsic factors, such as tarring are able to increase the cancer rate in well-known races. In several cases, gross extrinsic factors may be suitable to bring such predispositions to manifestation.

What conclusions may be drawn from these experiments for human pathology? At first we must not forget that these results were achieved by extreme inbreeding and strongest selection of white mice, the most degenerate species we know. Therefore we cannot expect to find similar percentages in man and we may not try to transfer these figures, astonishing and impressive as they may be by themselves, to human

circumstances. But the fundamental knowledge gained in this way is of the highest value. We can be certain that hereditary factors are highly important in the formation and localisation of tumours, and we have learned that one single factor is usually not sufficient to give rise to a tumour, that a number of factors have to work together. It is rather improbable that these conditions are fulfilled in man who is not at all pure bred and further we have seen that even the presence of all hereditary factors is often not sufficient for the manifestation of the cancer predisposition. Frequently, these factors do not even stipulate a stringent cancer predisposition, but only a certain predisposition for disturbances of metabolism or differentiation, out of which a cancer predisposition may rise only through other factors. Often it remains latent till it is brought into the open by other intrinsic or extrinsic factors. Therefore we must come to the conclusion that the ordinary human cancers are usually not due to heredity alone.

CANCER DUE TO EXTRINSIC FACTORS.

The investigation of the importance of extrinsic factors took its origin from observations in man. There were known three groups of cancers associated with extrinsic factors: first, in the group of parasitic cancers, the Bilharzia-cancer, which we can retrace in history for several thousand years, secondly, in the group of physical factors, the kangri-cancer of the abdominal wall of the Tibetans (they carry a hot basket of charcoal under their clothes for purposes of warmth and after many years cancer often originates in that part of the body where cancer is very uncommon), further Roentgen-radium, and mesothorium-cancer. Thirdly, in the group of the chemical cancers, the arsene-aniline dye- and the chimney sweeper-cancer were known.

By experimental research endeavours have been made to extend our knowledge in all these directions. To the first group belongs Fibiger's great discovery. Another similar tumour is the liver sarcoma of the rat which is produced by the *Cysticercus fasciolaris*. We saw that it very soon became a certainty that the parasites were responsible only for a chronic inflammation which later gave rise to a tumour. The metastases developed without any co-operation of the parasites. Their effect is a poisonous one at the place of their invasion and is not to be compared with their effect in the production of inflammation. This kind of research work therefore was not likely to have further success.

The observation of the production of cancer by radiant energy led to an exact investigation of all circumstances in question. The lung cancer in the mines of Schneeberg and Joachimsthal, could be attributed to the proportion of radium emanation in the air. The Roentgen and radium-cancer is only too well-known. A new source of cancer production has lately been discovered in America in factories producing luminous dial plates. The luminous compound contains radio-active substances which pass into the bodies

of the girls who paint these dial plates by shaping the brush into a point with their lips. These substances are deposited in the reticulo-endothelial system, especially in the bones and give rise here to a diffuse sarcomatosis. Another observation is the cancer of the skin of the face in farmers and sailors, an occurrence which depends on the effect of the ultra-violet rays of the sunlight.

All these observations were verified by experiments and new results achieved. In 1929 Bloch succeeded for the first time in producing a cancer of the rabbit's ear by X-rays. Roentgen, radium, mesothorium have proved themselves also as carcinogenic in experiments. To-day we know exactly the necessary quantity of rays required. Below a certain amount only benign papillomas originate, above it only necrosis. In experiments ultra-violet rays also gave rise to cancer.

All these observations and experiments have apart from their practical value for the prevention of injuries an essential theoretical value which we shall later consider.

In discussing the group of chemical factors I may only mention that experimental production of cancer by arsene and aniline dye has also succeeded. Scarlet dye was experimented with for a long time as it was known that it produces epithelial exuberances in surgical treatment. But it was not possible to produce real cancer by this dye.

Yoshida succeeded in 1932 in producing liver cancer in mice only by feeding a definite quantity of the scarlet dye for a long period of time. After 250 days all animals developed cancer. Feeding less necessitated a longer time for the development.

All these experiments show that the formation of tumours depends on the quantity of the compound and the duration of the treatment.

Of far greater importance are other experiments which took their origin from the observation of the chimney-sweep cancer. In imitation of the natural conditions many tried to produce cancer by application of tar on the skin, but all these experiments were unsuccessful until in 1915 two Japanese, Yamagiva and Ischikawa, had the necessary patience to continue the experiments for nearly a year. Thus they succeeded for the first time in producing a tar cancer on a rabbit's ear. A short time later the method of tarring the skin of the back of mice was developed, a method which to-day has become the standard method for verifying all carcinogenic substances. Experiments in producing cancer of the internal organs by tar also succeeded. In this way new knowledge was gained, especially about the first stages of carcinogenesis. But the question could not be answered and this fact always overshadowed the satisfaction of all these results: the question, what have all these substances to do with the rise of cancer in man? Men do not normally come into touch with all these often very uncommon compounds. Does then anything at all result from these experiments for the explanation of human cancer? The first

answer to these questions came from an unexpected source. The tar has proved its high carcinogenic qualities. Naturally as tar is one of the most complicated of substances the question had to be asked, on which of the thousands of substances contained in the tar does the rise of cancer depend? This question certainly seemed to be unanswerable at first sight. It is one of the most wonderful achievements of the human intellect that it was really possible to come nearer to the solution of this problem. The first step was made by Bloch and Dreyfus (1921) who were able to show that the carcinogenic agent is to be found in a mixture of nitrogen-free substances boiling above 400° C. By this means a great many substances were eliminated, but the number of the remaining was large enough. Further progress was made by an admirable co-operation of the pathologists and chemists of the Research Institute of the London Cancer Hospital under the direction of Cook. In 1924 Kennaway was able to show that the highly condensed hydro-carbons contain the carcinogenic agent. Thereby it was demonstrated that the carcinogenic substances had nothing to do with poisons, dyes, remedies and so on which our chemical industry has produced in such great numbers from tar. The next great success is due to Mayneord (1927) who was able to show that only those hydro-carbons are carcinogenic which have a certain fluorescence spectrum. Thus the number of the compounds in question was considerably narrowed. Cook and his fellow workers succeeded in isolating the first substance, already well-known in its chemical structure and that was the 1.2 benzanthracene. This compound was not very strongly carcinogenic but very nearly related compounds especially the 1.2, 5.6 dibenzanthracenes were highly active. Very soon it became clear that the effect was dependent on the molecular structure. Even trifling changes made the compounds ineffective. It is interesting that at most, one nitrogen atom may be added, as two make every substance inert. The 1.2, 5.6 dibenzanthracene could be produced synthetically by Kennaway. It was till then the most highly efficient compound and he succeeded in producing skin cancer as well as spindle-cell sarcomata of the connective tissue also cancer of the internal organs (lung, kidney, liver, testes, uterus). These tumours made metastases and could be transplanted into other animals. The great advance chiefly was that the research work stood now on an exact chemical basis but all these compounds were not so efficient as the tar itself. Finally the chemists of the London Cancer Hospital, succeeded in gaining from 500 lbs. of tar, a substance which the tar contains only in 0.003%, the 1.2 benzpyrene. It differs from the 1.2, 5.6 dibenzanthracene only in this, that its 5th ring is not added at 5.6 but at 1.9. Adding the ring at another place results in inefficient compounds. Cook was able to produce it synthetically. It is a highly efficient compound. Painting it in a 5% solution on the skin, produced a cancer in 56% of the mice after 120 days. Injected into the connective tissue it gives rise to spindle-cell sarcomas.

Figure 1.

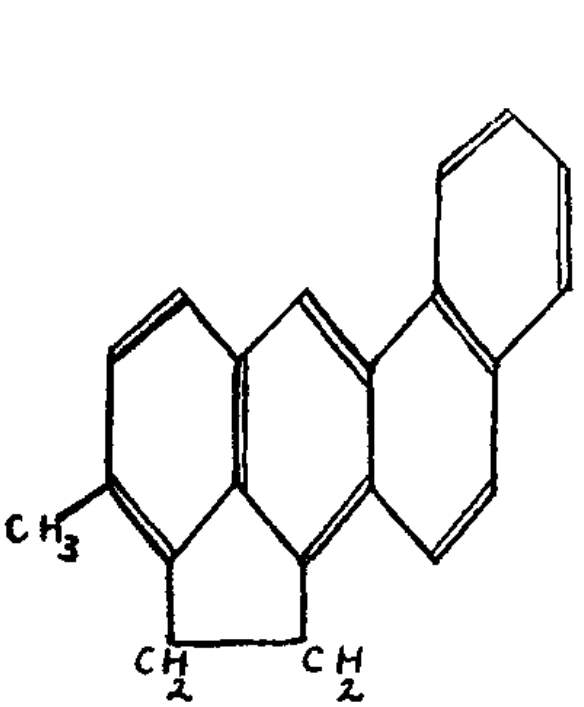
1,2 BENZPYRENE

1,2, 5,6 DIBENZANTHRACENE

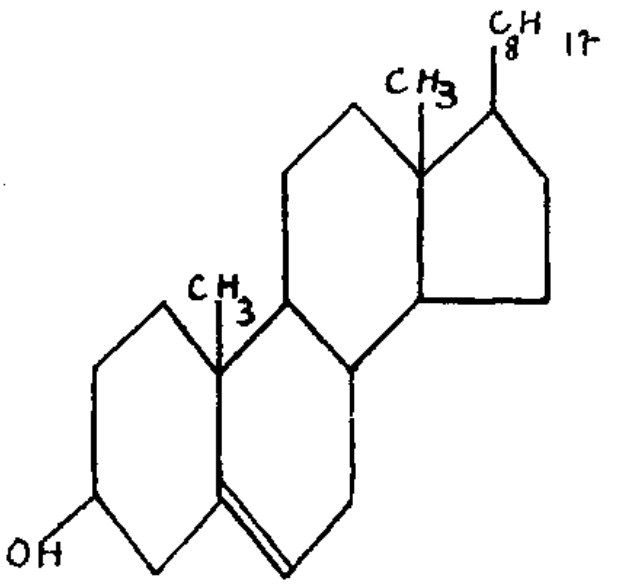
1,2 BENZANTHRACENE

Interesting as these results may be they do not yet answer the question:—what has all this to do with human cancer? The first answer to this question however became possible: From benzanthracene is to be derived by addition of a cyclopenthane ring and a methyl-group, methylcholanthrene which is more efficient than all compounds till then known. This methylcholanthrene is closely related to the cholic acids and the cholesterol as it contains the same sterol-skeleton composed of three 6 rings and one 5 ring. And it is interesting in the highest degree that Cook succeeded in transforming the

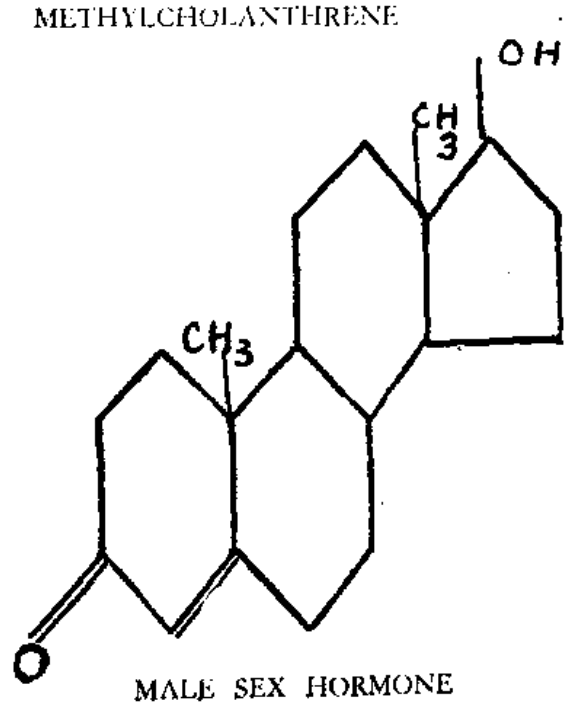
Figure 2.



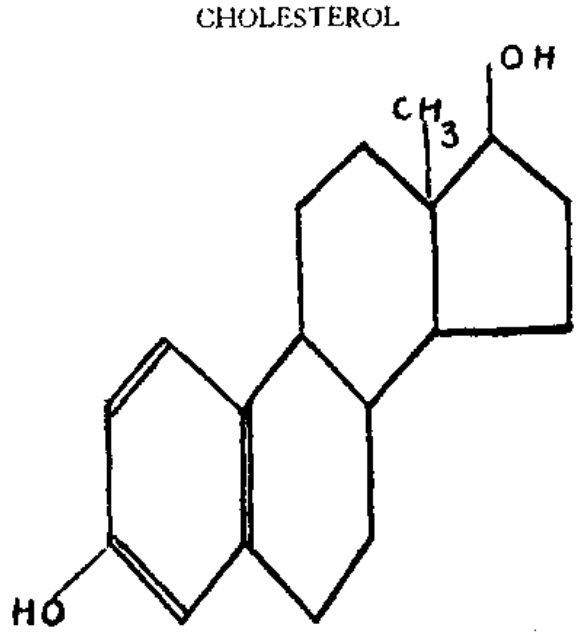
METHYLCHOLANTHRENE



CHOLESTEROL



MALE SEX HORMONE



FEMALE SEX HORMONE

cholic acids and the cholesterol by way of the desoxycholic acid in the test tube into the methylcholanthrene. That means the production from a physiological compound of a carcinogenic agent. And now we shall naturally ask if what was possible in vitro, may also happen in vivo.

