apatite' and makes formation of true solid solutions of the two compounds highly unlikely. Formation of lamellar mixed crystals of the two compounds, as described in the following communication, is more probable.

The channel in the water layer explains both the ease with which OCP loses water and the difficulty of establishing a definite degree of hydration. The formula for OCP used here is based on the assumption that the partially filled water site for O(43) is completely filled in the ideal compound. There is sufficient room at the site for a water molecule, where it is co-ordinated to eight oxygens by distances less than 3·5 Å. Complete loss of water from this site would yield the formula $Ca_4H(PO_4)_3.2H_2O$, which is sometimes given[3,4] for OCP. There is no space in the unit cell large enough to accommodate another water molecule, and it appears that earlier indications[7,8] of more than 2·5 moles of water are in error. Hayek *et al.*[3] found that two samples of OCP dried for a short time at 100° C contained 2·5 moles of water, indicating that drying at this temperature removes non-essential water without much loss of water from the lattice. In view of these results, the formula $Ca_8H_2(PO_4)_6.5H_2O$ would be a better designation for OCP because it avoids fractional moles of hydration, it represents the asymmetric unit, and it is consistent with the common name.

The asymmetric unit of OCP contains two non-water protons which may form interphosphate hydrogen bonds. One such hydrogen bond is indicated by a distance of 2·47 Å between oxygens O(20) and O(36). This hydrogen presumably contributes to the weak 2,400 cm^{-1} infra-red absorption reported for OCP (ref. 10) and for 'calcium-deficient' apatites[11]. The other interphosphate oxygen-to-oxygen distances are greater than 2·9 Å, and a second interphosphate hydrogen bond cannot be located definitely on the basis of the present information.

The great variety in the anion–cation combinations which form apatite-type structures indicates that a high degree of stability is associated with this atomic arrangement. OCP appears to be the first-established compound with this arrangement in a layer-type structure, and it is noteworthy that this structural feature persists even though it is present in only about one-half of the unit cell. Arnold[1] and Carlström[5] suggested that OCP is a hydrated, layer-type modification of HA. Their views that the layers are formed simply by replacement of calcium ions by hydronium ions and that the layers are normal to the *c* axis were not borne out by the structure determination.

The two most common habits of HA (following communication) are such that the forms (100) could be the major contributors to the surface area of the crystals. Since the layers of OCP also are parallel to the 100 face, the structure of the water layer may prove to be a useful model for describing the interface between the apatite crystal and the aqueous phase.

The two-dimensional phase of this work was done at the University of Amsterdam on a grant from the Rockefeller Foundation, Agriculture, with advice of Prof. Caroline H. MacGillavry of the Laboratory for Inorganic Chemistry. Mr. Abraham Krouger of the Netherlands Organization for Pure Scientific Research (Z.W.O.) prepared the films from which the intensity data were collected.

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Crystallographic and Chemical Relations between Octacalcium Phosphate and Hydroxyapatite

MANY investigators[1,5,6,12-16] have observed that precipitated calcium phosphates that give apatitic X-ray patterns often have mole ratios Ca : P less than that of hydroxyapatite (HA), $Ca_5(PO_4)_3OH$. Most of these investigators have advanced explanations for this apparent anomaly, none of which is entirely satisfactory. On the basis of a recent determination (preceding communication) of the structure of octacalcium phosphate (OCP), $Ca_4H(PO_4)_3.2{\cdot}5H_2O$, we offer another explanation which is consistent with the crystal structures of these two calcium phosphates. We have suggested[7] that HA and OCP form crystalline interlayered or lamellar mixtures analogous in this respect to clays. Such intra-crystalline mixtures not only account for apatitic precipitates with ratios Ca : P less than that in HA, but also explain observed chemical and physical properties of precipitated basic calcium phosphates.

We have obtained further evidence in support of this explanation from X-ray and petrographic investigations of basic calcium phosphates the mole ratios of Ca : P of which ranged from 1·33, that in OCP, to 1·67, that in HA, and of products obtained from OCP by dehydration in air, hydrolysis in boiling water, and treatment with fluoride solutions. Many of the alteration processes were observed with single-crystal X-ray techniques. The basic calcium phosphates were prepared in several ways, including titrations of phosphate solutions with solutions of calcium salts, ammoniation of acidic calcium phosphate solutions, hydrolysis of dicalcium phosphate, and diffusion of solutions of calcium acetate and sodium phosphate. The temperatures of the preparations ranged from 20° to 100° C.

