year. The soil is unreduced, and saturated with H_2O in the outermost layers of the grains. The hydrogen desorbs in the form of H_2O with a mean surface density of 1.6×10^6 cm^{-3}. (iii) $R > 650$ Å per year. The soil is unreduced and unsaturated with H_2O. The atmosphere will not be derived from the solar wind, but will consist of products of meteoroid volatilization.

If model ii prevailed on Mercury for a significant period in its history, ice could have accumulated in the polar regions in permanently shaded areas, as suggested for the moon by Watson *et al.* (*16*). Furthermore, if stirring of the soil layers were dominant, the equivalent of about a meter in depth of unreduced metals would be distributed within the regolith. This "smelting" process due to the combined action of solar heating and solar wind reduction would occur for any large bodies in the inner solar system. It has been suggested that the moon may have originally formed in this region (*17*) and later been captured by the earth. If so, the presence of pure metals at large depths in the lunar regolith would strengthen arguments for the moon's origin as a twin of Mercury.

Ultraviolet measurements from the Mariner 10 flyby of Mercury in March 1974 should provide definitive evidence of the present existence of H_2O in its atmosphere. The Lyman-alpha (1216 Å) channel will measure the scattered light from atomic hydrogen produced by photodissociation from both H_2 and H_2O. Knowledge of the scale height and intensity of the dayglow emission will lead to the identification of a photodissociation component and its parent molecule. If planetary outgassing is unimportant and the atmosphere is indeed a minimum atmosphere, these results will determine which of the three regimes is the best description and thus provide useful bounds on the present surface erosion rate.

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Stimulation of 24,25-Dihydroxyvitamin D_3 Production by 1,25-Dihydroxyvitamin D_3

Abstract. *Vitamin D–deficient rats produce [^{3}H]1,25-dihydroxyvitamin D_3 from [^{3}H]25-hydroxyvitamin D_3 regardless of dietary content of calcium or phosphate. A daily dose of 130 picomoles of 1,25-dihydroxyvitamin D_3 for a period of 5 days reduces production of [^{3}H]1,25-dihydroxyvitamin D_3 to essentially zero and stimulates production of [^{3}H]24,25-dihydroxyvitamin D_3. A daily dose of 325 picomoles of 25-hydroxyvitamin D_3 has a similar but less dramatic effect. On the other hand, 650 picomoles daily of 24,25-dihydroxyvitamin D_3 given to vitamin D–deficient rats had no effect. Thus it appears that 1,25-dihydroxyvitamin D_3 is an important factor in the regulation of kidney metabolism of 25-hydroxyvitamin D_3.*

There is strong evidence that 1,25-dihydroxyvitamin D_3 [1,25-$(OH)_2$-D_3] represents a metabolically active form of vitamin D in the stimulation of intestinal calcium transport and bone calcium mobilization (*1*). Its production in the kidney is strongly regulated in a complex manner by serum calcium (*2*), parathyroid hormone (*3*), and serum inorganic phosphorus concentrations (*4*). It has been suggested that hypocalcemia results in parathyroid secretion which in turn stimulates production of 1,25-$(OH)_2$-D_3. Hypophosphatemia, which results from low dietary phosphorus, also stimulates 1,25-$(OH)_2$-D_3 production (*4*). Generally, when 1,25-$(OH)_2$-D_3 production is diminished, 24,25-dihydroxyvitamin D_3 [24,25-$(OH)_2$-D_3] production is increased (*2*). However, in vitamin D–deficient rats or chicks only 1,25-$(OH)_2$-D_3 is produced regardless of dietary content and serum concentrations of calcium and phosphorus (*2, 3*). The present report emphasizes that vitamin D–deficient rats produce [^{3}H]-1,25-$(OH)_2$-D_3 from [^{3}H]25-OH-D_3 regardless of dietary contents of calcium and phosphorus and further demonstrates that 1,25-$(OH)_2$-D_3 inhibits [^{3}H]1,25-$(OH)_2$-D_3 production in vitamin D–deficient rats and stimulates the production of [^{3}H]24,25-$(OH)_2$-D_3.