And that, says Butenendt, one of our experts on sex hormones, may well happen, for the sex hormones are also derivatives of the cholic acids and the cholesterol and are closely related to the methylcholanthrene. This being known, the production of cancer by sex hormones was naturally tried but not successfully. But certainly relations do exist. In male mice belonging to races in which all females get breast cancer but from which the males are exempt, the males did get cancer if they were treated with follicle hormone. And on the other hand from the dibenzanthracene can be derived the so-called dioles which are not exactly hormones but which are oestrogenic.

Cook and Kennaway have brought forward the hypothesis based on these observations that misled processes of the cholesterol metabolism may be the cause for the originating of carcinogenic compounds, and Lacassagne suggests that perhaps the stagnation of secretions which contain substances related to the cholesterol may be sufficient for the formation of such carcinogenic compounds.

That is the present situation. The great progress is that for the first time some light is thrown on the possible relations between physiological functions and the originating of tumours. Cancer research work is no longer a mere affair of laboratories with mice, rats and rabbits, but patho-physiology will have to come into the discussions and will perhaps become the leading partner. But it will have to give its best for experimental research work does not stand still. New carcinogenic compounds not related to these yet known have been found and the near future may perhaps bring new and surprising results.

We have reviewed now the operation of the intrinsic as well as of the extrinsic factors, and we may ask for the connection which may exist between them, for it is certain that they are not disconnected and do not exclude each other. Under extreme conditions such as strongest inbreeding or the application of highly efficient means there may originate tumours from intrinsic or extrinsic factors alone but even in these cases, differences between the various races are to be seen. Usually the extrinsic and intrinsic factors co-operate and the reaction of the organism is as important as the external causes.

These striking results do not remain without effect on practical medicine. Impressed by the fact that X-rays which in high doses produce cancer, in small doses, cure it, K. H. Bauer, whose reports I follow for some length has asked the question: what happens to a cancer if it be treated with the carcinogenic substances in small doses?

And the answer was that he was able to cure by applying benzpyrene, 7 cases out of 22. Bauer himself says, that this is by no means the solution of the cancer problem, only a preliminary success, under especially favourable conditions, a success however which has a great theoretical value and which leads us to our other question: what importance have these results on the theories of carcinogenesis?

The older theories of Virchow, Cohnheim, Ribbert have been abandoned more and more. The parasitic theory also, has now hardly any followers, especially if it is meant as an explanation of the genesis of all tumours. All these theories may be able to explain one or the other group of tumours but they cannot be applied to the explanation of the formation of all the various kinds of benign and malignant tumours. Many scientists content themselves with declaring that tumours have very many causes and that we know very little about them. In more recent times two new theories have been developed in Germany which deserve our interest. First, it is the regeneration theory of Fischer-Wasels. It is a kind of modernisation of the old Virchow's irritation theory. Fischer-Wasels emphasises the importance of precancerous changes. He teaches that the first step is an irritation which causes a chronic inflammation. In the course of this chronic inflammation regeneration processes arise. If these are disturbed by the same or another factor, that may be external or internal ones, not seldom chronic intoxications, the condition for the transition of the regeneration into the tumourous growth may be given. Fischer-Wasels and his fellow workers have tried by many experiments to supply proofs for this theory and it is a plausible explanation for many tumours but it cannot answer all questions. First, it is not applicable to all kinds of tumours. There are a considerable number of which we know nothing of a chronic inflammatory precancerous stage. Likewise, the tumours originating only by intrinsic factors cannot be explained in this way. Above all it states nothing about the question: what happens at the moment of the transition of the regenerating cell into a tumour cell? We have seen that the tumour cells have fundamentally different qualities from the usual cells. Their metabolism, their practical immortality not only in tissue culture but also in the body, the manner of their growth, in short summarising all that which we call their autonomy, places them in fundamental contrast to all other cells. K. H. Bauer brought forward his new theory, based on these facts. He postulated that these qualities are not qualities of any individual cell but are passed down from one generation to the following ones, they cannot be accidental qualities but must be inherent in the genes. If the tumour-cells have different chromosomal qualities from the usual cells, then a mutation must have taken place. That is, according to him what must happen at the moment of the transition of a normal cell into a tumour cell. This theory attacks the problem from quite another side. It answers the question which all the other

theories hardly dealt with and were never able to answer and in this way links up medicine with the wider field of general biology. Certainly it does not state (and does not intend to state) anything about the preliminary stages which might produce the causes for such a mutation. Therefore I think that the objection made by Ascanazy against this theory has not much weight. He said, that as we know so little about mutation and the prospect of learning much more is not very great, this theory might paralyze our efforts to find out the causes of cancer and that would be very regrettable because these efforts have been so fruitful in recent years. But from its wholly different point of view, this theory will certainly not hinder these efforts as it only shifts the question into another track. We may no longer have to search for an unlimited number of causes, but our research work may now be led in a definite direction, and that will I hope, produce even better results. Other objections against the theory have not been made. It seems to be a well acceptd explanation for the fundamental difference between normal and tumour cells. Has experimental research provided any support for this theory?

All observations of the application of carcinogenic substances show that the formation of a real tumour is preceeded by processes which correspond to Fischer-Wasels' ideas. In this the experiments give support to his theory. On the other hand, experimental cancer research also shows the sometimes deciding importance of the intrinsic factors, so therefore we cannot accept this theory as a general explanation of tumour genesis. The mutation theory is not contradicted by any result of experimental research work. We can very well imagine that in the case of the rare tumours caused only by extrinsic or only by intrinsic factors, as well as in the case of the usual tumours caused by a combination of extrinsic and intrinsic factors the decisive step is a mutation. The whole later behaviour of tumours points in this direction. But have we any evidence, if not proofs that this really happens? Exact proofs we cannot expect. Nobody has ever seen a gene, we can only deduct their existence and their changes from their effect. Experimental research work was indeed able to give at least some clues. We know that X-rays are able to produce cancer and it is now also known that X-rays are the best experimental means of producing mutations. Furthermore other substances which are efficient in mutation-experiments are also carcinogenic. The last link in this chain is still missing: the answer to the question: are the new-found carcinogenic compounds able to produce mutations in biological experiments? I should think that is only a matter of time.

Thus, experimental cancer research proves that none of the theories is able to answer all questions. We can divide them all into two groups. To the first one belong all, from the older ones of Virchow and Cohnheim up to Fischer-Wasels. The only representative of the second group is that of Bauer. All of the first group tend to emphasize

the conditions which induce the origin of tumours. They are all wrong so long as each claims to be the sole explanation of tumour-genesis. They are all right as soon as each is taken as an explanation for a certain kind of tumour. And it must be emphasised that taken in this way none contradicts or excludes any of the others. Bauer endeavours to give an explanation for the happening at the moment of the transition of the normal cell into the tumour cell and gives thus the necessary completion. And so we can say that all the theories together valued in the proper way give us a fair insight into the processes of tumour genesis.

It is a long way from Fibiger's spiroptera-cancer to the abundance of all these latest discoveries. The decisive point is that the experimental cancer research is no longer working apart and wholly separated from clinical work, but that the connection between the clinic and the laboratory has been made and we can hope that the results of research work will now benefit the sick. And the welfare of our fellow men is, and remains the highest aim of us all, what ever place we may hold in the wide field of medicine.

THE INFLUENZA EPIDEMIC OF 1936 IN ST. HELENA.

by

P. B. Wilkinson.

Government Medical Department, Hong Kong.

A number of catarrhal conditions of the respiratory tract was noted during the early part of June this year. On June 2nd in the out-patient clinic at the Civil Hospital one adult was found to be suffering from laryngitis, two adults and a baby from bronchitis, and the label coryza was affixed to one adult and one infant. On the 3rd a man seen at home was tentatively given the diagnosis of influenza, and the same tentative diagnosis was made in a case seen at hospital on the 4th, and in two more cases seen in the country on the 5th. One other similar case was seen on the 6th. It is thus obvious that there were a number of "heavy colds" in the island during the first week of June, and they would doubtless have passed unregarded had they not been noted in inverted commas as "influenza'.' One of the 5 cases lived in town, 4 in the country.

On June 7th, the S.S. *Llandaff Castle* called at Jamestown, homeward bound. Her doctor informed me that he had a "few influenzal colds" on board. The ship was given pratique and many of her passengers came ashore for some hours. Within 72 hours of the arrival of this ship influenza had gained a foothold in Jamestown, and for the next month it continued to spread both in town and country. 307 cases of the disease were seen in the town from June 4th to June 30th. The town figure for the month of July was 194, and by the beginning of August the epidemic was clearly abating.

The following curves give a good picture of the explosive onset of the disease in Jamestown and they also show the time lag which one would expect before the disease reached Longwood and Sandy Bay. The disease appeared in the Longwood area between June 16th and June 22nd. It was first noted in the Sandy Bay district on June the 17th.

It proved to be highly infectious, and attacked people of all ages and of either sex. The aged and the very young suffered most severely from the disease, and the mortality which it occasioned was practically limited to these two age groups. At the height of the epidemic one, at least, of the flax mills had to close down because so many of the hands had been stricken with the disease.

It is noteworthy that very few of the Europeans on the island suffered from the disease.

Jamestown had but little rain during the four months preceding the epidemic, and during June the weather in the town was warm and

dry. The decline of the epidemic appeared to be related to some comparatively heavy showers which fell on July 11th and 12th. It is impossible to say whether there was any actual relation between this sudden change in the weather and the decline of the disease, but the number of fresh cases seen began to diminish during the week following this change. The rainfall figures for Jamestown and Plantation for the months February, March, April, May, June and July were as follows:—

February.	Plantation.	1.69 ins.	
	Jamestown.	.84 ins.	
March.	Plantation.	3.67 ins.	
	Jamestown.	.61 ins.	
April.	Plantation.	2.33 ins.	
	Jamestown.	.25 ins.	
May.	Plantation.	4.42 ins.	
	Jamestown.	1.24 ins.	
June.	Plantation.	3.94 ins.	
	Jamestown.	.81 ins.	
July.	Plantation.	4.40 ins.	July 12th .81"
	Jamestown.	1.36 ins.	July 11th .40"

The total numbers of cases of influenza seen during the three months June, July and August were as follows:—

June	550 cases.
July	324 ,,
August	84 ,,
Total population 4200.	958 cases.

These figures are not absolutely accurate for several reasons. First, a certain number of islanders very sensibly suffered in silence and at home. Second, Sandy Bay was not visited on July the 8th, nor was the hospital visited on July the 7th, 8th, and 9th. These unavoidable inaccuracies are probably not of such significance as to detract from the graphic value of the curves.

The clinical features of the disease were as follows. The incubation period, as determined from households, in which one member conveyed the infection to others appeared to be short; 24-48 hours seemed to be the average period. Onset was usually sudden, sometimes even abrupt. Within a few hours of onset the victim was prostrated, and showed fever which ranged from 100-103°. No rigors at onset were noted. The symptoms chiefly complained of were frontal headache, backache, joint pains, coryza and a slight cough. This cough as a rule was non-productive. Many cases also complained of 'aching' in the nose and soreness or rather dryness of the throat. A

mild degree of injection of the pharynx was noted in many of the cases, and in some of the children who were attacked there was an accompanying tonsillitis. Conjunctival infection was noted in a small percentage of the cases, and a number of the children who were attacked had one or more sharp attacks of epistaxis. Pain in the eyeballs on conjugate deviation of the eyes was a common symptom and not infrequently the eyeballs were tender on pressure. Another very common symptom was giddiness, and a feeling of dizziness. In the majority of the cases complaining of these symptoms, no organic lesion was found to account for them. The sense of prostration usually became intense about the 3rd or 4th day of the disease, but passed off, rapidly or slowly, according to the temperament of the patient as the fever abated. As most of the cases were treated at home, it was not possible to determine whether the fever declined by crisis or by lysis, but the impression obtained was that defervescence by crisis was very much rarer than by lysis.

The above picture was typical of the majority of cases seen during the epidemic. That is to say, the cases differed from the "common cold" only in the abruptness of onset, the higher degree of fever, the slighter involvement of the upper respiratory passages, and the prostration.