The crystals used in the single-crystal X-ray studies were prepared by diffusion at 50°–60° C of 0·5 M sodium phosphate solution into a 0·5 M calcium chloride solution. Both solutions were also 0·5 M in sodium acetate, as was the barrier solution; all were adjusted to *p*H 8. The optical properties of some of the crystals showed that they had partially hydrolysed.

The optical properties of OCP were measured on crystals that were prepared by slow hydrolysis at 40° C of dicalcium phosphate in 0·5 M sodium acetate solution[7].

OCP crystallizes as thin (100) blades of triclinic : pinacoidal symmetry. The blades are elongated along *c* and modified by the set {010} and the terminating set {011}. Contact twinning with (100) as the twin plane was commonly observed optically. Single-crystal X-ray patterns commonly revealed twinning with *c* as the twin axis, and this is probably the polysynthetic twinning observed optically. In both modes of twinning the (100) is the composition plane.

The crystals are biaxial (–) with a $2V$ of 50°–55° (calc. 54°). The refractive indexes measured by the immersion method at 25° C are $N_\alpha = 1{\cdot}576$, $N_\beta = 1{\cdot}583$, and $N_\gamma = 1{\cdot}585$. The optic plane is inclined to the (100), where its trace on that face is at 78° relative to *c* in acute α. The acute bisectrix lies in the quadrant defined by *a*, *-b*, *-c*. One optic axis is roughly normal to (100), which accounts for the very low birefringence of crystals in their preferred orientation. Dispersion ($r > v$) is very weak. The specific gravity obtained by the sink–float method is

2·61 g/cm^3, and the value calculated from refractive indexes[17] is 2·59 g/cm^3.

The indexes of refraction of microscopically coarse, euhedral crystals of synthetic HA with the correct chemical composition are $n_\varepsilon = 1·640$ and $n_\omega = 1·646$.

Preparations with ratios Ca : P between those of HA and OCP give X-ray powder-diffraction patterns with lines of both salts, and the relative intensities of the OCP lines generally decrease and those of the HA lines increase as the ratio Ca : P increases. Individual preparations may appear homogeneous under the microscope because of the uniform appearance of the crystals. Optically, however, the individual crystals display wavy extinction, symmetrical extinction without the expected conoscopic figures, or marked variation in refractive indexes from one crystal to another. In some preparations, the variation in refractive indexes is slight; but in others it extends over much of the range between OCP and HA. The optical properties of individual crystals show them to be intra-crystalline mixtures, even when they appear superficially homogeneous.

The idea that crystals of this type are lamellar mixtures of HA and OCP (ref. 7) was supported by the features of close structural similarity in the two salts (preceding communication). Proof of this idea was supplied by a single-crystal X-ray study of an optically homogeneous 'crystal' the indexes of refraction of which were between those of HA and OCP. Its zero-layer Weissenberg pattern from a *c*-axis setting could be indexed on the basis that it contained both salts with the *b* and *c* axes of the HA collinear, respectively, with those of the OCP.

The mean index of refraction of a lamellar mixed crystal should increase roughly in proportion to the HA content, and Posner and Perloff[18] found a nearly linear relationship between the mean index and the ratio Ca : P in their preparations. An exact relationship of this type is unlikely, however, because both non-essential water[19] and the history of the sample have considerable effects on the refractive index. The optical indicatrix does not change in a simple manner with the ratio Ca : P because the mixed crystals are very thin, the OCP component has a pronounced tendency to twin, and the conoscopic figures are rarely visible and are indistinct and composite when they can be seen. Lamellar intra-crystalline mixtures should produce indistinct conoscopic figures when viewed normal to the plate because the direction then is nearly parallel to an optic axis of the OCP component and perpendicular to the optic axis of the HA. On edge view, OCP is optically length slow and HA is length fast. In a lamellar mixture these effects should tend to compensate each other, and the birefringence should be minimum in a crystal containing about two parts of HA and one part of OCP. This mixture would have a mean refractive index of about 1·625, and crystals with indexes near this value show feeble birefringence on edge view.

