

ON THE EXCHANGE MECHANISM IN BONE

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BASED on their phosphate exchange reactions *in vivo*,¹⁻⁵ the calcified tissues have been regarded⁵ as composed, physiologically at least, of two parts; the one, that rapidly comes to equilibrium with the blood minerals, and changes its composition in conformity with the mineral composition of the blood, has been designated as labile, and the other, which is relatively much less affected by the composition of the blood, has been designated as stable or non-labile. Though no experimental proof so far has been produced to support this theoretical division of the calcified tissues into labile and non-labile parts, the exchange reactions, which the calcified tissues, more particularly the bones, enter with the mineral constituents of the blood, have, nevertheless, been sought to be explained on the basis of this hypothesis. Recently, it has been shown^{6,7} that bone salt also exhibits similar exchange reactions *in vitro*. When bone salt is equilibrated with a solution of NaF, it is observed that fluoride is removed by the bone salt, and that the corresponding quantity of the anions like $\text{CO}_3^{=}$ and $\text{PO}_4^{=}$ is released from the bone salt into the liquid phase in the manner of Freundlich adsorption isotherm. It was thought that the anions of the bone salt that are thus exchanged with the fluoride of the liquid phase, which gets adsorbed, are probably likewise already adsorbed on the bone salt, and constitute what has been termed as its labile part, and that by repeatedly equilibrating a given quantity of bone salt with a solution of NaF, and determining the quantity of the fluoride adsorbed, and the quantities of the anions of the bone salt liberated into the liquid phase, it should be possible to determine the relative quantities of labile and non-labile fractions in a given quantity of bone salt, and thus experimentally substantiate the above hypothesis. Based on these observations and arguments, an attempt has been made to determine the amounts of labile and non-labile parts of bone salt. A sample of bone salt (percentage composition: N = 4.97, Ca = 26.42, P = 12.72, Mg = 0.47, Na = 0.36, F = 0.073, $\text{CO}_3 = 4.25$, Residual Ca = 23.59, Ratio Residual Ca : P = 1.85), weighing 1.002 g., was equilibrated with a solution (2.5 per cent.) of NaF. At equilibrium, the quantity of fluoride adsorbed, and the corresponding quantities of $\text{CO}_3^{=}$, and $\text{PO}_4^{=}$, released from the solid phase into the liquid phase,

were determined. As the replacement of adsorbed anions of bone salt, and their consequent release into the liquid phase, when a sample of bone salt is equilibrated with a solution of NaF, is determined by the concentration of fluoride in the liquid phase, and as the concentration of NaF in the liquid phase cannot be raised beyond 4 per cent., that being approximately the solubility of NaF in water, and as the quantity of adsorbed anions released into the liquid phase with a 4 per cent. solution of NaF may either be the total quantity of adsorbed anions in a given quantity of bone salt or a part thereof, the same bone sample, after its quantitative separation from the liquid phase, was again equilibrated with a fresh aliquot of NaF solution. This process of repeated equilibration was continued till the liquid phase at equilibrium was not found to contain phosphate or carbonate. The process of equilibration of the above quantity of the bone salt with a solution of NaF was carried out 12 times. In the twelfth equilibration study, it was observed that the liquid phase at equilibrium contained no carbonate, about 0.3 mg. of P (per 50 c.c. of the solution), and had the fluoride concentration little higher than that of the original solution, indicating that the capacity of the above quantity of the bone salt to enter into exchange reactions had been reached, and that the further quantity of fluoride was not only not being adsorbed but that part of the previously adsorbed fluoride was being released back into the liquid phase. At this stage, the bone salt was quantitatively collected and analysed, and was found to contain a trace of carbonate, 10.12 mg. of P, and 233.7 mg. of F, as against the initial values of 43.43 mg. of CO_3 , 130.0 mg. of P, and 0.7459 mg. of F. Thus, it can be seen that about 94 per cent. of the anions in the above quantity of bone salt, by the process of repeated equilibration with a solution of NaF, has been replaced by fluoride in the manner of Freundlich adsorption isotherm, and that it has not been found possible to replace likewise the remaining percentage of anions with fluoride. Can it now be assumed that the remaining percentage of anions represents that part of the bone salt, which has been termed non-labile and real, and that the considerably large percentage of anions, that have been replaced with fluoride, represents that part of the bone salt, which has been designated as

labile or adsorbed? Before answering this question, it is desirable to consider the theoretical possibility of the replacement with fluoride of the remaining percentage of anions in the bone salt. There does not seem to be any reason as to why it cannot be assumed that it is possible to replace, in the manner of Freundlich adsorption isotherm, the remaining percentage of anions in the bone salt with fluoride, provided, fluoride, under such conditions, is adsorbed by the bone salt. It can be seen from the data presented that, in the twelfth equilibration study, the liquid phase contained no carbonate, about 0.3 mg. of P per 50 c.c. of the solution, and had the fluoride concentration little higher than that of the original solution, indicating that further quantity of fluoride was not only not being adsorbed but that part of the previously adsorbed fluoride was being released back into the liquid phase. As fluoride was not being adsorbed, the remaining anions were not being replaced with it, and consequently were not being released into the liquid phase. Such a circumstance, however, can be viewed differently also. Further quantities of fluoride were not being adsorbed by the bone salt, because there were no replaceable anions left in it. In that case, the remaining percentage of anions will have to be regarded as that fraction of the bone salt, which has been designated as non-labile and real, and the rest of

bone salt, as labile and adsorbed. However, it does not seem to stand to reason to assume that so large a fraction as 92 per cent. of the total P in the bone salt is adsorbed on the remaining 8 per cent. Under such circumstances, the only other alternative has to be accepted that all the anions in the bone salt, at least theoretically, can be replaced with fluoride by the process of repeated equilibration, and in the manner of Freundlich adsorption isotherm. Thus, the theoretical division of bone salt, on the basis of its exchange reactions *in vivo*, into labile and non-labile parts, has not been found to be correct *in vitro*. It seems to be the fundamental property of the bone salt to enter into exchange reactions with the anions of the liquid phase in the manner that can approximately be denoted by the Freundlich adsorption isotherm. Such a property of the bone salt may be the basis of the exchange mechanism in bone *in vivo*.

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EUROPEAN ORGANIZATION FOR NUCLEAR RESEARCH

THE European Organization for Nuclear Research has emerged from its planning phase and will shortly become a reality under the terms of a Convention signed recently in Paris by representatives of twelve nations.

The programme for the new European Organization includes the construction of a new international laboratory for nuclear research, and the continuation of co-operation between existing laboratories in the various countries.

The construction of the laboratory and its equipment is expected to require seven years. The cost of all activities during those seven years will total 120 million Swiss francs, including construction of the laboratory and its equipment. This will consist mainly of two large

accelerators, a synchro-cyclotron, which will probably be completed in four years, and a proton synchrotron that will take seven years to construct.

When the Convention becomes effective, it is planned to build the laboratory near the French border three miles north-west of Geneva.

The research will be fundamentally scientific and of non-military character. None of the work will be secret. The laboratory will not include an atomic reactor and will not be used for the production of high-energy materials. It will be used only to study the properties of atomic nuclei, and of such elementary particles as protons, neutrons and mesons.