CHEMICAL NATURE OF SALTS FROM BONES AND TEETH AND OF TRICALCIUM PHOSPHATE PRECIPITATES

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ACCORDING to recent papers[1], it seems that much confusion still prevails concerning the physical and chemical properties of tricalcium phosphates. Experimental researches, performed during the War, enabled us, however, to elucidate many difficulties in this field and to demonstrate our misinterpretation of many previous experimental results. Our researches originally dealt particularly with the molecular nature of salts from bone and teeth, but were later extended to the nature of tricalcium phosphate precipitates.

(1) It is generally believed that bone salts are constituted either of hydroxylapatite which has adsorbed calcium carbonate or of carbonato-apatite, because bone salts give the same powder diffraction photograph as apatites. We have shown that in fact bone salts diffract X-rays similarly to the apatites because they are mainly made of a salt 'isomorphous' to apatites, namely, α tricalcium phosphate, in a merely physical association with carbonate. The main arguments in favour of our views are as follow :

(*a*) If we submit bone to the fractional solubility method, we observe that small quantities of acid in contact with bone salts first dissolve only calcium carbonate, but no phosphorus. It is thus possible, with accurate quantities of citric acid, to separate chemically the carbonate of bone from the phosphate without destroying the latter. Hence, bone salts are a simple physical complex of phosphate and carbonate. If we were dealing with carbonato-apatite, the two constituents of the compound could not possibly be separated by using the same chemical method.

(*b*) Our X-ray diffraction studies show that ignition will transform the purified osseous α phosphate into tricalcium phosphate, while it has no action upon apatite. The raw bone salts are transformed into carbonato-apatite after ignition at 900° C. by combination of the tricalcium phosphate with carbonate ; in fact, this operation does not essentially modify the X-ray pattern obtained from bone salts. The main constituent of the non-ignited complex is thus 'isomorphous' with the ignited compound in spite of the alteration of the chemical properties. After ignition, however, the lines of the pattern are sharper than before because the individual crystals of carbonato-apatite are bigger than those of α tricalcium phosphate .

(*c*) The refractive index of bone salts is equal to that of a mixture of 90 per cent pure α tricalcium phosphate precipitate with 10 per cent calcium carbonate, namely, 1·590 ; after ignition, on account of the chemical change produced, the value of the refractive index becomes equal to that of natural apatites, namely, 1·649[5].

(2) Similar observations were made with complexes of tricalcium phosphate and lime such as are obtained after partial hydrolysis of precipitated tricalcium phosphate. Indeed, it is well known that precipitated tricalcium phosphate often contains more calcium than required by its theoretical composition ; in fact, its Ca/P ratio, theoretically equal to 1·94, often reaches 2·15 (characteristic value of apatite) and may even be greater. A partially hydrolysed tricalcium phosphate with a Ca/P ratio of 2·15 resulting from production of lime and adsorption during hydrolysis is not an apatite, though it shows an X-ray diffraction pattern similar to that of apatite ; its main constituent is, as in bone salts, a compound 'isomorphous' with apatite, namely, α tricalcium phosphate. The merely physical complex of tertiary and lime becomes an apatite when ignited at 900° C. This can be demonstrated in the same way as we did for bone[3,4]. We cannot admit, therefore, that the tertiary, with a Ca/P ratio of 1·94, is hydroxylapatite with adsorbed PO_4 ions[6]. That its powder diffraction pattern is the same as that of apatites is not a conclusive argument, because the tricalcium phosphate itself is 'isomorphous' with those compounds.

(3) Finally, we have shown, using up to now optical methods only, that the mineral fraction of ivory and cement from tooth is the same as that of bone. Enamel, however, has a more complex composition, its prisms being formed of real carbonato-apatite, while its interprismatic substance is organic matter impregnated mostly with α tricalcium phosphate[7].

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BRITISH EMPIRE CANCER CAMPAIGN

REPORT FOR 1945

AS the twenty-second annual report of the British Empire Cancer Campaign* is the first to be published since the end of the War, it is appropriate that reference should be made to the steady progress in cancer research which has been maintained during the war years. In particular, the first practical chemotherapeutical advance—the treatment of cancer of the prostate with œstrogens—has been made. War research has developed new methods, tools and substances, and some of these should be of help in cancer research in peace-time. The present report summarizes the recent progress.

Interesting results are being obtained in experiments on animals with 2-acetylaminofluorene. Workers in Leeds and Sheffield using this compound have induced tumours of many organs, including bladder, pancreas, liver, lung, breast and ductus acusticus. By dosing mice with 2-acetylaminofluorene a number of bladder tumours have been obtained, and some of these resemble papillomata of the human bladder. In these experiments the carcinogenic agent

* British Empire Cancer Campaign. Twenty-second Annual Report, 1945. Edited by J. P. Lockhart-Mummery. Pp. 102. (London : British Empire Cancer Campaign, 1945.)

was injected into the stomachs of the mice and was presumably absorbed and may have produced its effect after it was secreted in the urine. This fluorene derivative appears to be suitable for studies of anti-carcinogenic or neutralizing agents; but its carcinogenic action is less easily modified by dietetic changes than is the action of the azo compounds such as dimethylaminoazobenzene.