The lamellar crystals are so thin that the different layers cannot be distinguished under the microscope, so it is not known how many layers are in any given crystal or whether the usual number of layers is large or small. There are two processes by which the lamellar mixed crystals might be formed: one of these, epitaxial overgrowth, might produce crystals with many layers; and the other, hydrolysis, might produce crystals with few layers.

Because of similarities between the structures of HA and OCP (preceding communication), epitaxial overgrowths of one compound on the other should occur easily. Variations in the composition of the liquid phase in the immediate vicinity of a growing crystal, as in a dropwise neutralization, could cause alternate deposition of first one compound and then the other. This type of lamellar growth could result in crystals with many layers.

Hot aqueous solutions cause OCP crystals to hydrolyse to pseudomorphs the properties of which progressively approach those of HA. Crystals produced in this manner may contain few layers, such as a layer of OCP sandwiched between two layers of HA.

It would be difficult to demonstrate that the lamellar mixed crystals can be formed by epitaxial overgrowth alone. OCP hydrolyses so readily to HA, particularly at temperatures above 50° C, that this alteration could be occurring even under conditions where the epitaxial overgrowth mechanism appears predominant.

Hydrolysis of Octacalcium Phosphate. In boiling water the progressive hydrolysis of OCP to HA is reflected in a gradual increase in indexes of refraction. At the same time, the intensities of the OCP lines in the X-ray powder pattern of the residual solids decrease, and after continued boiling the solids give sharp patterns of HA. The Weissenberg pattern of an OCP crystal which had been boiled in water for 6 h showed reflexions from both OCP and HA, with the *b* and *c* axes, respectively, of OCP collinear with those of HA. The pattern of an OCP crystal that had been in boiling water for 72 h, however, was essentially that of HA alone. The reflexions were sharp, and the pattern showed the full hexagonal symmetry of HA, which indicated that there had been considerable re-organization of the lattice during the hydrolysis.

Even after prolonged boiling, the index of refraction of the residue was never higher than 1·635. It then appears either that the hydrolysis is never completed or, more probably, that the resulting pseudomorphs contain fissures that result from incomplete closure of the lattice after loss of water and phosphate ions, and possibly calcium ions. The fissures, which probably are parallel to the (100) face of the original OCP, could be sites of entry and retention of carbonate and other foreign ions in sedimentary phosphorites, hard tissues, and other apatitic materials that may be formed from OCP, and they could also contribute to internal or 'entrapped' surface area[20]. Pseudomorphs formed by hydrolysis of OCP in the presence of carbonate ions give strong tests for carbonate.

Anhydrous dicalcium phosphate (DCPA), $CaHPO_4$, is sometimes formed as a separate phase in the hydrolysis of OCP, in agreement with phase-rule considerations of the system $CaO–P_2O_5–H_2O$ (ref. 21).

Magnesium, even in concentrations as low as 0·001 N, markedly inhibits the hydrolysis of OCP. This inhibition may result from the formation of a magnesium complex on the terminal edges of the crystals that impedes loss of water molecules and ions from channels in the 'water layers' (preceding communication) of the OCP, and may be important in the growth and development of hard tissues.

OCP probably was not the most stable calcium phosphate under any of the conditions of its preparation, even though OCP precipitated in preference to HA and DCPA. The rapid precipitation and subsequent alterations of OCP go far to explain some complications in the chemistry of basic calcium phosphates. As an example, when 3 g of dicalcium phosphate dihydrate, $CaHPO_4.2H_2O$, was added to 100 ml. of distilled water at 85° C with continuous stirring, OCP crystals were observed as a separate phase within 5 min. These crystals grew for about 15 min until the dicalcium phosphate dihydrate nearly disappeared. At about this time, aggregates of extremely fine acicular crystallites of HA appeared, and soon rounding of edges of the OCP crystals indicated that the continued precipitation of HA was maintained by dissolution of OCP. The remaining OCP was converted to apatite, mostly through hydrolysis *in situ*, when the mixture was allowed to cool and stand overnight. Thus, HA apparently was produced by two mechanisms, and its acicular or platey habit showed whether it had been produced by direct precipitation or hydrolysis, respectively. At lower temperatures, conversion of dicalcium phosphate dihydrate to DCPA, rather than formation of HA, appeared to terminate the precipitation of OCP.