A certain number of cases conformed to the so-called gastro-intestinal type. These cases were relatively infrequent, and seemed to occur mainly in young adults. They differed from the simple febrile type in that vomiting and anorexia supervened immediately after onset. No case of this type proved fatal. A larger number of cases of the respiratory type was seen. In this type of case the disease presented the usual picture of the simple febrile type until about the 5th to the 8th day of the illness, when some recognisable involvement of larynx, trachea or bronchi became apparent; laryngitis and tracheitis were the two commonest conditions noted. Frank bronchitis, judging by physical signs, seemed to be relatively uncommon. If the catarrhal process involved the bronchial tubes and lungs, as it frequently did in the elderly victims of the outbreak, the outstanding feature of the case was capillary bronchitis with generalised pulmonary congestion. The physical sign of importance in these cases was the presence of numerous fine non-consonating crepitations, usually heard best over both bases, but occasionally over the whole lung. The percussion note was never impaired. No effusions either serous or purulent were demonstrated, but in the case of one elderly woman of 74, an effusion at the right base was suspected. She was not needled and ultimately recovered. In this type of case cough was the symptom which troubled the patients most. It was not, as a rule, productive, and many cases never produced any sputum. In no case was the pathognomonic rose-red sputum noted. When sputum was coughed up, it was generally tenacious and green in colour.

Only two cases of the malignant type occurred. One was a woman of 35, the other a man of 49. Both died within 24 hours of admission to hospital. Both these patients were gravely ill on admission and both showed heliotrope cyanosis. The fever abated in each case as the toxaemia increased and the signs of impending cardiac failure became apparent. The cyanosis was intense in the man, who became slate coloured within 6 hours of death. As no measures are of value in treating this type of case, the Hippocratic aphorism 'do not attempt to treat a patient overwhelmed with disease' was scrupulously observed. A post-mortem examination was made on the woman. Both lungs were found to be acutely congested, and they exuded an abundance of pink frothy fluid on section. No areas of actual consolidation were found, but the surface of each lung was covered with discrete, white, slightly raised areas. On cutting into the parenchyma of the lung through one of these white areas, the appearances in the underlying tissue were those of a diffluent abscess.

Certain sequelae were common. Frontal sinusitis was observed as a sequela in 6 cases, and in 1 case the right antrum became infected. These sinus complications all occurred in young adults. A catarrhal otitis media was observed in 10 cases. The process was bilateral in 1 case, unilateral in 9. The mallcolar vessels were found to be injected on examination, and in 2 cases a collection of fluid was observed. In only one case did these changes progress to suppuration. This little girl of 5, when first seen, presented the picture of a right sided mastoiditis with head retraction and tenderness of the neck muscles on deep pressure. The right ear drum was acutely inflamed and bulging in the postero-inferior quadrant. The child was admitted to hospital. Lumbar puncture yielded a cerebro-spinal fluid which was normal to the naked eye and showed no pleocytosis on examination. Pandy's test was negative. Two days after admission the drum ruptured, and there was a small amount of purluent discharge for the next 5 days. She made an apparently complete recovery. Recovery from this complication in the other cases was slow. The condition caused discomfort rather than pain in the majority of cases, and the usual complaint was of deafness and a "feeling of fullness" in the affected ear.

In a certain number of cases, mostly among the older patients, signs were noted suggestive of some persistent degree of cardiac insufficiency. One man of 86, who had had a generalised bronchiolitis during the febrile phase of the illness recovered but developed marked oedema of the feet and legs ten days after his fever abated. No physical signs were elicited to account for this and his urine was normal. The oedema disappeared on treatment with digitalis and nux vomica. In other cases the effort syndrome was marked and there were no accompanying physical signs. The symptoms were excessive fatiguability, dyspnoea on exertion, palpitation and in a few cases

praecordial pain. These symptoms persisted for weeks in some cases, but in none could any sign of organic involvement of the heart be made out. There was a marked degree of vasomotor instability and a very irritable pulse in two or three of these cases.

In three septuagenarians there has been persistence of basal bronchiolitis. They all had their acute attacks of the disease many weeks ago now, but the lung signs continue unchanged. Cough is a prominent and distressing symptom of these 3 cases.

The only organic nervous sequela noted was a left Bell's palsy which occurred in a little girl of 4. Her mother noticed 4 days after the onset of her influenza, that her left eye had "gone funny." On examination she was found to have a peripheral facial nerve palsy on the left side. Both ear drums were normal and the mother denied any history of ear discharge in the past. The appended photograph shows Bell's sign well.

The mental depression was marked and persistent in not a few cases, but in many of these it appeared to be aggravated by the persistence of the highly irritating "essential" cough so characteristic of the disease. Persistent headache was a rare sequela noted in only 4 cases.

One child of 10 who had an attack of influenza ten weeks ago, developed vague abdominal symptoms six weeks later. She complained of pain in the region of the umbilicus and her bowels became obstinately constipated. Her condition appeared to improve somewhat and she returned to school, but only for a fortnight. Her symptoms then became intensified and further examination showed a slight degree of abdominal distention. A doughy mass could be made out lying transversely across the abdomen at the level of the umbilicus. There is now little doubt that the child was suffering from tubercular peritonitis, despite the absence of specific signs in the other systems, and a negative family history on both sides. It is of interest to note that her mother states that her milk has always been boiled.

Relapses were common, especially among the poorest and worst fed islanders. More second attacks of the disease were noted in the Longwood area than in any other part of the island, and there is little doubt that the explanation for this fact is to be found in the deplorable conditions in which the working-class people of Longwood exist.

Epidemic influenza has occurred not infrequently in the island in the past, though unfortunately no detailed accounts of the past epidemics are extant. An account of the 1900 epidemic, which killed 46 people, is to be found in the Blue Book for that year. Ten deaths were attributable directly to influenza during the 1936 epidemic. Mention has already been made of the only two malignant cases seen, both of which perished rapidly. Of the other eight victims, two were

young children and the others were all over 70 years of age. Of this particular outbreak it can be said with truth that, apart from the malignant type of the disease, influenza takes its toll from the two extremes of life.

The appended list of figures shows the number of deaths from influenza recorded in each of the past outbreaks. The figures have been obtained by examining the Death Registers from 1853 down to the present day.

1863	21	
1867	2	
1868	5	
1888	2	
1895	1	
1896	1	
1900	45	
1904	1	
1909	1	
1914	5	
1915	1	
1919	1	
1925	1	
1927	4	
1929	3	(All recorded as "influenzal pneumonia")
1936	10	

The three influenza epidemics with the highest mortality occurred in 1863, 1900, and 1936. In 1867 it is worthy of note that three young adult deaths are attributed to "bronchitis" and one to "bronchitis with epistaxis." These deaths occurred within a few days of the ones attributed to influenza, and one cannot help surmising that they also may possibly have been due to influenza.

In 1895, although only 1 death is recorded from influenza, there is a note in the Register to say that the disease was reported in epidemic form on October 11th that year. No account of the epidemic exists. The Blue Book for 1900 gives a graphic picture of the widespread distress caused by the disease in that year.

The epidemic was of interest because sera from St. Helena had been examined in 1935 in an attempt to obtain further evidence as to the nature of the virus responsible for the pandemic of 1918.

In 1931 Shope found that swine influenza was due to the combined action of a filter passing virus and an organism, *Haemophilus influenzae Suis*. It was shown by Laidlaw and his co-workers in 1933 that this virus produced a disease in ferrets which was clinically indistinguishable from that caused by human influenza virus. That the two viruses are antigenically related to one another was shown by the fact that infection with either conferred some immunity to the other.

As swine influenza had been unknown up to 1918 and as antibodies to swine virus were found in many human sera after 1918, Laidlaw suggested in 1935 that swine influenza might represent a survival in the pig of the virus which caused the 1918 pandemic.

This suggestion was supported by the fact that both American and English children under 10 years of age showed no antibodies to swine virus, whereas many adults showed antibodies to both human and swine virus. The absence of antibodies to swine virus in children under 10 was explicable on the hypothesis that the virus producing them had not been widespread among human beings, at any rate during the last 10 years. No such contrast between the adult and childhood levels of antibody was noted when dealing with human virus.

As St. Helena was one of the three places in the world reputed to have escaped the pandemic of 1918, it was felt that an investigation of the antibody level to both human and swine viruses made on islanders who had never left St. Helena, might throw some light on the question.

In September, 1935, twenty-three St. Helenans, who had been alive in 1918 and had never left the island, were bled and their sera were tested against both human and swine influenza viruses at the National Institute for Medical Research, Hampstead. One serum had fair antibody to human virus and one to swine virus. Of the remaining 21 sera, five only had small amounts of antibody to swine virus, the rest had negligible amounts, and none of the 21 had a high level of antibody to human virus. These results seemed to confirm the hypothesis that had led to the examination of the sera, for it was known that St. Helena had not been exposed to the 1918 pandemic and ex hypothesi antibodies to swine virus were not expected to be in St. Helenian sera. That antibodies to human virus were practically absent was thought to be due to the fact that the island had not suffered from an influenza epidemic for at least six years when the sera were collected.

The epidemic described in this paper occurred in June, 1936 and more sera were obtained from convalescents three months after the epidemic ended. These showed considerable variations in antibody content, both to human and swine virus. In December, 1936, seven months after the onset of the epidemic 22 of the 23 islanders who were originally bled in 1935 volunteered to give further samples of blood.

The results were interesting. Antibodies to both human and swine virus had appeared in good amount, and the antibodies to swine virus were present in amounts equalling those in European sera. As little is yet known about the antigenic structure of these viruses, it is impossible to draw conclusions from these results, more especially as it was not possible to determine the antigenic structure of the virus responsible for this epidemic. But as all recently isolated strains of virus

have shown serological affinities to the Wilson Smith virus, it was probable that the virus responsible for this epidemic was related to W. S. virus, and therefore the rise in titre of antibody to W. S., virus was not unexpected. What was unexpected was the appearance of swine virus antibody in people who had had none the year before.

Only 9 of the 22 people bled a second time had had symptoms of any sort during the epidemic, yet a good rise of antibody was found in many of the remaining 13. This finding strongly supports the conception of widespread subclinical infection during epidemics of influenza.