Weanling male rats (Holtzman) were fed a vitamin D–deficient diet that contained either 0.02 percent calcium and 0.3 percent phosphorus (low calcium–adequate phosphorus), 1.2 percent calcium and 0.1 percent phosphorus (high calcium–low phosphorus), or 1.2 percent calcium and 0.3 percent phosphorus (high calcium–adequate phosphorus) (*5*). The diet and water were given without restriction for 2 weeks. At the end of 2 weeks the rats were given, intraperitoneally, either 325 pmole of 25-hydroxyvitamin D_3 (25-OH-D_3) (*6*), 650 pmole of 24,25-$(OH)_2$-D_3, or 130 pmole of 1,25-$(OH)_2$-D_3 dissolved in 0.1 ml of ethanol every day for 5 days. The control group received the ethanol vehicle in the same manner.

After the 5 days of treatment, 325 pmole of 25-[26,27-^{3}H]OH-D_3 dissolved in 0.05 ml of ethanol was given intrajugularly to all rats. Twelve hours later the rats were killed and their blood was collected to yield serum. A portion of the serum was used for the determination of inorganic phosphorus by the colorimetric assay (*7*) and an-

other portion was used for the determination of calcium in the presence of 0.1 percent $LaCl_3$ by using a Perkin-Elmer model 403 atomic absorption spectrometer. The remaining serum was extracted with chloroform and methanol (*8*). The chloroform-soluble fraction was chromatographed on columns (2 by 10 cm) of Sephadex LH-20 by using a solvent system of a mixture of chloroform and Skellysolve B (65 : 35 by volume) (*9*). Fractions of column effluents (5.5 ml) were dried and added to a toluene counting solution (*10*). The radioactivity was determined in a Packard liquid scintillation counter model 3375.

Vitamin D–deficient rats convert [^{3}H]25-OH-D_3 in vivo to [^{3}H]1,25-$(OH)_2$-D_3 while converting little or none to [^{3}H]24,25-$(OH)_2$-D_3 regardless of dietary contents of and serum concentrations of calcium and phosphorus (Fig. 1; Table 1). This has been emphasized before in both chicks and rats and confirmed in the present study. Administration of 1,25-$(OH)_2$-D_3 each day for 5 days almost completely eliminates the ability of animals to make [^{3}H]1,25-$(OH)_2$-D_3 and instead markedly stimulates production of [^{3}H]24,25-$(OH)_2$-D_3 from [^{3}H]25-OH-D_3. Only in animals on a low calcium diet does some ability to produce [^{3}H]1,25-$(OH)_2$-D_3 remain. Even under conditions of hypophosphatemia, the 1,25-$(OH)_2$-D_3 administration turns off synthesis of [^{3}H]1,25-$(OH)_2$-D_3 and stimulates that of [^{3}H]24,25-$(OH)_2$-D_3. Since in vitamin D–deficient animals 25-OH-D_3 is metabolized to 1,25-$(OH)_2$-D_3, administration of 25-OH-D_3, as might be expected, produces similar but less dramatic results (Fig. 1). On the other hand, 24,25-$(OH)_2$-D_3 at doses which produce

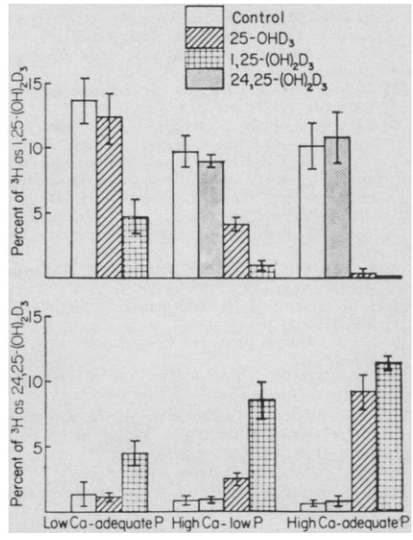

Fig. 1. Effect of vitamin D metabolites on conversion of [^{3}H]25-OH-D_3 to [^{3}H]1,25-$(OH)_2$-D_3 and [^{3}H]24,25-$(OH)_2$-D_3 in vivo. Rats were fed a low calcium (0.02 percent)–adequate phosphorus (0.3 percent), high calcium (1.2 percent)–low phosphorus (0.1 percent), or high calcium (1.2 percent)–adequate phosphorus (0.3 percent) diet for 2 weeks and then given either 325 pmole of 25-OH-D_3, 650 pmole 24,25-$(OH)_2$-D_3, 130 pmole 1,25-$(OH)_2$-D_3, or the ethanol vehicle alone every day for 5 days. After 5 days of treatment, 325 pmole of 25-[26,27-^{3}H]-OH-D_3 was given to all the rats. Twelve hours later the rats were killed and chromatographic analyses of their serum was carried out as described in the text. The number of rats in each group and the serum concentrations of calcium and phosphorus are shown in Table 1. The values show the percentage of the total radioactivity recovered from the columns as the indicated metabolite. The standard error of the mean is shown at the top of each vertical bar.

physiologic responses (*11*) had no effect on the conversion of [^{3}H]25-OH-D_3 to [^{3}H]1,25-$(OH)_2$-D_3. Thus 24,-25-$(OH)_2$-D_3 and its metabolites do not appear capable of exerting a regulatory effect on the kidney hydroxylation reactions.