Precipitates with low indexes of refraction and with ratios Ca : P near those of OCP usually are relatively large thin blades similar in morphology to OCP. As the compositions and indexes approach those of HA, the typical habit becomes rosette clusters of very small scalar crystals. Precipitates in which the ratio Ca : P was essentially that of HA consisted of stellate clusters of delicate needles and only then did the crystallites have the hexagonal habit of HA.

Apatitic crystallites in bone are present with both scalar and needle habits[22]. The co-existence of crystals of two habits is consistent with the two mechanisms of formation of HA—scalar crystals from partial or complete hydrolysis of OCP (ref. 7), and needle crystals by direct precipitation of HA. There is a possibility, however, that a few layers of OCP in the seeds from which the scalar crystallites developed may have modified the directly precipitating HA into a platey habit. These crystallites, however, are (100) plates and not distortions of the (001) platey habit of HA as has been implied[1].

Reaction of Octacalcium Phosphate with Fluoride. In aqueous systems containing low concentrations of fluoride ion, fluorapatite is the most stable calcium phosphate[23], and OCP is reported to react with fluoride to produce an apatite[24]. It is significant that this reaction also occurs *in situ*, and the resulting crystals are pseudomorphs after the original OCP. In an examination of this reaction, a single crystal of OCP was mounted on an X-ray goniometer and its zero-layer Weissenberg pattern from a c-axis setting was obtained after the crystal had been immersed in 0·1 N sodium fluoride solution at 45° C for different times. Only OCP reflexions were present in the pattern of the untreated crystal; both apatite and OCP reflexions were present in the pattern after 5 h of immersion, and, except for a few very faint OCP reflexions, only apatite reflexions were present in the pattern after 9 h of immersion. The apatite reflexions were less sharp than the OCP reflexions, indicating that the apatite 'crystal' was composed of oriented sub-units. The orientation of the apatite crystallites relative to the original OCP was the same as for the OCP–HA crystals described previously.

The multicrystalline character of the apatite crystal was indicated further by the fact that it fell apart while being handled for optical study. In contrast to dehydrated or hydrolysed OCP crystals, fluoride-treated OCP crystals are very soft and smear easily, and their multicrystalline character implies that they may adsorb or occlude relatively large amounts of impurities. If OCP is present in tooth enamel, fluoride treatment would increase its chemical stability but may decrease its mechanical strength.

When a 1-g sample of OCP was treated with 100 ml. of 0·1 N sodium fluoride solution at 45° C for 7 days, the residue dried at 105° C for 1 h weighed 0·844 g and contained CaO 52·9, P_2O_5 41·2 and fluorine 4·0 per cent. This composition and the loss in weight indicate that the product was an impure fluorapatite (theoretical for $Ca_5(PO_4)_3F$, CaO 55·6, P_2O_5 42·2, fluorine 3·8 per cent). It is probable that the impurities can be attributed to the multicrystalline character noted here. With the same treatment, fine-grained HA took up only 0·4 per cent fluorine, indicating that HA reacts much slower with fluoride than OCP. Similar treatment of materials with compositions between those of HA and OCP caused fluorine uptakes roughly proportional to the OCP contents calculated from the ratios Ca : P. It is concluded that, when a lamellar mixed crystal of HA and OCP is treated with fluoride solution, the resulting crystal is largely fluorapatite interlayered with HA.

Dehydration of octacalcium phosphate. On drying at temperatures slightly above 100° C, OCP loses some of its water of crystallization without apparent change in its X-ray powder diffraction pattern (preceding communication and ref. 3), although the mean refractive index increases slightly. As the drying temperature is raised, the material progressively loses water, the 18·7-Å line of OCP shifts to slightly lower spacings, the OCP lines in the X-ray pattern gradually weaken and disappear at about 180° C, and the refractive index rises to a maximum of 1·61, which is well below that of HA. Except for the 002 line, the powder pattern of material dried at 180° C is very diffuse; it resembles that of a poorly crystallized apatite, and it contains no DCPA lines. The presence of DCPA in a sample heated at 220° C, however, has been detected[7] by X-ray diffraction.

The Weissenberg patterns of a single crystal of OCP which had been dried at 180° C contained diffuse spots which corresponded in position and intensity to those of an apatite. Their positions indicated also that the c axis and $h00$ planes of the apatite were parallel to the corresponding elements, respectively, of the original OCP. Present also were rather sharp reflexions of DCPA the positions of which indicated that the b axis and $00l$ planes of DCPA were parallel to the c axis and $h00$ planes, respectively, of the original OCP.