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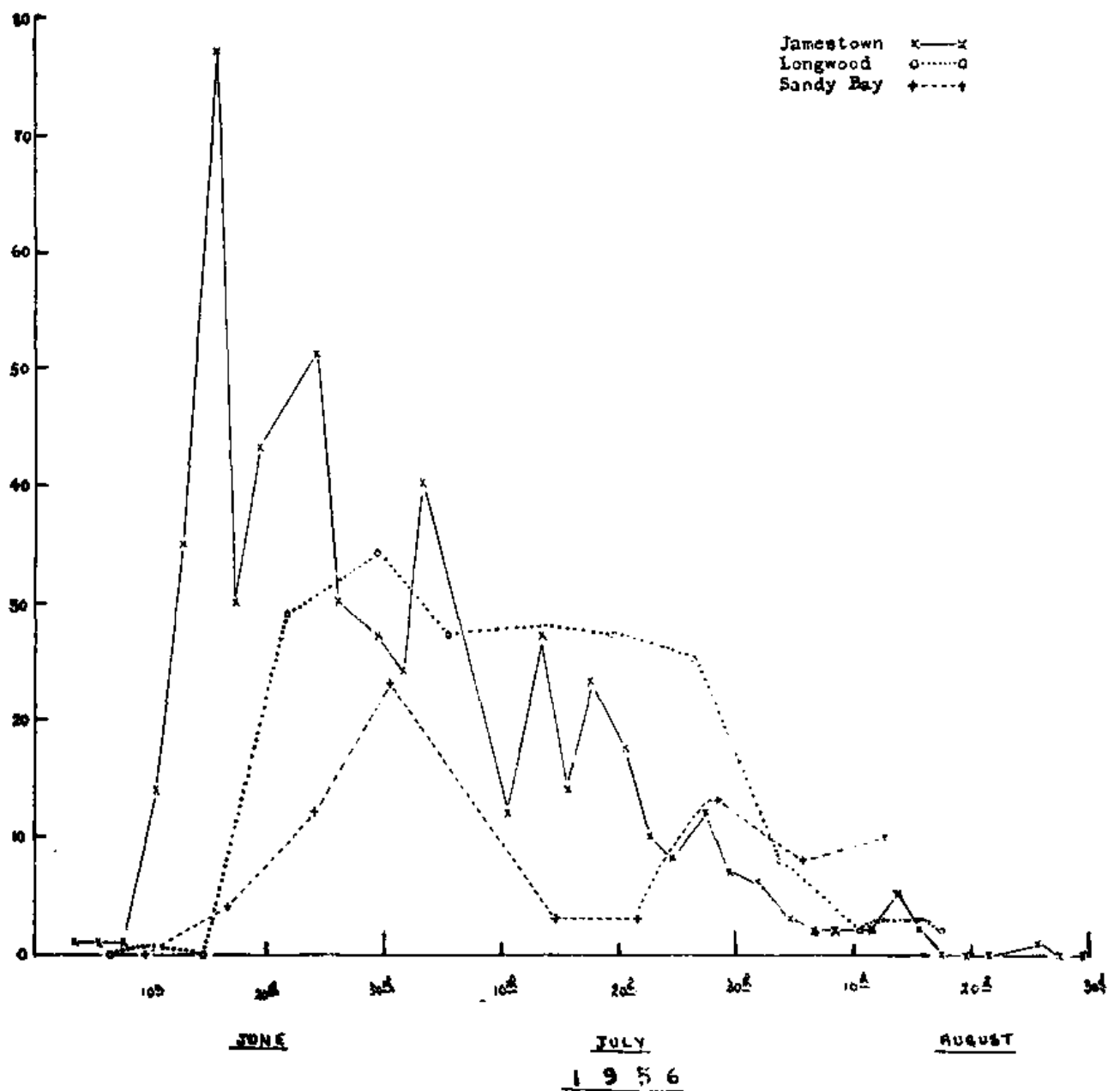
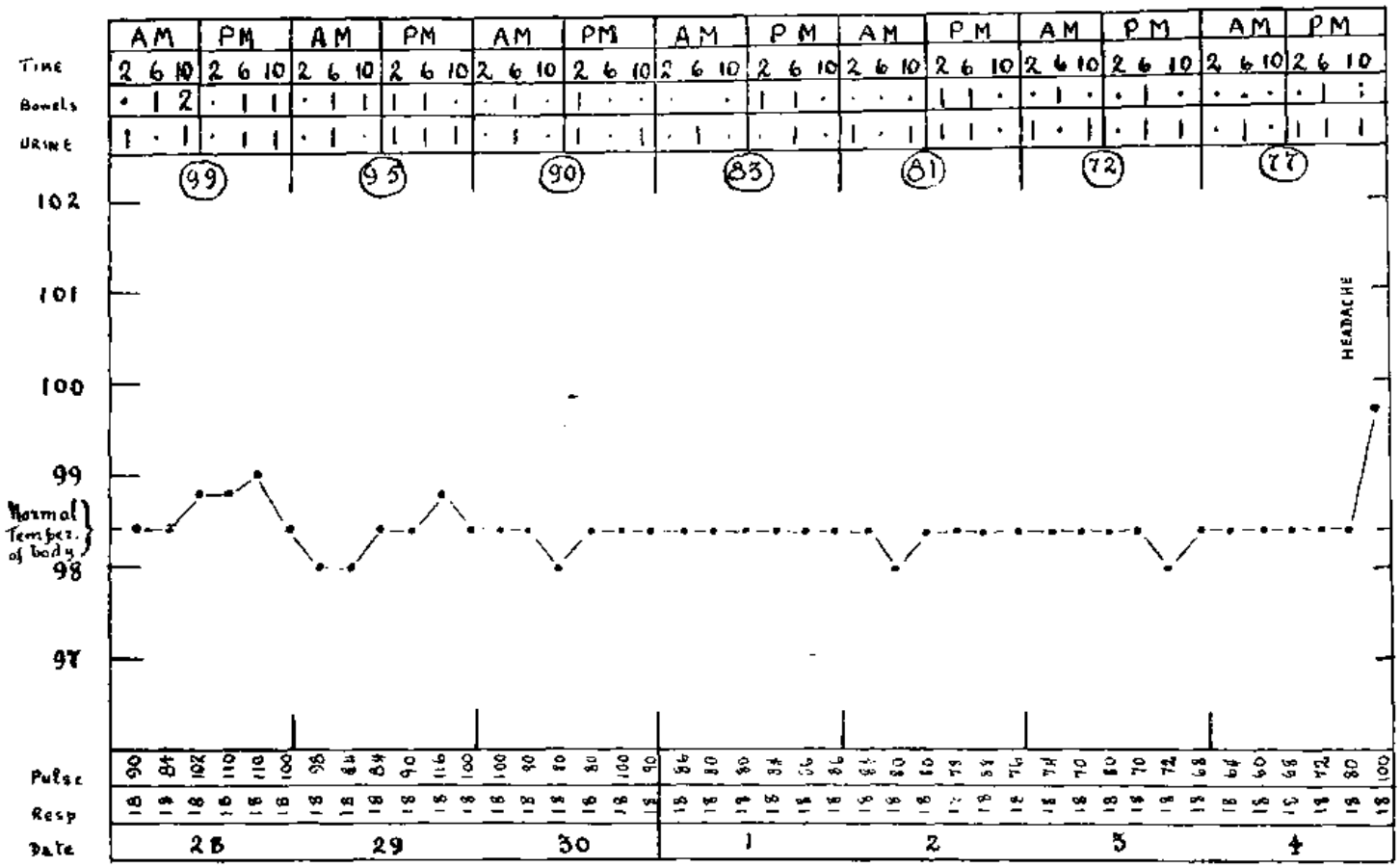
Showing left facial paralysis of D. H., aged 4, who developed a facial palsy (peripheral) four days after she developed influenza. Both drums were normal and remained so, while there was marked disinclination to attempt shutting both eyes.

Frequency polygons of the 1936 Influenza Epidemic.





JUNE, 1936. JULY, 1936.

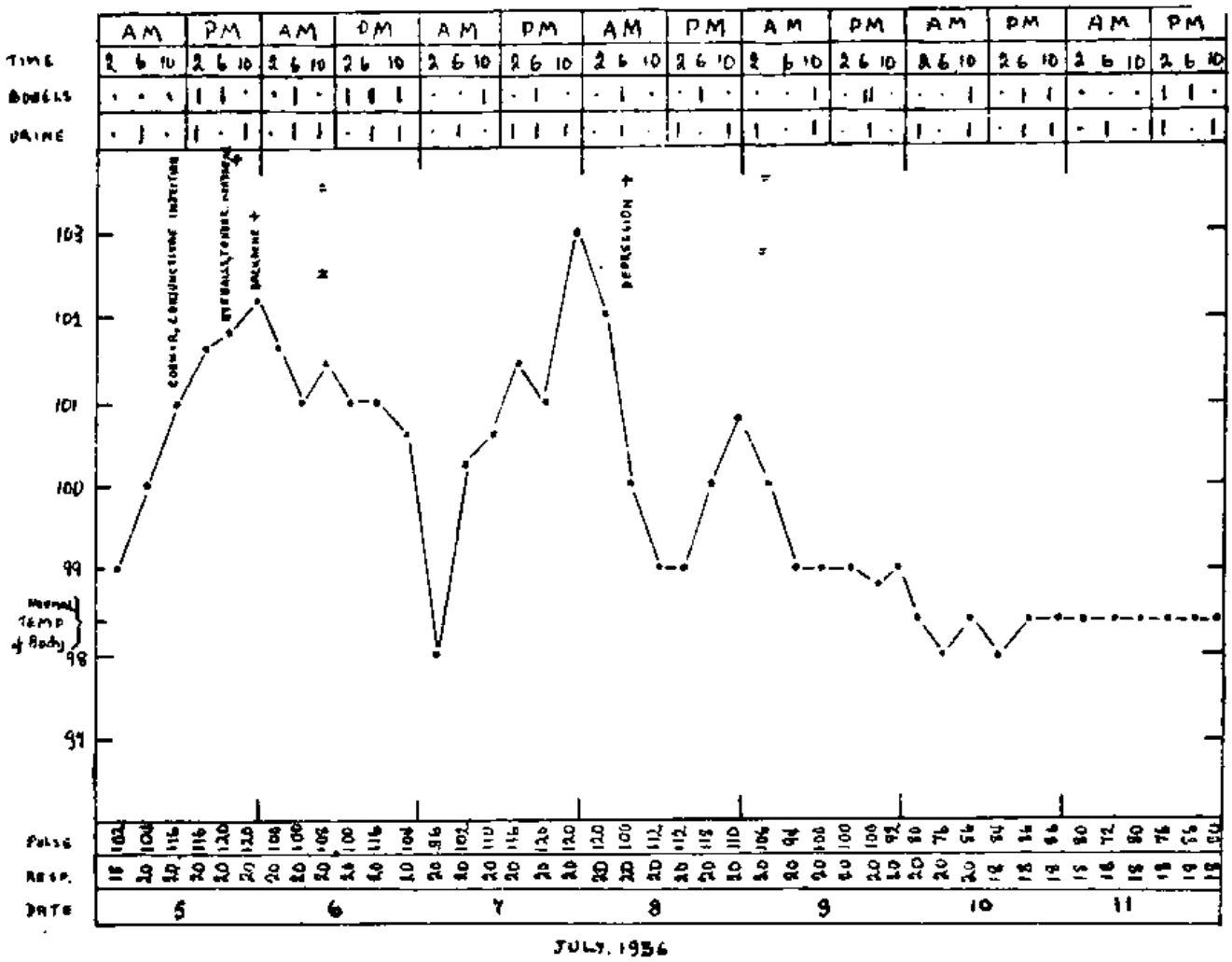
Louisa Wright. 32 years.

Puerperal Supraemia Beriberi. "Influenza"

Admitted :— 10.5.36.

1.7.36. Urine Tested.

Sp. Gr. 1010
React. Acid
Alb. Nil
Sugar. Nil.

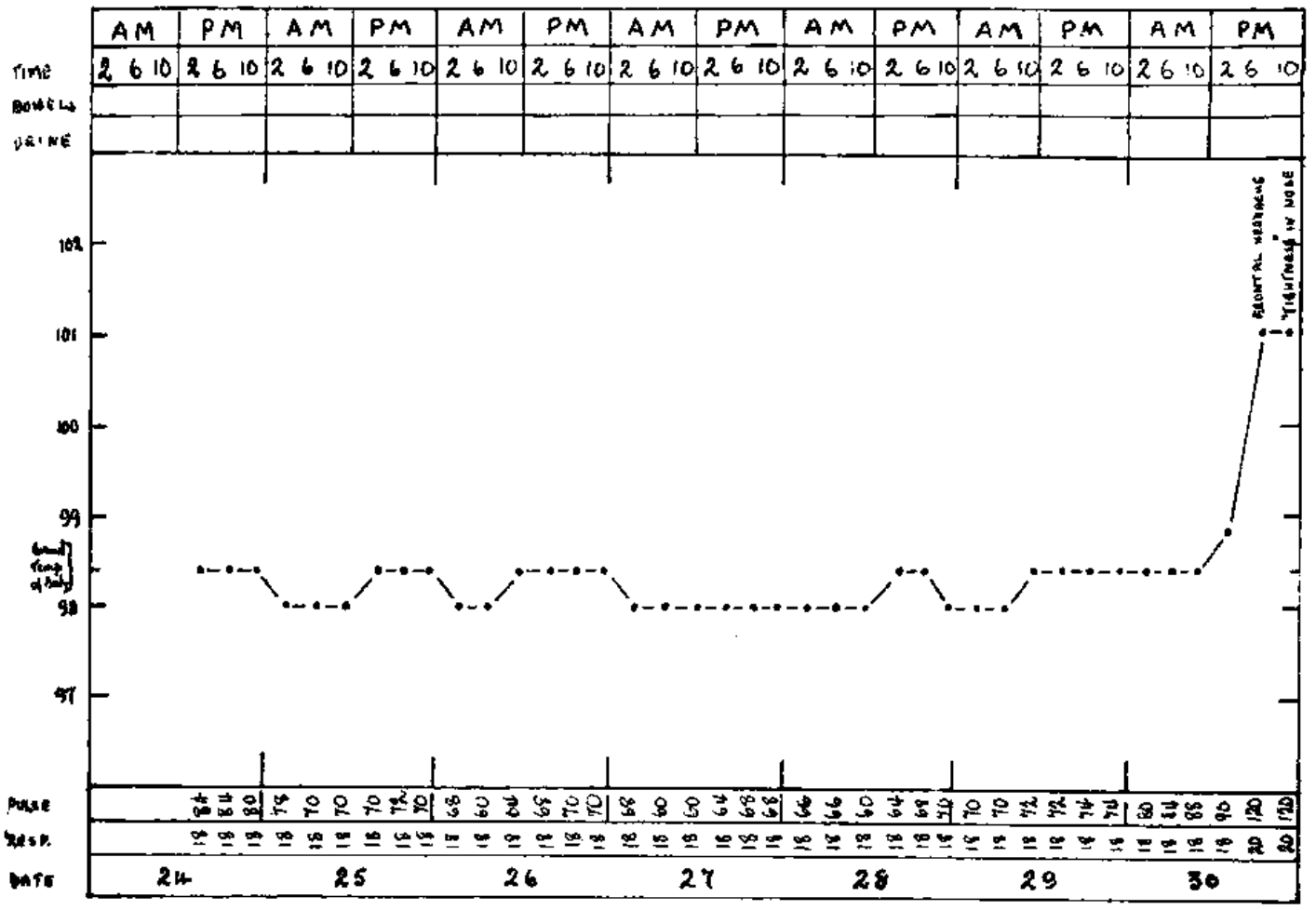


Louisa Wright. Age: 32 years. Puerperal Sapraemia Beriberi "Influenza"

Admitted:—10.5.36.