It might be speculated that the apparent regulation exerted by 1,25-$(OH)_2$-D_3 may result from changes in plasma calcium or phosphorus (*2–4*). However, the data in Table 1 show, especially with the high calcium–adequate phosphorus diet, that the changes in hydroxylation as a result of metabolite administration occur without significant change in plasma calcium and phosphorus concentrations.

In viewing the data on plasma calcium and phosphorus, it must be kept in mind that the column designated as control represents the vitamin D–deficient animals that had received [^{3}H]-25-OH-D_3 12 hours before. Thus the serum calcium values of 6.0 represent a response to the [^{3}H]25-OH-D_3 from a deficiency level of 4.5.

The present results show that, in addition to parathyroid hormone and hypophosphatemia, 1,25-$(OH)_2$-D_3 itself plays an important role in regulating biosynthesis of 1,25-$(OH)_2$-D_3 and 24,25-$(OH)_2$-D_3. In fact, it is possible that 1,25-$(OH)_2$-D_3 may induce 25-OH-D_3-24-hydroxylase in the kidney.

The molecular mechanism whereby the 25-OH-D_3 hydroxylases of kidney are regulated remains unknown. However, it seems clear that the 25-OH-D_3-1-hydroxylase is always present in vitamin D deficiency and it seems likely that the 1,25-$(OH)_2$-D_3 must be present before other factors, such as inor-

Table 1. Serum calcium and phosphorus values in rats used for study of the production of [^{3}H]1,25-$(OH)_2$-D_3 and [^{3}H]24,25-$(OH)_2$-D_3 shown in Fig. 1. Controls are vitamin D–deficient animals that received 325 pmole of [^{3}H]25-OH-D_3 12 hours before the blood samples were taken. All values are expressed as milligrams per 100 ml of plasma ± the standard error of the mean. Numbers in parentheses indicate the number of rats.

Diet		Pretreatment			
		Control	1,25-$(OH)_2$-D_3	25-OH-D_3	24,25-$(OH)_2$-D_3
Low calcium–adequate phosphorus	Calcium	6.0 ± 0.4 (5)	6.4 ± 0.3 (5)	6.5 ± 0.2 (5)	
	Phosphorus	9.5 ± 0.4	9.4 ± 0.6	10.7 ± 0.6	
High calcium–low phosphorus	Calcium	11.1 ± 0.2 (4)	11.9 ± 0.3 (5)	11.0 ± 0.3 (6)	10.7 ± 0.5 (3)
	Phosphorus	3.4 ± 0.4	6.0 ± 1.2	6.5 ± 0.8	3.0 ± 0.8
High calcium–adequate phosphorus	Calcium	10.9 ± 0.7 (4)	11.2 ± 0.4 (5)	11.6 ± 0.4 (4)	11.0 ± 0.5 (3)
	Phosphorus	11.4 ± 0.7	10.4 ± 0.6	10.0 ± 0.7	11.5 ± 0.5

ganic phosphate or parathyroid hormone, can effect a change from the 1-hydroxylation system to the 24-hydroxylation system. Because this changeover is slow (*3, 4*), requiring days, it seems possible that new enzyme synthesis and enzyme turnover are involved.

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Collagen Polymorphism: Characterization of Molecules with the Chain Composition $[\alpha 1(III)]_3$ in Human Tissues

Abstract. *Collagen molecules with the chain composition* $[\alpha 1(III)]_3$ *have been isolated from pepsin-solubilized collagen of dermis, aorta, and leiomyoma of the uterus by differential salt precipitation. On denaturation, approximately 90 percent of this collagen is recovered as a* γ *component (300,000 daltons). Reduction and alkylation of the high-molecular-weight component yields* $\alpha 1(III)$ *chains (95,000 daltons). In addition to containing cysteine,* $\alpha 1(III)$ *chains exhibit several other compositional differences when compared to* $\alpha 1(I)$, $\alpha 1(II)$, *or* $\alpha 2$ *chains from human tissues.*

The majority of the triple-stranded collagen molecules in several connective tissues such as bone, mature dermis, tendon, and dentin contain two distinct α chains. These chains, $\alpha 1(I)$ and $\alpha 2$, occur in this type of molecule in a ratio of 2 to 1; that is, the chain composition is $[\alpha 1(I)]_2\alpha 2$ (*1*).