The patterns also contained diffuse streaks along the reciprocal lattice lines parallel to the reciprocal axis a^* of the original OCP. The streaks indicate the presence in the dehydrated OCP of amorphous, partially oriented, 'collapsed OCP layers' that remain after destruction of 'water layers' (preceding communication) of the OCP lattice. The diffuse streaks showed a two-fold symmetry about the c axis, in keeping with the pseudosymmetry of OCP, the 'apatite layers' of which presumably tend to persist in the collapsed lattice, and not with the hexagonal symmetry of HA. The intensities of the diffuse streaks indicated that the collapsed OCP layers comprised a considerable fraction of the dehydrated crystal.

Since DCPA was detected by the single-crystal method but not by X-ray powder diffraction, it is possible that DCPA has been present and overlooked in many apatitic materials. The strongest line of

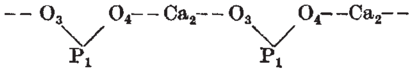
DCPA nearly coincides with the 002 line of HA or OCP which is frequently used to measure the particle size of apatitic material by line broadening. This measurement can be reliable only if DCPA, OCP and collapsed OCP are absent.

Results of previous studies[7] of dehydrated OCP were taken to indicate that the product was a defect apatite. The fact that OCP breaks down on drying into an apatite and DCPA, as shown by the single crystal X-ray investigation, makes it unnecessary to postulate the existence of a defect apatite, and the quasi-amorphous material, collapsed OCP, which is presumed to give rise to the diffuse streaks in the X-ray pattern, cannot properly be called hydroxyapatite.

The reasons for the orientations of the apatite and collapsed OCP relative to the original OCP crystals are apparent from structural considerations. The orientation of the DCPA relative to the original OCP crystal is understandable in terms of the three lattice elements of OCP (preceding communication) and DCPA (ref. 25) that lie in the plane of juncture; these are shown as follows:

OCP	DCPA
$b = 9{\cdot}63$ Å	$a = 6{\cdot}91$ Å
$c = 6{\cdot}88$ Å	$b = 6{\cdot}66$ Å
$\alpha = 89°\ 17'$	$\gamma = 89°\ 11'$

Although the difference between *b* of OCP and *a* of DCPA precludes a normal epitaxy between the two compounds, there is a structural similarity which may orient the DCPA. In the notation of MacLennan and Beevers[26], DCPA has calcium phosphate chains of the type:



$$--\mathrm{O_3}\underset{\mathrm{P_1}}{\vee}\mathrm{O_4}--\mathrm{Ca_2}--\mathrm{O_3}\underset{\mathrm{P_1}}{\vee}\mathrm{O_4}--\mathrm{Ca_2}--$$

that are parallel to the *b* axis. These chains are similar to those parallel to the *c* axes in OCP and HA that involve the 'hexagonal' calciums (preceding communication). The ratio of the length of *b* of HA to that of *a* of DCPA is close to 3/2, which may be conducive to the orientation.

The zero-layer Weissenberg pattern of dehydrated OCP has strong reflexions with *d* values of $3{\cdot}37_5$, 2·70 and 2·25 Å on the central lattice line coinciding with that of the *h*00 reflexions of the original OCP. These spacings coincide almost exactly with the fourth, fifth and sixth orders of a 13·50-Å lattice spacing. This was first interpreted to mean that removal of the water had collapsed the OCP layers so that they had an average spacing of 13·50 Å instead of 18·68 Å as in OCP. It was found, however, that the $3{\cdot}37_5$- and 2·25-Å spacings could be indexed as the 002 and 003 reflexions, respectively, of DCPA, and the 2·70-Å spacing as the 300 reflexion of HA. The closeness of the fit shows that the thickness of the unit cell of HA, d_{100}, is very nearly equal to 5/6 of d_{001} of DCPA. The 002 and 003 reflexions of the DCPA component were relatively strong, and the possibility that some of their intensities arose from collapsed OCP layers with a spacing of 13·50 Å cannot be ignored.