1.7.36. Urine Tested:—

Sp. Gr.	1010
React.	Acid
Alb.,	Nil
Sugar.	Nil.



JULY, 1936.

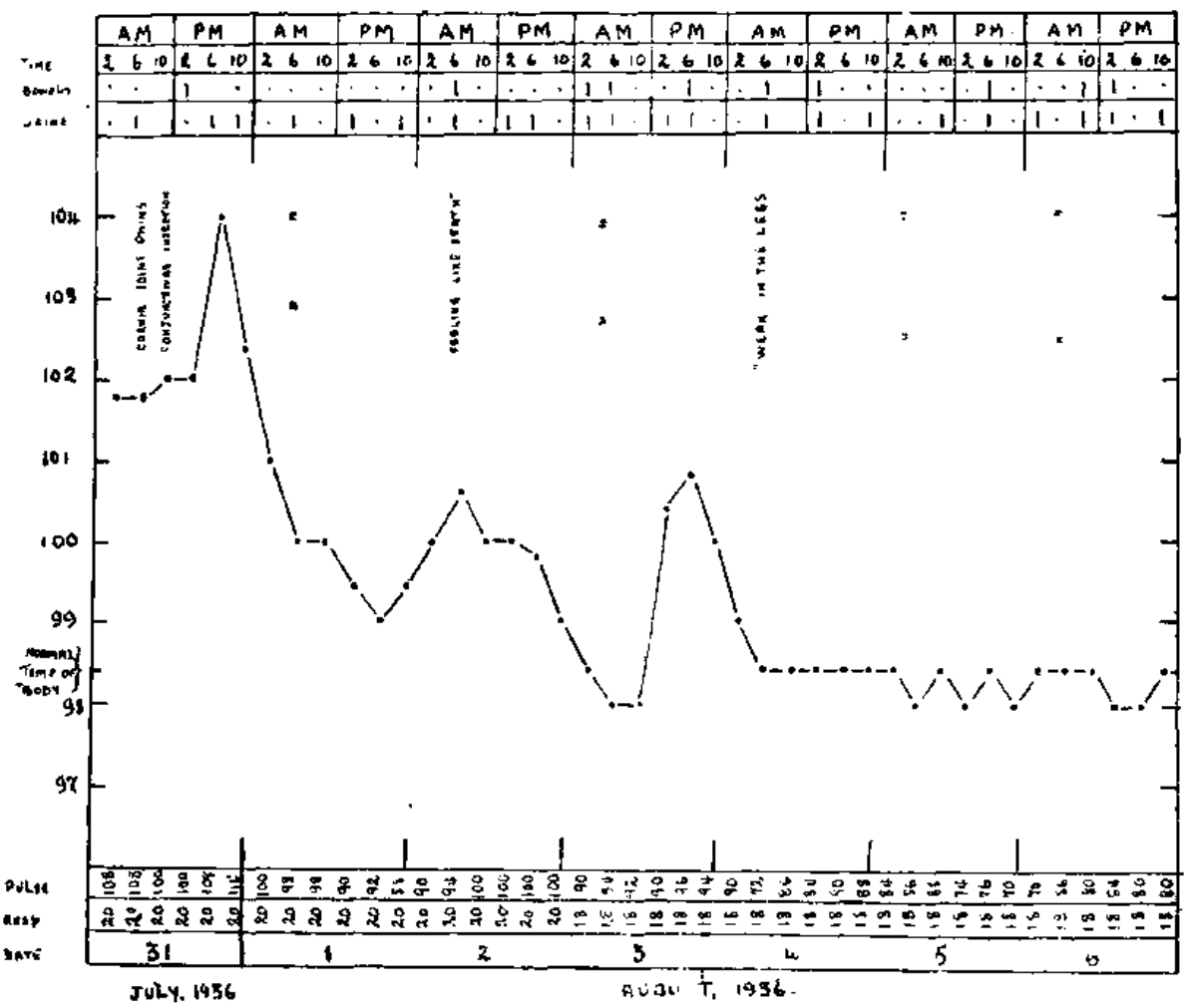
Rosnia O'Dean. Age, 37 years.

Admitted:—24.7.36.

Endometritis post-abortion "Influenza"

24.7.36. Urine Tested:—

Sp. Gr.,	1025
React.,	Acid
Deposits.	Nil.
Alb.,	Nil.
Sugar.	Nil.



Rosnia O'Dean. Age, 37 years.

Admitted :—24.7.36.

Endometritis post-abortion "Influenza"

24.7.36. Urine Tested :—

Sp. Gr.,	1025
React.,	Acid
Deposits.	Nil.
Alb.,	Nil.
Sugar,	Nil.

THE OCCURRENCE OF ZINC IN FOODSTUFFS AND IN THE HUMAN BODY.

William George Elford Eggleton.

Associate, The Henry Lester Institute of Medical Research, Shanghai.

During the last two decades evidence has been accumulated to show that the metal zinc is very widely distributed in nature. It is present in all plants and parts of plants with a few doubtful exceptions and in all animal organs and structures. There is a growing body of evidence in favour of its being regarded as an essential element but exactly what rôle it plays in vital processes is as yet unknown. Lack of zinc in certain soils of the Florida Everglades is held to account for the occurrence of the disease known as "little leaf disease" of citrus and other plants growing in these areas since applications of zinc salts to these soils cause the disappearance of the disease. In the higher animals the accumulation of zinc in the foetal liver together with copper, manganese and iron is regarded as strong evidence of its indispensability. A low-zinc diet produces various abnormalities in rats, such as loss of hair, lesions round the eyes and mouth and a slower growth rate, all of which abnormalities do not appear when the animals receive a small supplement of zinc. Various workers have produced evidence regarding its essential nature and have advanced theories regarding its function. These have been reviewed by the author (1938).

Since the complete elucidation of the eventual part played by the metal in vital processes depends upon a wide knowledge of its occurrence and distribution in nature a useful purpose is served by bringing together for comparison under one cover all the existing data regarding its presence in foodstuffs and in the human body. It is only when this is done and the various figures are examined in relation to one another that irregularities can be recognised. Moreover, the assembled information makes it possible to calculate speedily and with fair accuracy the zinc content of any combination of foodstuffs. Many diets have been examined by the author in this way and four of special interest are given in detail.

Zinc in Natural Waters.

Zinc is present in almost all soils in amounts not usually exceeding 50 p.p.m. The author has found 10 and 33 p.p.m. respectively in two Shanghai soils. It is present also in almost all waters but its concentration rarely exceeds 0.1 p.p.m. and is frequently much less. In tap waters, as a result of the solvent action of dissolved CO_2 on galvanised tanks and piping, the amount of zinc in the water as delivered for use may frequently reach higher levels according to the length of time the water is in contact with the metallic parts.

Thus Pritzker (1922) finds some Swiss tap waters to contain 2.5 p.p.m., Birckner (1919) detected 0.25 p.p.m. in tap water as supplied in Washington, D.C., and the author has found 0.5 p.p.m. in Hong Kong tap water. Bartow and Weigle (1932) find that natural waters from the Missouri/Kansas/Oklahoma region may contain as much as 50 p.p.m. This locality is rich in zinc bearing minerals and the waters are without doubt contaminated by wastes from the many zinc mines and refineries in the neighbourhood. The U.S. Public Health Service recommends that service water should not contain more than 5 p.p.m., but this figure is well within the limit of safety, for Bartow and Weigle have shown that men consuming water containing as much as 45 p.p.m. for several years suffered no ill effects.

The concentration of zinc in sea water is usually very much higher near the shore than it is in the open sea. For instance Severy (1923) finds .390 p.p.m. near the shore at Pescadero, whereas one mile from the shore there was as little as .002 p.p.m. The water of the English Channel has been reported by Atkins (1936) to contain less than .008 p.p.m. and Hiltner and Wichmann (1919) failed to find any zinc in a sample of sea water taken from a distance of one mile from the coast at Sayville, N.Y.

The existing data concerning the occurrence of zinc in natural waters is summarised in Appendix I.

Zinc in Vegetation.

The amount of zinc occurring in plants is usually of the order of 20 p.p.m. of dry matter, the amount naturally varying according to the zinc content of the soil in which the plant is grown. In general more zinc is found in the quickly growing parts of the plant such as the leaves, roots and seeds than in the stems and stalks. Bertrand has reported that green leaves contain more zinc than etiolated leaves and the author has found that the large white sepals of *Mussaendra pubescens,* Ait., commonly known in the East as Buddha's lamp contain only 29 p.p.m. whereas the green leaves contain nearly three times as much. In seeds the zinc is almost wholly concentrated in the germ and pericarp. For this reason, nuts, legumes and whole-meal cereals contribute relatively more zinc to the diet than do tubers, roots and greens. The fleshy parts of fruits contain only 2-4 p.p.m. of zinc in the fresh material.

Zinc in Animals.

With regard to the occurrence of zinc in marine animals it should be mentioned that the higher concentration of zinc in coastal waters is reflected in the fact that inshore marine organisms usually contain larger amounts of the metal than deep sea fish, thus shell fish in general are usually found to contain between 20-60 p.p.m.

whereas ordinary fish rarely contain more than a tenth of this amount in the fresh muscle, although larger amounts are found in the pancreas, liver, spleen and certain other parts of the organism. Oysters have been reported to contain amounts of zinc ranging from 150 to 2,300 p.p.m., notably by Hiltner and Wichmann (1919) and Birckner (1919) working in America. For Californian oysters, however, Severy (1923) reports values of 15-99 p.p.m. coinciding within close limits with the values given by Koga (1934) for Japanese oysters. There is, therefore, reason for believing that the high values recorded by Birckner and by Hiltner and Wichmann are a reflection of an unusually high degree of contamination of the waters from which they obtained their samples and consequently may serve only as an interesting illustration of the oyster's remarkable degree of tolerance for the metal.

In land animals the zinc is associated mainly with the protein-containing tissues such as muscle, kidney, spleen, pancreas and liver, particularly the last mentioned, but the values for these portions of the animal are on the whole not widely different. Milk is a very poor source of zinc, containing only about 3.4 p.p.m. in the fresh material, but colostrum contains several times this amount. Eggs are relatively rich, the metal being concentrated wholly in the yolk to the extent of about 40 p.p.m. The white of egg is the only substance of animal origin which has been reported consistently to be entirely devoid of zinc in the natural state.

The zinc conents of the principal plant and animal products used as foodstuffs as found by various workers together with those determined by the author by means of the more accurate and less laborious dithizone method (65), have been collected and arranged in Appendix II. Some disagreement will be seen to exist and there are still numerous articles of food for which figures are lacking. Nevertheless little difficulty will be experienced in making a reasonably accurate estimate of the zinc content of any required material and the amount of zinc supplied in any particular diet may be ascertained with fair accuracy. Certain portions of fish, such as the gills, scales and skeleton are not commonly used as food except in the case of sardines where the skeleton and scales are retained and in whitebait where the small fish are usually consumed whole. Certain portions of shellfish are also commonly rejected. Nevertheless, for the sake of completeness the zinc content of such parts have been included where they exist. For similar reasons figures for the distribution of zinc in the blood of the ox, goose and chicken and for the zinc content of bone, skin and hair of rabbit and horse are also given.

The existing data concerning the distribution of zinc in the human body together with those secured by the author are given in Appendix III.

Influence of the Composition of the Diet on Its Zinc Content.

It has already been mentioned that most of the zinc occurring naturally in foodstuffs is associated with the protein-containing tissues. Fats, oils and carbohydrates contain less zinc weight for weight than protein foods and it is probable that the small amount of zinc which they do supply is due to their containing small amounts of protein with which the zinc is associated. As a result of this the zinc content of the diet is controlled very largely by the amount of protein which it contains. Apart from this, the actual intake of zinc varies of course directly with the amount of food consumed. In order to illustrate these points the zinc contents of two typical diets, and two specialised diets, have been calculated. The results are shown in Tables 1 to 4.

TABLE I.

Estimation of the daily consumption of zinc on the basis of the average American diet (Sherman).