One of the simplest carcinogenic agents is urethane or ethylcarbamate. American workers first found that this compound induced tumours of the lung in mice, and the same result has now been obtained in Britain. When one considers that urethane was used as an anæsthetic and that acetylaminofluorene was introduced as an insecticide, it might seem desirable that all new chemotherapeutic agents should be tested for carcinogenic action before they are widely used in medicine.

Experiments on the antagonism to the carcinogenic action of benzpyrene carried out by Dr. F. Dickens and Dr. H. Weil Malherbe at Newcastle have revealed something of the nature of the anticarcinogenic material present in mouse fat. The action of the fat appears to be due to unsaturated fatty acid derivatives. The most active anticarcinogenic material was present in the phosphatide fraction, and phosphatides inhibit both carcinogenic action and benzpyrene excretion. Cholesterol increases the rate of excretion of benzpyrene and accelerates the production of tumours. The results suggest that metabolism of the hydrocarbon is necessary for carcinogenesis, and that the true or ultimate carcinogen may be a metabolite. The same investigators have studied the remarkable solvent action of aqueous solutions of purines on polycyclic hydrocarbons. The solvent power of purines increases with the number of carbonyl groups and with the number of N-methyl groups in the purine molecule; hypoxanthine with no methyl or carbonyl groups has very little solvent action, but tetramethyl uric acid is a very good solvent for 3 : 4-benzpyrene. Nucleosides and nucleotides have some solvent action but less than that of the corresponding unsubstituted aminopurines.

Work at the Mount Vernon Hospital has thrown light on the relationship of mitosis and carcinogenic action. Thus croton oil, which has a cocarcinogenic effect, induces hyperplasia of the skin, and cantharidin inhibits both mitosis of epidermal cells and the carcinogenic action of benzpyrene. The same workers have shown by fluorescence spectrography that benzpyrene applied to the skin of mice is absorbed in about four hours and disappears within twenty-four hours following a single painting. The specific carcinogenic action of benzpyrene therefore probably occurs within a few hours of application to the skin. Mice were painted with benzpyrene on one flank at midday and on the other flank at midnight. The midnight paintings induced more tumours than did the midday applications. With midnight applications the benzpyrene content of the tissue would be highest during the day when mitosis is most frequent. The evidence obtained indicates that the process of carcinogenesis by benzpyrene occurs while cells are dividing. This is in agreement with the fact that hyperplasia and carcinogenesis are often interdependent.

The results obtained in Newcastle and at the Mount Vernon Hospital taken together suggest that the actual carcinogenic process may involve the action of a metabolic product of a carcinogen on some cell constituent during the process of mitosis.

By investigating statistics of mortality from cancer, Prof. and Mrs. E. L. Kennaway have been able to show that though the incidence of cancer of the scrotum is very much higher among chimney-sweeps than among the general population, the mean age of death from this cause is about the same in the two classes. This is an example of an external factor which increases the incidence of cancer among the population yet has no effect upon the incubation period. A similar effect is shown in the incidence of lung cancer in chromate workers in Germany. There appears to be some mechanism resisting any acceleration in the development of cancer. The fact that types of cancer which tend to be inherited show differences in age of incidence in susceptible families and in the general population suggests that the resistance has a genetical basis.

In addition to work on carcinogenesis, experiments have been carried out on the chemotherapy of cancer, on the relation of viruses to cancer and carcinogens and on the immunity to subsequent tumours which develops when animals bearing tumours are suitably irradiated with X-rays. The report includes accounts of treatment of cancer in several hospitals by irradiation and surgery. The Clinical Cancer Research Committee presents a detailed analysis of the data from more than five hundred cases of cancer of the pharynx and larynx. E. BOYLAND.

INTERNATIONAL ASTRONOMICAL UNION

IN order to set the wheels of international co-operation in astronomy turning smoothly again after the gap necessarily caused in many cases by the war years, the Executive Committee of the International Astronomical Union recently called together as an advisory body representatives from the United States of America and from a number of European countries. At a meeting which took place during March 7–13, in the rooms of the Danish Academy of Sciences, Copenhagen, the following countries were represented: Belgium, Czechoslovakia, Denmark, France, Great Britain, Netherlands, Norway, Poland, Sweden, Switzerland, U.S.A., U.S.S.R. and the Vatican City State. The British representatives were the Astronomer Royal, Prof. W. M. H. Greaves and Prof. F. J. M. Stratton. After a welcome from Prof. Elis Strömgren on behalf of the Danish National Committee of Astronomy and from Prof. Niels Bohr on behalf of the Danish Academy, the meeting settled down to business under the presidency of Sir Harold Spencer Jones, with the guidance of the general secretary, Prof. J. H. Oort, director of the Leyden Observatory.

Committees were appointed to advise the Executive Committee on Publications on Solar Phenomena, on Variable Stars (names, catalogues and ephemerides), on Bibliography, on Fundamental Astronomy and Minor Planets and on Exchanges between Astronomers of different Countries. Annual grants were recommended in connexion with the above and for certain institutions for which the Union has been partly responsible in past years. Among other projects which were discussed favourably, mention may be made of an International Observatory, for which it was realized that the backing of the United Nations Educational, Scientific and Cultural Organ-