HA and DCPA, the two crystalline phases in dehydrated OCP, are the stable solid phases at the invariant point near the water corner of the system $CaO–P_2O_5–H_2O$. Treatment of dehydrated OCP with boiling water then should cause these phases to increase at the expense of the amorphous phase, and, in accord with this, 6 h of this treatment sharpened the X-ray powder pattern of dehydrated OCP. This treatment of dehydrated OCP may be a method for preparing mixtures of HA and DCPA in which each particle would contain both phases. Such a product would be useful in studies of the uptake of phosphate by plants and in physiological studies because, according to the phase rule, the presence of the second solid phase reduces the number of degrees of freedom by one. We have no evidence of the formation of intracrystalline mixtures of HA and DCPA by direct precipitation or by hydrolysis of OCP; but, in view of the stability of the two solids, such mixtures should be anticipated.

Ignition at 500°–600° C converts DCPA to a pyrophosphate. The net process for OCP, then, could occur according to either of the equations:

$$4[Ca_4H(PO_4)_3 . 2{\cdot}5H_2O] = 2Ca_5OH(PO_4)_3 + 3Ca_2P_2O_7 + 11H_2O \quad (1)$$

$$4[Ca_4H(PO_4)_3 . 2{\cdot}5H_2O] = 4Ca_3(PO_4)_2 + 2Ca_2P_2O_7 + 12H_2O \quad (2)$$

Half the phosphate would be converted to pyrophosphate in the reaction of equation 1, but only a third in that of equation 2. Gee and Deitz[27] determined the pyrophosphate contents of several apatitic preparations with different ratios Ca : P that had been ignited at 600° C for 60 h. The experimental points shown in Fig. 2 of their paper are poorly represented by the line labelled 'equation 4' which corresponds, in effect, to our equation 1. They fall very close, however, to a line defined by the condition that all the OCP in the precipitates reacted according to equation 2. It appears from their results that little of the calcium pyrophosphate produced according to equation 2 reacted at 600° C. with the original HA (that is, in the HA layers) to form more tricalcium phosphate, but that this reaction did occur above 800° C. This behaviour is more readily understandable in terms of crystals which are interlayered than ones in which the acidic groups are distributed homogeneously in the lattice as they should be if the crystals were defect apatites or solid solutions.

Detection of octacalcium phosphate by X-ray diffraction. An unsuccessful attempt was made to use the intensities of the 100 (18·68 Å) and 700 (2·67 Å) lines in the powder pattern of OCP as quantitative measures of the amount of OCP in precipitates of intermediate composition. The intensities of these lines varied irregularly and disproportionately with change in the ratio Ca : P. For example, the pattern of a sample with mole ratio Ca : P of 1·52 contained neither line, whereas the 18·68-Å line was obvious in the pattern of a physical mixture of 5 parts of OCP and 95 parts of HA which had a mole ratio Ca : P of 1·65. Since these lines, which are the strongest lines distinguishing OCP from HA, did not appear in the pattern of a sample that contained about 50 per cent OCP, it is not surprising that OCP is not detected in bones and teeth from their X-ray patterns even if it is present.

The reasons for the faintness of the distinguishing lines of OCP are not far to seek. The lines arise from planes parallel to the platey direction of the crystals, so that the intensities of lines of very thin crystals, such as those in bones and teeth, would be expected to be low. Lamellation and twinning also are parallel to the platey direction, and so decrease further the effective particle thickness. Furthermore, loss of water from OCP crystals may also lower the intensity of the distinguishing lines.

Since X-ray powder methods are not reliable for the detection of OCP in its mixtures in poorly crystallized materials, suitable chemical or physical methods for its detection would be highly advantageous. Such a test might be based on differences in the reactions of OCP and HA with fluoride ions.

Infra-red absorption. Posner, Stutman and Lippincott[13] report infra-red absorption data on synthetic 'calcium-deficient' apatitic materials in which the intensity of the peak at about 3,400 cm^{-1} is inversely proportional to the ratio Ca : P. This relationship is interpreted to indicate that the positive charges of the missing calcium ions are supplied by hydrogen ions that form interphosphate hydrogen bonds in the apatite lattice. Winand, Dallemagne and Duyckaerts[11,16] disagree and state that the frequency of the absorption band is too high to be caused by a hydrogen bond of the type $O_3PO\text{–}H\cdots OPO_3H$; they suggest that the absorption is due to water adsorbed by the crystals.