Food	*Food/day*[1] *g.*	*Estimated zinc content of food*[2] *p.p.m.*	*Estimated amount of zinc consumed/day mg.*	
Meat and fish				
Beef	111	34	3·774	
Pork (including lard)	40	30[3]	1.200	
Lamb and mutton	9	37	·333	
Poultry	14	24[4]	·336	
Fish	19	6	.114	5·757
Eggs	32	15[5]	.480	.480
Milk and milk products				
Milk	280	3·4	·950	
Cheese	5	30[6]	.150	
Butter and fats	32	2	.064	1.164
Grain products				
Wheat: patent flour	104	7	.728	
Bread, Crackers, &c.	72	5	.360	
Sweet cakes	5	5	.025	
Entire flour & Graham	22	20	.440	
Graham bread	10	10	.100	
Corn: Meal & flour	72	9	.648	
Preparations	15	9	.135	
Oatmeal & prepns.	3·5	33	.116	
Rice	2	15	.030	
Rye, Barley & Buckwheat	12	18	.216	2.798
Legumes				
Fresh	7	25	.175	
Dried	3	30	.090	.265
Vegetables				
Tubers and yams	133	3	·399	
	195	4	·780	1.179
Nuts	1	15	.015	.015
Fruits	139	3	·417	·417
Sugar and molasses	72	2	.144	.144
	1409.5			12.219

Footnotes:
1. Calculated from calorific values after Cowgill.
2. Values for raw uncooked food.
3. Assuming 16% lard of negligible zinc content.
4. Mean of values for chicken, duck and goose.
5. Assuming egg consists of two-thirds white containing no zinc and one-third yolk containing 45 p.p.m.
6. Assuming zinc of milk is concentrated in the cheese.

TABLE 2.

Estimation of the daily consumption of zinc on the basis of the average N. China diet (Adolph).

Food	*Food/day g.*	*Estimated zinc content of food p.p.m.*	*Estimated amount of zinc consumed/day mg.*	
Meat and fish				
Beef, mutton, mule	1.6	34	.054	
Pork (including fat)	11.7	20	.351	
Fish	6.9	6	.041	
Shrimp and shellfish	5.2	24	.125	.571
Eggs	10.5	15	.158	.158
Milk and milk products				
Milk	6	3.4	.020	
Cheese	—		—	
Butter and fats (chiefly oils)	42	2	.084	.104
Grain products				
Wheat and wheat products	330	8	2.640	
Corn	8	9	.072	
Rice	187	15	2.808	
Millet	47	20	.940	
Kaoliang	30	20	.600	7.060
Legumes (soybean)	34	32	1.088	1.088
Vegetables				
Tubers and roots	30.8	3	.093	
Greens, Cabbage, &c.	83	4	.332	.425
Nuts				
Chestnuts	3	2	.006	
Peanuts	3	20	.060	.066
Fruits (12 varieties)	4	3	.012	.012
Sugar and starch	18	0		
	861.7			9.484

The first diet, which is that given by Sherman (1924) as the average American diet, derives most of its proteins from flesh foods, whereas grain products and legumes supply the bulk of the protein in the N. China diet given by Adolph (1925). The amount of zinc consumed in the American diet is estimated to be 12.22 mg./day against the value of 9.48 mg./day for the N. China diet. These figures correspond to 8.67 and 11.00 mg. of zinc per kg. respectively.

Another diet to which considerable interest attaches is the Steffanssen-Anderson diet. This diet consists exclusively of meat and animal products and was advocated by Steffanssen for use in arctic regions where considerations of weight are almost as important as the calorific and dietary values of the foods carried. The zinc content of this diet is uncommonly high, supplying 24 mg. of zinc per day which corresponds to over 29 mg./kg. of food. Steffanssen lived for a whole year on this diet and remained in perfect health.

TABLE 3.

Estimation of the daily consumption of zinc in the Stefjanssen: Anderson exclusive meat diet (20).

Food	*Food consumed per day* g.	*Estimated zinc content of food* p.p.m.	*Estimated amount of zinc consumed* mg.
Lean beef	390	34	13.26
Fatty tissue	175	2	.35
Liver	200	45	9.00
Marrow	70	20(?)	1.40
	835		24.01

The figures in Table 4 refer to another diet which is of particular interest in that it is a diet which is known to have produced the very high beri-beri rate of 200-600 per mille. This diet it will be seen provides 7.3375 mg. of zinc per day corresponding to the rate of 5.65 mg. for every kilogram of food taken.

TABLE 4.

Estimation of the zinc content of the diet of the native sailors in the Dutch East Indian Navy prior to 1874 (20).

Braddon (1907).

Food	*Food day*	*Estimated zinc content of food* p.p.m.	*Estimated amount of zinc consumed/day* mg.
Meat and fish			
Beef	225 (150)*	34	5.100
Pork	75 (37.5)*	37	1.3875
Fat (beef)	75	2	.150
(pork)	37.5	2	.075
or			
Fish, fresh	300	6	1.800
or			
Fish, dried	300	15	4.500
Rice	1000	3**	3.000
Salt, vinegar, coffee, &c.	?	?	very small
		Totals:	
		With meat	9.7125
		With fresh fish	4.8000
		With dried fish	7.5000
	1300	Average	7.3375

* On the reasonable assumption that the beef and pork consist of one-third and one-half fat respectively.

** The 1000 g. of rice presumably refers to cooked rice, consequently the average zinc content of cooked rice has been used in the calculation.

The amounts of food, zinc consumed per day and the zinc contents of the four diets which have been mentioned are summarised for comparison in the following table.

TABLE 5.

Comparison of the zinc contents of the four diets and the amounts of zinc ingested per day.

Diet	*Amount/day g.*	*Zinc/day mg.*	*Zinc content p.p.m.*
Steffanssen	835	24.01	28.75
American	1409.5	12.219	8.67
North China	861.7	9.484	11.00
Dutch Native Sailors	1300	7·3375	5.65

Consideration of the figures given will show that, assuming the daily intake of three to four litres of water containing on the average 0.5 p.p.m. of zinc, the average daily intake of zinc from an adequate diet is in the neighbourhood of 10-13 mg./day. A number of other published diets have been examined in this manner and all have been found to supply closely similar amounts. In fact it might be said that it is impossible to choose a well balanced diet which supplies less than 8 mg. or more than 16 mg. of zinc per kilogram of food.

Daily Excretion of Zinc in Urine and Feces.

The amounts of zinc excreted daily in the urine and feces have been determined by Rost (1921) and by Drinker, Fehnel and Marsh (1927), and Giaya (1920), Fairhall (1926) and Derrieu and Cristol (1930) have published figures either for the average zinc content of urine or for the amount of zinc excreted in the urine daily. The various figures are summarised in the following table from which it will be seen that the average value for the combined daily zinc excretion in urine and feces is 12 p.p.m., which value falls within the estimated limits given above for the amount of zinc ingested daily.

TABLE 6.

Daily excretion of zinc in urine and feces.

	Urinary mg.	*Fecal mg.*	*Total mg.*
Giaya (1920)	0.5*	—	—
Rost (1920)	0.6—1.6	3—19	3.6—20.6
Fairhall (1926)	1.0	—	—
Drinker, Fehnel and Marsh (1927)	0.25—2.0	2.67—19.9	2.92—21.9
Derrieu and Cristol (1930)	1.0	—	—

* Estimated from his figure for the zinc content of urine, viz., 0.17 mg./1.

DISCUSSION.

One point of importance emerges from this study. The three foods, marine fish, cooked polished rice and cabbage, which constitute the bulk of the diet of the poorest type of Chinese are, as is commonly known, very deficient in vitamin B_1. As will be seen from Appendix

II they also contain minimal quantities of zinc. Simple calculation shows that the zinc intake on a diet consisting largely of these three foods cannot supply appreciably more than 5-6 mg./day. Apart from being obviously less than 12 mg./day, the zinc requirement of man is unknown. Consequently, the extent to which the lower zinc intake of 5 mg./day may be reflected in the health of the subject is purely a matter of conjecture. Attention is drawn, however, to the fact that a diet producing beri-beri may supply minimal quantities of zinc, and presumably also copper and manganese. To what extent shortage of minor elements may be the cause of certain symptoms usually associated with beri-beri remains to be shown, but it is considered possible that this shortage may account, in part at least, for the peculiar appearance of the hair, the dry skin and the abnormal finger and toe nails which are sometimes observed in beri-beri patients. This question is receiving further attention.

SUMMARY.

Data for the zinc contents of natural waters, foodstuffs, and various organs and structures of the human body, collected from many sources, have been classified and tabulated, together with figures secured by the author, thus permitting the rapid estimation of the zinc content of any desired combination of foodstuffs. Examination of a number of diets four of which are given in detail shows that the zinc content of the diet is controlled largely by the proportion of protein which it contains and that the average daily intake of zinc from a well balanced diet closely corresponds, when calculated in this way, with the average amounts of zinc which various workers have observed to be excreted daily in the urine and feces, viz 12 p.p.m. Diets which are associated with the appearance of beri-beri may be deficient in zinc and certain other minerals.

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Appendix I.

ZINC CONTENT OF NATURAL AND SERVICE WATERS.

	Zinc content mg./l.	*Reference Nos.*
Sea Water		
English Channel (presumably)	not less than .002	25
,, ,,	less than .008	4
Galveston Coast (30 ft. from shore)	.140	16
Pescadero, U. S. A.		
Near shore	.390	
1 mile out	.002	58
West Sayville, N. Y. 1 mile out	nil	36
Fresh Water		
U. S. A. Washington, D. C., tap water	.250	15
Portland, Me., tap water in Natural Science Building	8	*cited by* 5
N. Dakota, water from Devil's Lake...	15	1
Natural waters from the Missouri/ Kansas/ Oklahoma region. (Zinc mining area)	0.9 — 50	5
Germany.		
Berlin tap water	5	49
Tübingen University tap water	2.5	70
Australia, Brisbane. Rain water stored in galvanised tanks	17.1	34
Hong Kong.		
Tap water from University Buildings...	.5	
Water from spring in rear of School of Physiology	.0088	
Switzerland. Tap water	2.5	50

Appendix II.
ZINC CONTENT OF FOODSTUFFS.

	Zinc content. dry matter p.p.m.	fresh matter p.p.m.	*Reference Nos.*
MEATS			
Ox: meat (beef)		21	23
,,		26.3	42
,,		46-52	71, 72
,,		46.6-50.4	54
,,		26-56	53
,,		25-37	14
,, (lean beef)	15		46
liver		35.4-83.3	52
,,	126.6	34.5	39
,,		42	14
,,		43	23
,,		58-84	71, 72
,, (dried)	117.4		30
,, (dried at 100)	283		67
pancreas		32.4-43.2	55
,,		23	23
,,	135.2	34.8	39
,, (9 years and over)	57, 60, 80	15, 16, 21	30a
spleen		13.5	54
,,	135.9	27.6	39
kidney		24	14
,,	114	18.9	39
brain		9.0	54
,,	56.6	13.5	39
testicle		18.0	11, 13
,,	98.7	13.6	39
blood, whole		21.4	23
,, ,,		5.3-5.7	71, 72
,, ,,		5.1	45
,, ,,	23.7	4.4	39
,, ,,		4.7-7.45	6
,, red cells	25.3	7.6	39
,, plasma	19.6	1.9	39
,, plasma B		3.32-3.35	6
suparenals	121	24.4	39
thyroid	71.1	19.5	39
Calf: meat (veal)		25-50	52
pancreas		33.3-43.2	55
,, (6-8 weeks)	75, 90	21, 25	30a
,, foetal (5-7 months)	55, 70, 75	14, 18, 19	30a
,, ,, (under 5 months)	153	33	30a
brain		17	14
blood	32		46
Sheep: meat (mutton)		25-50	52
liver (N.Z.)	254.6		3
pancreas		19.04, 25	55
testicle	64-81		3
,,	76	15	13
epididymis	69	12	13
seminal vesicles	113	40	13
Pig: meat (pork)		25-50	52
pancreas		28.2-44.4	55
testicle	76	14	13
epididymis	162	30	13
seminal vesicles	357	72	13
prostate	156	38	13
Cowper's glands	43	10	13

		Zinc content. dry matter p.p.m.	Zinc content. fresh matter p.p.m.	Reference Nos.
Horse:	meat		25-50	52
	,,		29	54
	,,	263	60	10
	liver	243	75	10
	spleen	203	45	10
	kidney	324	57	10
	lungs		11	54
	,,	182	39	10
	brain	203, 284	43, 62	10
	heart		15.8	54
	,,	263	71	10
	pancreas	243		10
	stomach	203		10
	testicle	089,729,243	214, 227	10
	spermatic fluid	486	13	13
	ovary	203	33	10
	mammary gland	981,851,203	363, 346	10
	lymphatic ganglion	243, 981	42, 172	10
	parotid	263	49	10
	thyroid	163		10
	suprarenal capsule	365	91	10
	bone (femur)	405	310	10
	marrow	324	32	10
	skin	203		10
	hair	284		10
	hoof	203		10
	cerebrospinal fluid	203, 122	73, 37	10
Rabbit:	foetal, embryo		44, 31	12
	,, 9 days		40	12
	,, 1 month		45	12
	,, 2 months		44	12
	,, 4 months		49	12
	meat		17-23	14
	,,		20	23
	,,	33-42		33
	liver	121-506	30-135	14
	,,		45-48	23
	,,		19.3	54
	,,	79-90		33
	kidney		32	14
	,,		43	23
	brain		31-64	14
	,,	33-45		33
	lung		36	14
	heart		45	10
	,,	45-69		33
	testicle		38-76	14
	blood, whole		19-26.1	23
	,, ,,	148		14
	bone (with marrow)	51		14
	skin	> 300		14
	hair	> 300		14