In contrast, cartilage collagen is comprised almost entirely of molecules containing three identical α chains, which differ from $\alpha 1(I)$ and $\alpha 2$ chains with respect to amino acid composition and sequence as well as to the content of hydroxylysine-linked carbohydrate. These identical chains have been designated $\alpha 1(II)$ chains (*2*). The predominance of collagen molecules with the chain composition $[\alpha 1(II)]_3$ has been established for several cartilaginous structures in a number of species (*3–5*).

In addition, evidence has been presented for the occurrence of yet another genetically distinct α chain in interstitial collagens. This chain, designated $\alpha 1(III)$, has heretofore been detected only in the form of two cyanogen bromide peptides derived from insoluble collagen of infant dermis (*6*). We report here the isolation of collagen molecules with the chain composition $[\alpha 1(III)]_3$, with the amino acid composition of $\alpha 1(III)$, and indicate some of the tissues in which this type of molecule occurs.

Samples of skin, aortic arch, and thoracic aorta were obtained postmortem from both premature and normal infants who had died from respiratory complications. Uterine leiomyoma was obtained from several cases at surgery. Samples of skin, vascular tissue, and leiomyoma were pooled, cleaned of adhering tissue, and sliced into small pieces approximately 1 mm^3 in size. Each sample was extracted for 4 days at 4°C in 100 volumes of 1.0*M* NaCl containing 0.05*M* tris-HCl, *p*H 7.5, and for an additional 4 days at 4°C in 100 volumes of 0.5*M* acetic acid. As indicated previously, these solvents were capable of solubilizing a portion of the collagen in infant skin (*7*); however, none of the vessel or leiomyoma collagen was brought into solution.

After the extraction procedures, the tissues were lyophilized and portions (1 g) were stirred in 0.5*M* acetic acid containing pepsin as described for cartilage collagen (*8*). Collagen rendered soluble by incubation of the tissues with pepsin was precipitated from the digestion mixture by the addition of NaCl to a concentration of 0.9*M*. The precipitates were redissolved in 1.0*M* NaCl, 0.05*M* tris, *p*H 7.5, and dialyzed exhaustively against 0.5*M* acetic acid at 4°C and lyophilized. The proportion of original tissue collagen recovered as soluble native collagen by this procedure was 65, 55, and 20 percent for skin, leiomyoma, and vessel, respectively.

Collagen samples were redissolved at a concentration of 5 mg/ml in 0.02*M* (Na^+) sodium acetate, *p*H 4.8, containing 1.0*M* urea, denatured by warming to 45°C for 30 minutes, and chromatographed on a column (1.8 by 10 cm) of carboxymethylcellulose as described for cartilage collagen (*4, 8*). A representative elution pattern (Fig. 1A) indicates the presence of three major peaks which were identified as containing $\alpha 1(I)$, $\alpha 1(III)$, and $\alpha 2$ chains by examination of the cyanogen bromide peptide pattern obtained from the material in each peak (*6*). Although Fig. 1A depicts the elution pattern of collagen from leiomyoma, collagen from the vascular tissue and dermis showed the same pattern. Some heterogeneity was observed in each peak, and this may be ascribed to chemical heterogeneity introduced by the activity of pepsin as well as to the presence of a small amount of β_{12} cochromatographing with $\alpha 1(III)$.

The above results suggesting that pepsin-solubilized collagen from these tissues is comprised of a mixture of molecules with the chain compositions $[\alpha 1(I)]_2\alpha 2$ and $[\alpha 1(III)]_3$ were confirmed by the use of differential salt precipitation similar to the technique used to fractionate mixtures of $[\alpha 1(I)]_2$-$\alpha 2$ and $[\alpha 1(II)]_3$ molecules (*9*). For this purpose, the collagen samples were redissolved at 4°C in 1.0*M* NaCl, 0.05*M* tris, *p*H 7.5; and the NaCl concentration was increased in successive steps by 0.1*M* over the range 1.1 to 3.0*M*. Utilizing this procedure we ob-