An alternative explanation, which is consistent with interlayering in these materials, is that the intensity of the infra-red absorption peak is proportional to the amount of OCP in the preparation and so inversely proportional to the ratio Ca : P. Because of its water content, OCP has a broad absorption peak in the 3,400 cm^{-1} region[10].

Winand, Dallemagne and Duyckaerts[11] report a weak absorption at 2,400 cm^{-1} for some of their calcium-deficient apatitic materials. This absorption could be caused by the shortest interphosphate oxygen-to-oxygen distance in OCP which is 2·47 Å (preceding communication). Although these results indicate that the materials studied by Winand and co-workers contained OCP, the 2,400 cm^{-1} peak may have arisen from DCPA. Samples treated in a hydrothermal bomb[16] should not contain OCP, but may contain DCPA and HA.

Causes for low ratios Ca : P. It is apparent that at least two compounds, OCP and DCPA, are difficult to detect by X-ray powder diffraction in the presence of apatite, and each may contribute to low ratios Ca : P in apatitic materials. Collapsed OCP may behave similarly. The present results do not preclude the existence of calcium-deficient or defect apatites, occluded phosphate, solid solutions, or dubious crystalline compounds which have been suggested to explain the observed variations in the ratio Ca : P in apatitic materials, but to a large degree they make it unnecessary to hypothesize the existence of such materials. Surface adsorption certainly influences both the ratio Ca : P and the water content when the crystallites are small, as they are in bone and dentine. The crystals used in this investigation, however, were too large for the external surface to have had a significant effect.

The general formula for the unit-cell contents of calcium-deficient apatites, $Ca_{10-x}(H_3O)_{2x}(PO_4)_6(OH)_2$, given by Neuman and Neuman[6] has for $x > 0$ more atoms than can be contained in the unit cell of HA and, furthermore, is based on a degree of hydration of OCP that appears incorrect. The loss of two molecules of water for each mole of OCP postulated by them is in accord, however, with the reaction:

$$Ca_4H(PO_4)_3 . 2{\cdot}5H_2O = 3/2CaHPO_4 + 1/2Ca_5(PO_4)_3OH + 2H_2O \quad (3)$$

indicated by the single-crystal dehydration experiment described earlier. Dehydration experiments are difficult to interpret because of experimental ambiguity between waters of crystallization of OCP and non-essential water; the variability in the amount of water evolved when OCP is dehydrated, depending on whether the product contains collapsed OCP, HA and DCPA, or $Ca_2P_2O_7$ and $Ca_3(PO_4)_2$; and the uncertainty in the extent of reaction of hydrogen ions of the OCP layers with the hydroxyl ions of the HA layers. These factors prevent placing much reliance on dehydration experiments and probably account in part for the variation in the reported values for the degree of hydration of so-called tricalcium phosphate hydrate[15,20].

A general formula for lamellar mixtures of OCP and HA might be written as $Ca_{10-x}(PO_4)_6(OH)_{2-x}(H)_x . 2{\cdot}5xH_2O$, provided it is not considered to represent an isomorphous series.

The several general formulæ proposed for these materials may be written $(10\text{-}x)CaO . 3P_2O_5 . nH_2O$, where n has the value 1 for the formula of Winand and Dallemagne[16], $(1 + x)$ for that of Stutman, Posner and Lippincott[14], $(1 + 3x)$ for that of Neuman and Neuman[6], and $(1 + 2{\cdot}5x)$ for the one we give above for lamellar mixtures of HA and OCP. In this formula, n includes both water of constitution and water of crystallization, and, in practice, some non-essential water may also be included. The value of n should be obtained, therefore, by difference after accurate analysis for calcium and phosphorus, and not by dehydration. In the foregoing form, the general formula clearly shows the inadequacy of the ratio Ca : P as the sole compositional description of apatitic calcium phosphates.

Crystallographic methods are unlikely to distinguish between HA, OCP, and lamellar mixtures of the two salts when the crystallites are as thin as 25–75 Å as they have been reported for bone[28,29]. These dimensions correspond to no more than five d_{100} thicknesses of OCP. It appears, therefore, that a comparative study of the chemical reactivities and solubilities of HA, OCP and their lamellar mixtures is one of the more promising means for gaining an understanding of the properties of biological and other cryptocrystalline apatitic calcium phosphates.