	Zinc content. dry matter p.p.m.	Zinc content. fresh matter p.p.m.	Reference Nos.
Sea-lion: meat		50-56	58
liver		48-49	58
spleen		10-12	58
blood, whole		1.9	58
bile		2.4	58
Sperm whale: meat		40	58
liver		40	58
Chicken: meat (red)	141		61
,, (white)	29		61
blood, plasma		.95	47
,, nuclei		1.25	47
,, protoplasm		1.08	47
feather (web)	231, 240		28
,, (quill)	102, 105		28
Duck: meat		27	23
liver		67-76	23
Goose: meat	83.1	22.1	39
liver	233.8	67.5	39
stomach	120.7	32	39
intestines	144.7	44	39
lungs	59.4	13.1	39
heart	91.5	23.8	39
kidney	75.1	20	39
pancreas	122	41.7	39
brain	55.3	10.3	39
testicle	80.4	11.1	39
blood, whole		9.8	39
,, plasma	79	2.3	39
,, nuclei	83	2.9	39
,, protoplasm	30	4.6	39
FISH (marine)			
Red snapper:			
Lutjanus aya			
meat	2.3		17
liver	55.5		17
air bladder	3.6		17
spleen	43.5		17
stomach	19.1		17
branchial arches	18.4		17
gills	5.6		17
skin	10.6		17
fins and tail	10		17
skeleton	16.5		17
Catfish:			
Ailurichtus marinus			
meat	8.1		17
liver	31		17
gills and branchial arches	102.5		17
fins and tail	12.2		17
skeleton	93		17

	Zinc content. dry matter p.p.m.	Zinc content. fresh matter p.p.m.	Reference Nos.
Salmon: (Chinook)			
Onchorhynchus tschawytscha		8	58
Sam lai: (Hilsa-herring)			
Hilsa Reevesii (Richardson)			
meat	25*		28
skin	162*		28
scales	44*		28
Lo yue: (sea perch)			
Latelabrax japonicus, Cuv. et Val.			
skin	479*		28
scales	162*		28
Fish: (undesignated)	33-42		61
Sea fish: (undesignated)		4	52
Cod: liver, oil		trace	73
,, ,, (Torch brand)		1	
Fang fish:			
Dasyatis akijei			
liver, oil		3	
FISH (fresh water)			
Snake-head			
Ophiocephalus argus, Cantor			
meat	38.6	6.8	39
liver	133.5	33.2	39
digestive tube	108.5	22.2	39
blood, whole		7.3	39
,, plasma	180	3.6	39
,, nuclei	40	1.1	39
,, protoplasm	13	1.6	39
Grass carp: (Wan yu)			
Ctenopharyngodon idellus, Cuv. & Val.			
skin	87*		28
scales	110*		28
MOLLUSCS, CRUSTACEANS, &c.			
Oyster			
Ostrea s. Crassostrea laperousi, Schrenk			
whole	410.5	66.1	39
meat	233.2	43.2	39
hepatopancreas	245.3	67.7	39
mantle	500	70.2	39
gills	1002.1	134.8	39
remainder	660.9	115.3	39
Ostrea lurida (California)		15-99	58
Oyster (Eastern)		170	58

* fat-free.

	Zinc content. dry matter p.p.m.	Zinc content. fresh matter p.p.m.	Reference Nos.
Oyster (undesignated)			
meat		76.4	16
digestive tube		196	16
mantle		218.8	16
remainder		191.2	16
Oyster, shucked, (U.S.A.)		1157.25	15
,, ,, (U.S.A 31 sources)		26-620	*
,, ,, (,, 16 ,,)		133.7-1032	*
,, ,, (,, 10 ,,)		146-779	*
,, ,, (,, 27 ,,)		170-2298	36
,, ,, (,, 13 ,,)		398-1220	*
,, blue (Perth, N.J.)		2.903	36
Clam: (Pismo)			
Ensis americanus		15.03, 14.72	58
,, (Little neck)			
Venus kennicottii		5.09	58
Mussel:			
Mytilus californica		49.5, 40.22	58
Abalone: *Haliotis cracherodii*		20.6-25	58
"Mollusc"			
foot	265		61
mantle	1052		61
Shrimp: *Palaemonetis vulgaris*		22-23.8	58
Crab: *Callinectis hastatus*		11.5, 44.3	58
EGGS			
Hen: whole		10	65
white		tr.	15
,,		nil	14
,,		nil	73
,,		nil	65
,, commercial		21	37
yolk		44.5, 56.7	15
,,	99		14
,,		4	73
,,		2, 1.2, .6	74
,,		42.9, 38.1, 40.1	37
,,		23, 29	65
,,	67		46
MILK			
Cow: whole (range of 12)		3.6-5.6	15
,,		3.9	53
,, (range of 7)		2.69-2.75	67
,, (range of several)		2.7-3.2	63
,,		2.06-2.08	41
,,		2.96-4.11	56, 57
,,		3.4-3.6	39

* Cited by 36.

	Zinc content. dry matter p.p.m.	fresh matter p.p.m.	*Reference Nos.*
skimmed		4.4	15
plasma		4	74
colostrum		4.16-13.56	56, 57
Goat: whole		2.3	53
,,		4.56-4.28	41
,,		2.6-4.2	39
Sheep: whole		2.97-3.68	56, 57
colostrum		3.06-13.78	56, 57
Horse: whole		2.64-4.2	56, 57
Man: whole		1.3 1.4	53
,,		1.4-2.1	39
,,		1.3	32
,,		1.23-3.56	56, 57
,, negro, 4th day after parturition		5.66	15
,, 9th day ,,		11.5	15
,, 15th day ,,		13.78	15
colostrum		4.46-7.35	56, 57
,,		2.8-9.2	39
BUTTER		2.5	50
CEREALS			
Wheat: whole (4 varieties)	100	26.08-84.8	15
,,			64
,, (air dried)		22.1	67
flour, wholemeal		10-15	9
,, ,,		25	65
bran		139.2	15
,, (5 sources)		74-112	65
,, (air dried)	75	87.4	67
,,			46
germ	40	140, 145	65
flour, white			64
,, ,,		8	30
,, ,, (75% extraction)		6.7	9
,, ,,	tr.	6.5	65
,, ,,			46
bread ,,	50	5-8	52
,, ,,			64
,, ,,		4.1	30
shredded		40.5	30
"Graham" crackers		13	30
"Grapenuts"		13.9	30
Barley: whole (Chevalier, Pacific coast)		26.7	15
malt		11	15
Oats: whole (4 varieties)		31.71-49.37	15
rolled (air dried)		17.5	67
,,		40	30

	Zinc content. dry matter p.p.m.	Zinc content. fresh matter p.p.m.	Reference Nos.
Rye: whole		17.19	15
Rice: whole, Japanese		14.65	15
,, (unknown, ex Shanghai)		17.8	
,, Annam	23.5	22.4	
bran		30	9
,,	67.4		
polished		2.5	9
,, Siam $8.40 per picul	10.4	9.7	
,, ,, $8.00 per picul	15.3	14.3	
,, ,, ,, (cooked)	14.8	5.1	
,, ,, third class	14.8	13.6	
,, ,, ,, ,, (cooked)	13.4	5.3	
,, ,, broken	15.7	14.3	
,, ,, ,, (cooked)	12.4	3.8	
,, Saigon	16.1	14.5	
,, ,, (cooked)	12.1	2.8	
,, Tonkin, glutinous	15.7	14.2	
,, ,, ,, (cooked)	15.0	4.5	
,, Canton, red	25.9	23.9	
,, ,, ,, cooked	15.0	5.5	
,, Annam	11.1	10	
starch (undesignated)	9.6		
"Ryzamin" concentrate of rice polishings		6	
Corn: whole		25.24	15
degerminated		3.99	15
meal		8.8	37
Buckwheat		10	9
"Cereals"		12-19.5	9
Arrowroot starch	258		
Tapioca starch	9		
VEGETABLES			
Carrot		4.96	15
,,		1-2	9
,,		3.1	65
Potato		5	9
,,		1.8	65
Onion		13.8	9
Garlic		10	9
Beetroot		7.4	65
,, (in glass)		57.8	30
Sugarbeet		2	62
Radish		4.5	9

	Zinc content. dry matter p.p.m.	fresh matter p.p.m.	*Reference Nos.*
Cabbage (outside leaves)		3.7, 2.6, 3.4	65
,, (inside leaves)		4.2, 2.1, 4	65
Spinach		3.1	30
,,		6.2	9
,,		7.1	65
,, (in glass)		12.2	30
Lettuce		4.7	9
,, (air dried)	44.1		67
,, (outside leaves)		3.3	65
,, (inside leaves)		2.9	65
Cress		5.6	9
Dandelion		9.7	9
Alfalfa		4	9
,, (air dried)	11.98		67
,, leaves (dried at 100)	21		
,, hay (dried at 100)	17		
LEGUMES & PULSES			
Soybean:			
Glycine soja, S. et Z.		20	9
(dried)	120		15
(air dried)		44.1	67
,, ,,	38	34.4	
leaves	110		46
Mung bean:			
Phaseolus mungo L. var. radiatus, Bak.			
(air dried)	25	23.3	
Lentils:		24.4	9
Flat bean:			
Dolichos lablab, L.		21.4	
(air dried)	24		
Green pea:		44.5	9
Pisum sativum, L.			67
(range of 3 varieties)	26.40.4		67
(canned)	28		15
(smooth pea)	34.53		
Haricot bean		52.5	9
Green beans (in glass)		4.9	30
Peanut:			
Arachis hypogoea, L.			
Butter		20.6	30
Oil		tr.	73

	Zinc content. dry matter p.p.m.	Zinc content. fresh matter p.p.m.	Reference Nos.
NUTS & SEEDS			
Sweet almonds		10	9
Arachis nut		16	9
Sunflower seeds		17	9
Walnuts (dried)		20	9
Chestnuts		1·2	9
Pine kernels		55·5	9
FRUITS & BERRIES			
Orange		1·1	30
pulp		1·2	9
Lemon:			
juice		1·2	9
Peach:			
(in glass)		3·8	30
Fig:		1·2	9
Grape:		1·2	9
Coconut:			
oil		12·5-40	73
Apple:			
flesh		·26	65
peel		·33	65
Olive:			
oil		tr.	73
Loganberry		4·5	65
Raspberry		3·5	65
Tomato:		5·9	30
puree (tinned)		70	65
MISCELLANEOUS			
Mushrooms: (17 species)	41-279		48
Boletus edulis		5·1	9
Cane molasses		38	
Dextrose, B.P.		nil*	
Shred Agar (Merck)		13·71	15
Gelatin (A. H. Thomas No. 33)		27·40	15
Ah Chiao (Donkey skin glue)		17·8	
,, ,, (after hydrolysis & ether extn)		27·9	
Gum from tree of *Prunus* sp.		55·0	
Brewers' yeast (H.K. Brewery)	37	7·0	
Bakers' yeast (Chieftain)	138	47·0	

* Contained traces of copper and sulphurdioxide.

Appendix III.

ZINC CONTENT OF HUMAN ORGANS AND STRUCTURES.

	Zinc content. dry matter p.p.m.	fresh matter p.p.m.	*Reference Nos.*
Epidermal structures			
Head hair	9		53
,, ,, (pigmented)	84-444 mean of 11 = 225		28
Head hair (unpigmented)	198, 222		28
Beard hair	130, 167		28
Pubic hair	71-342 mean of 8 = 197		28
Finger nails	121-260 mean of 13 = 195		28
Toe nails	96-340 mean of 10 = 198		28
Skin (whole)	12-55 mean of 8 = 26		28
Epidermis	97		28
Teeth	250		22
,,	50-100		43
Nervous system			
Cerebrum		15.7	18
,,	43.5, 21.3	8.5, 4.6	
Cerebellum		17.5	18
,,	53.5, 44.4	12.6, 9.6	
Whole brain		11.0	52
,,		5.2, 8.8, 7.2	18
,,		10.6-12.5	54
,,		8.3	45
,,	36-84		33
,, (5 mos. foetus)		11.5	18
Dura mater	18.4		
Choroid plexus	119, 29		
Sciatic nerve (fat-free)	27, 35, 37, 48		29
Trunk			
Lung		6.1-7.1	45
Spleen	198	42	21
,,		10.0-12.7	45
,,	27-73		33
,,	59.9, 156.6	14.0, 25.7	
Pancreas	56-156		33
,,		97-164	45
,,	107, 122	25.3, 26.4	
Kidney	316	68	21
,,		19.5-49.0	45
,,	36-174		33
,,	123, 147	24.6, 22.6	
Liver		52,146	52
,,	356	115	21
,,	182.8(8)	47.7(8)	35

	Zinc content. dry matter p.p.m.	Reference Nos.	Nos.
Liver (cont.)		10.76	51
,,		53.6-68.3	45
,,	219-288		33
,,		39	44
,,		17.7-86.8(53)	69
,,	162.9,186.2	44.6, 48.8	
Gall bladder	32.7		
Viscera		12-22(62)	31
,, (infant, 3 months)		8.8	32
,, (young female)		14.5	32
,, (male, 18)		15.4	32
,, (male, also 18)		16.6	32
,, (female, 24)		20.5	32
,, (female, 40)		26.0	32
,, (male, old)		41.0	32
,, (male, 70)		48.6	32
Uterus	170		21
Endocrine organs			
Thymus (boy, age 13)	71	15.1	
Secretions			
Milk and Colostrum	see App. II		
Bile	12.8, 16.2	1.2,2.4	
Blood and Pus			
Blood whole		4.8-5.8	45
,, ,,	139		21
,, ,,		20.6	23
,, ,,		15-25	59
,, ,,	57		
,, plasma		2.89-3.68	19
,, cells		6.0-8.25	19
,, cell nuclei		10 times plasma value	23
Pus, whole	3-10		75
,, nuclei, (acute)	93.5		75
,, ,, (chronic)	24.8		75
,, plasma, (acute)	26.0		75
,, ,, (chronic)	42.3		75
,, protoplasm, (acute)	43.4		75
,, ,, (chronic)	108.0		75
Muscular and Fatty tissue			
Cardiac muscle		12.6-15.6	45
,, ,,	48-103		33
,, ,,	97.9,127.6	28.9, 26.6	
Striated muscle		47-52	52
,, ,,		25-36	45
,, ,,	119		61
Mammary gland		3.75	66

	Zinc content. dry matter p.p.m.	fresh matter p.p.m.	*Reference Nos.*
Reproductive organs			
Testicle		8-10.3	45
,, (age 28)	163	16	13
,, (age 2)	315	76	13
Prostate (age 28)	491	94	13
,, (age 60)	731	113	13
Seminal Fluid	572,1552,2020	53,152,220	13
Foetus			
whole, (7 months)		30	32
Bone		126	45
		227	27
Excretions			
Feces		3-19 mg./day	53
,,		2.67-19.9 mg./day	26
Urine		0.6-1.6 mg./day	53
,,		1.0 mg./day	30
,,		0.25-20 mg./day	26
,,		1.0 mg./day	24
,,		0.17 mg./l	32

A CASE OF GOUT IN A CHINESE.

by

C. H. Yeang.

Department of Surgery, University of Hong Kong.

Gout is supposed to be rare in this part of the wrold: at least many of the Hong Kong old timers have reportedly scarcely encountered a case. We should therefore like to put on record the following case of gout in a Chinese male of 56. We expect to hear other cases met with by our readers, as the patient mentioned that he had seen his friends in Kwangtung Province suffering from a similar complaint although in his own family there was no one else. It is a matter of etiological interest that our patient was a poor man, being an electrical fitter, but he had been drinking a great deal of wine since his youth. He explained that Chinese wine was to him accessibly cheap in those days.

The patient attended the University Surgical outpatient Clinic and was presented by a student in the usual routine manner. He merely complained of a firm, painless swelling 1½" diameter on the medial side of his right foot, at the deceptive situation typical for a bunion in hallux valgus. He also presented a much smaller similar one on the corresponding side of the left foot. (See photos attached). There is also one on each lateral malleolus. Interest is attached to the fact that they were easily mistaken for fibromata in view of the rarity of the occurrence of gout in Chinese. However, he also had these tophi over the olecranon processes, and small ones over the extensor tendons of the hand.

They were of gradual growth and were not tender but became exceedingly painful at times during rainy weather. He had 3 or 4 attacks of arthritis a year. As luck would have it, he developed an attack of multiple arthritis during his stay in hospital, with pain and stiffness of right wrist and hand and both knees. The left knee was particularly swollen, with effusion and signs of inflammation.

Before the attack, the blood uric acid was found to be 5.7 mgms % as compared with the normal of 2 mgms %; unfortunately, we have no figures for the amount during the attack. The urine contained excess of amorphous urates, but no casts.

His blood pressure was 138 systolic and 64 diastolic, which was not at all high in view of his age.

His Kahn test was negative.

The tophi were found to contain needle-shaped crystals of sodium urates and gave the positive uric acid test.

The x-ray evidences are certainly interesting in that they reveal the characteristic non-opaque mouse-eaten areas at the sides of the bases of the short long bones. The striking x-ray appearances are diagnostic, and these areas are due to the deposition of sodium biurate, which is not opaque. "A Manual of Radiological Diagnosis" by Ivan C. C. Tchaperoff, refers to this as calcium urate, which is obviously a mistake. The gross appearance of these deposits in the bones is similar to the tophi.

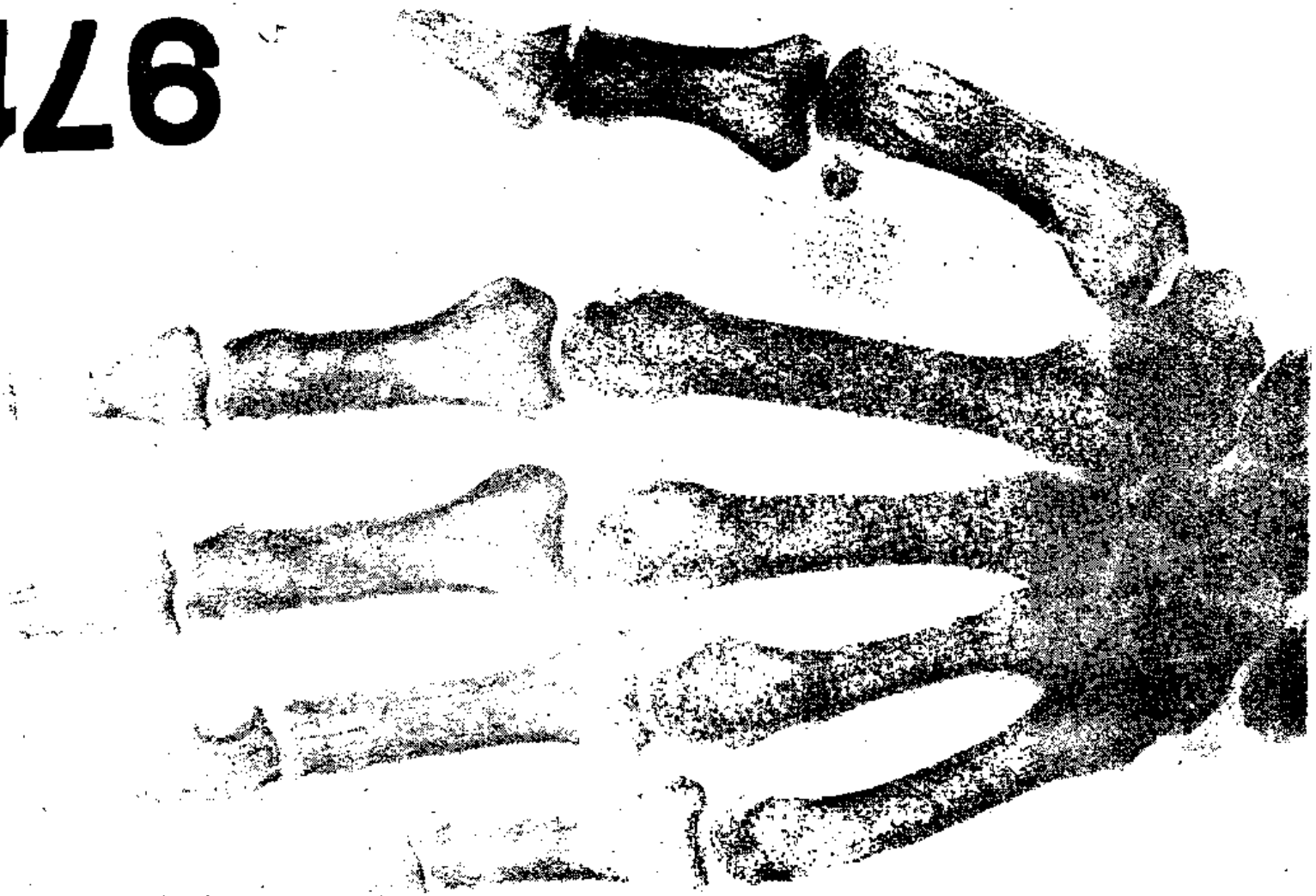
Another interesting point is shown in the accompanying photograph where the deposition of sod. biurate in the soft tissue adjacent to bone has given rise to indentation. Is this pressure atrophy?

The cartilaginous surface of the bone ends is replaced by a thin white chalky, coat, which accounts for the attacks of arthritis.

The patient died suddenly in hospital and at postmortem the kidneys showed chronic interstitial nephritis and the vessels arteriosclerosis.

I have to thank Prof. Digby for his encouragement and suggestions in preparing this article.


HOOKLEY



GOUT - Note rouso-ca[illegible] erosions at base of second
[illegible] ny of fourth finger, the actual bone being absent in
[illegible]

Review of Books

Volume Jubiliare, en l'honneur de Monsieur Louis. E. C. Dapples, President du Conseil d'Administration de Nestlé and Anglo-Swiss Holding Co., Ltd.

To those of us who have not the pleasure or honour of knowing M. Dapples personally, a glance through his Jubilee Volume will readily bring the conviction that the letter of Hommage with which the volume begins can not be mere pen or lip hommage.

The establishment and growth of an institution such as the Nestlé and Anglo-Swiss Holding Company Ltd., is only possible when it has been under the control and guidance of a man of exceptional qualities and character. Of the personal qualities of M. Dapples only those who have worked with and under him through years of difficulty as well as prosperity are undoubtedly the best judges; of his business acumen, the present status of the Company affords a sufficient indication; but to scientists in general and medical scientists in particular the most outstanding and most praiseworthy aspect of his activities is his recognition of the debt a company such as his owes to science. Just as a wise husbandman gives back elements to the soil in return for the crops he reaps, so the wise business man attempts to repay science for its benefits by means of furthering scientific research. This volume shows that the research work done in the Nestlé laboratories is done in the spirit of true scientific investigation and for the advancement of science as a whole and not only for their own particular pecuniary benefit.

So vast is the field covered by the examples of research work published in this Jubilee Volume that no one worker could adequately review all the articles, but to us here in Hong Kong there are a number of especial interest. In the last issue of this journal we published an article from the pen of Dr. Eggleton dealing with part played by the so-called trace elements in nutrition of the human body and in that article, mention was made of the work of Paul Dutoit and Christian Zbinden. Both these well known investigators contribute valuable articles in this volume, the former concerning mineral elements and the latter concerning the chemical constitution and synthesis of certain vitamins. As might be expected most of the articles deal with nutrition but their scope is by no means limited to the part played by milk therein.

If we might offer a suggestion from our own selfish viewpoint, we should like at some future date to hear what such a company has to suggest concerning the problem of feeding of native races, a problem which for us in China presents great difficulties both nutritional and economic as well as practical.

Of the original articles, it is interesting to note that a big percentage are written by members of the scientific staff of the Société Nestlé and the standard of these articles gives an idea of the scientific calibre at the disposal of the Société.

Now a word or two about the book itself. It contains 690 pages, is well printed and profusely illustrated. many of the illustrations being in colour. The print is clear and the binding excellent especially for our climate here in Hong Kong. It undoubtedly serves not only as a tribute to a worthy man but is of scientific value to workers in many parts of the world. After reviewing this work we are left with the feeling of pleasure that such a university as the University of Lausanne has seen fit to recognise the work of M. Dapples by conferring on him their Doctorate, *honoris causa.*

"*Catechism Series.*" Botany. Part I, 76 pages, paper covers, one shilling and sixpence, Edinburgh, E. & S. Livingstone, 16 & 17 Teviot Place.

The advantage of a little book of this type is that it presents a large number of facts in a very small compass. The disadvantages are many. Owing to the brevity of the statements it means that unless the student already understands the subject he will not understand the statements. Secondly, there is a tendency to use teleological arguments which are not only unsound but bad for the students. A statement is made that a certain structure is for a definite purpose, the student will remember this and will forget or ignore the far more important aspect of the problem,—how did such a structure arise? An example of where this book fails is quoted.

"*Give some examples of the materials deposited in or on cell-walls.*

(*b*) CUTIN may be deposited to render the walls less permeable to water. Such deposition is *cutinisation* or *cuticularisation* and when on the outer walls of the skin or *epidermis* the layer is called *cuticle.*"

Here are all the sins,—teleology, a plethora of synonymous terms and no explanation of what cuticle is and why and how it is formed.

Acknowledgements

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