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SOME POSSIBLE RELATIONSHIPS OF CARBOHYDRATES AND OTHER BIOLOGICAL COMPONENTS WITH THE WATER STRUCTURE AT 37°

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IN two previous publications[1,2] some suggested conformations for polypeptides were discussed based on hexagonal arrangements of the carbonyl oxygens of the peptide bonds. One of the interesting aspects of these suggested hexagonal patterns was the very close correlation with a similar regular hexagonal arrangement of the 'second neighbour' oxygen positions in water at a temperature of about 37°. (My calculations were based on a 'first neighbour' oxygen distance of 2·93 Å at 37° as explained in ref. 2. Later, I found a brief mention by Brady and Krause[3] to a 'first neighbour' oxygen distance of 2·94 Å at 30°. This suggests a value of 2·95 Å at 37°, and would represent a 'second neighbour' oxygen distance of 4·82 Å in liquid water at this temperature, compared with our calculation of 4·79 Å.) Thus, a water layer lying over a peptide layer in this suggested conformation would have the possibilities for exact collinear hydrogen bonding between the respective oxygen atoms of the two layers at this temperature.

In view of these similar dimensions it seemed expedient to examine other biological substrates and see if their reactive groupings also permitted definite interactions with the water structure at about 37°. Because the conformations of the cyclitols have been extensively studied and are well defined, a specific example, *scyllo*-inositol, was selected to serve as a model for some of the interrelations which may exist. Many other substances have been studied in less detail, and I will mention some relevant points about them.

Scyllo-inositol and the water structure. Scyllo-inositol is a hexahydroxy *cyclo*hexane having the all-*trans* conformation with the six hydroxyl groups equatorial[4]. A model of this compound was constructed from the Dreiding stereomodels using the stable chair conformation for the *cyclo*hexane ring. (It was interesting to note that even in the models the boat form of *cyclo*hexane is non-rigid and allows considerable rotation around the bonds between carbons. However, once the model is forced into the chair form, this conformation is very rigid and allows no rotation about the carbon–carbon bonds. Only the hydroxyl hydrogens can rotate around the C–O axis.) The conformation of *scyllo*-inositol is given in Fig. 1. Measurements made on such a model indicate that the oxygen atoms 1, 3 and 5 form the corners of an equilateral triangle with sides which measure about 4·86 ± 0·02 Å on the Dreiding scale. This oxygen pattern has, therefore, approximately the same dimensions as the pattern formed by three 'second neighbour' oxygen atoms in the water structure at 37° (4·82 Å on a side). In a similar manner oxygen atoms 2, 4 and 6 form an equilateral triangle of the same dimensions.

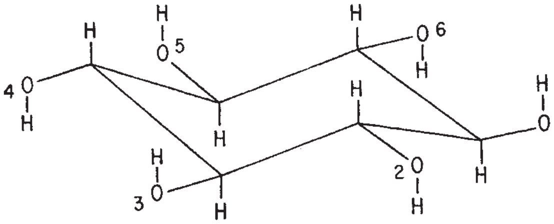

Fig. 1. *Scyllo*-inositol

The six oxygen atoms of *scyllo*-inositol when joined by imaginary lines are observed to have the conformation of a chair. At first glance, it might be presumed that the six positions would duplicate one of the hexagonal chair arrangements of six 'nearest neighbours' in the water structure[2]. However, more accurate measurement of the adjacent oxygens in *scyllo*-inositol (for example, oxygens 1 and 2) indicates that they are about 2·82 ± 0·02 Å apart compared with 2·94 ± 0·01 Å between 'nearest neighbour' oxygens in water at 37°. It was further observed that the respective 1–3–5 and 2–4–6 oxygen planes in *scyllo*-inositol are only about 0·48 Å apart, while the corresponding 'second neighbour' planes in water would be about 0·98 Å apart at 37° (Fig. 2, layers *C–D*, for example). The shorter distance between the oxygen layers in inositol and other sugars may bear some relation to the frequent occurrence of these compounds in nature as phosphate or sulphate esters; and the possibility should be kept in mind that the accommodation of these larger atoms into the water structure could require molecules with some alterations in the attaching positions to fit them into a possible stabilizing water pattern.

These possible interactions of inositols (and other sugars such as α- and β-D-glucose) with the water structure, especially with the 'second neighbour' pattern at 37°, indicate that such carbohydrates or their polymers could also interact in an orderly manner with peptide (or protein) layers arranged in