ciples in the inhibitor fraction have been purified. However, the alkali treatment known to destroy ACI inhibition of adenylate cyclase (*8*) destroys all the biologic effects we describe. Although it is possible that the demonstrated effects are nonspecific, ACI itself had no major effect on basal cardiac contractility and calcium exerted its normal inotropic effect. It seems unlikely, therefore, that nonspecific effects on membranes or other tissue components are responsible for the observations described.

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First Occurrence of the Garnet-Ilmenite Transition in Silicates

Abstract. *Pyrope garnet ($Mg_3Al_2Si_3O_{12}$) has been found to transform to an ilmenite-type phase at a loading pressure between 240 and 250 kilobars and at about 1000° to 1400°C in a diamond-anvil press coupled with laser heating. The lattice parameters for the ilmenite-type phase of $(Mg_{.75}Al_{.25})(Si_{.75}Al_{.25})O_3$ are $a_0 = 4.755 \pm 0.002$ and $c_0 = 13.360 \pm 0.005$ angstroms. The zero-pressure volume change associated with the garnet-ilmenite transition is calculated to be −7.1 percent. This result verifies the prediction that pyrope garnet would transform to the ilmenite structure at high pressure first suggested in 1962 by Clark* et al. *and Ringwood.*

Ferromagnesian garnet $(Mg,Fe)_3$-$Al_2Si_3O_{12}$, especially the magnesium-rich variety, is an important mineral in the earth's upper mantle. Accordingly, studies of phase transformations of pyrope garnet ($Mg_3Al_2Si_3O_{12}$ or $3MgSiO_3 \cdot Al_2O_3$) at high pressure have an important implication for our understanding of the earth's transition zone and the lower mantle.

Table 1. X-ray diffraction data (room temperature and 1-bar pressure) for the ilmenite-type phase of $MgSiO_3 \cdot \frac{1}{3}Al_2O_3$ quenched from a loading pressure of about 300 kbar and temperature of 1000° to 1400°C of pyrope-garnet ($Mg_3Al_2Si_3O_{12}$) with CoK_α radiation; obs, observed; cal, calculated.

I/I_{100}*	d_{obs} (Å)	d_{cal} (Å)†	*hkl*
5	4.46	4.45	003
85	3.51	3.51	012
10	2.98		‡
95	2.592	2.594	104
5	2.48		‡
15b	2.44		‡
40	2.380	2.378	110
100	2.097	2.097	113
< 5	1.93		‡
< 5	1.86		‡
40	1.752	1.753	024
15	1.723		‡
90	1.623	1.625	116
5	1.546	1.548	018
		1.546	211
5	1.518	1.516	122
35	1.410	1.411	214
5	1.392		‡
45	1.373	1.373	030
5	1.269	1.271	1, 0, 10
5	1.258	1.259	119
5	1.188	1.189	220
< 5	1.12	1.126	312
		1.121	0, 2, 10
10	1.080	1.081	134
20	1.049	1.050	315
		1.049	226
10	1.013	1.017	042
		1.014	2, 1, 10
		1.008	1, 1, 12
10	0.9570	0.9575	1, 2, 11
5	0.9430	0.9427	318

*Estimated visually; "b" denotes broad line. †Calculated from a hexagonal lattice cell with $a_0 = 4.755$ and $c_0 = 13.360$ Å. ‡Corresponding to the lines for the orthorhombic perovskite modification.

Clark *et al.* (*1*) and Boyd (*2*) have suggested that pyrope garnet might transform to an ilmenite-type structure at high pressures. This parallels the suggestion by Ringwood (*3*) that the ilmenite-type phase of $MgSiO_3$ would probably display extensive solid solution with Al_2O_3 (corundum, a disordered ilmenite structure in which the cations are identical).

Ringwood and Major (*4*) investigated the system $Mg_3Al_2Ge_3O_{12}$–$Mg_3Al_2Si_3O_{12}$ to 170 kbar at 1000°C in attempting to establish the garnet-ilmenite transition. They observed a series of ilmenite-type solid solutions containing up to 20 mole percent $Mg_3Al_2Si_3O_{12}$. Extrapolation of phase boundaries suggests that pressures of 200 to 300 kbar would be required to transform pyrope to an ilmenite structure (*5*).

I have previously reported that pyrope garnet disproportionates into a mixture of the orthorhombic perovskite phase of $MgSiO_3$ plus Al_2O_3 (corundum) at loading pressures greater than 300 kbar and at about 800° to 1200°C (*6*). Since the zero-pressure density for the assemblage $MgSiO_3$ (perovskite) plus Al_2O_3 is greater than the estimated density for the ilmenite modification with the pyrope composition, it is expected that the pyrope garnet-ilmenite transition, if one exists, should take place before the pyrope garnet breaks down to the assemblage perovskite plus corundum.

Kawai *et al.* (*7*) synthesized a hexagonal form of $MgSiO_3$, which was later confirmed as the ilmenite-type structure by me (*8*). Success in synthesizing the ilmenite-type phase of $MgSiO_3$ would lend considerable support to the possibility of pyrope garnet transforming to the ilmenite structure, representing a solid solution between $MgSiO_3$ (ilmenite) and Al_2O_3 (corundum) at high pressure.

In the present work, I have made eight experimental studies of pyrope glass in the loading pressure region between 100 and 300 kbar and temperature of about 1000° to 1400°C. Very fine powder of the glass form of $3MgSiO_3 \cdot Al_2O_3$, which was provided by A. Major (Australian National University), was intimately mixed with a few percent of graphite as the starting material. The graphite serves to absorb the laser irradiation and thus heats the sample while under compression. The sample so prepared was compressed in a diamond-anvil press fitted with a lever-and-spring type assembly and heated by a continuous YAG laser while the sample was maintained at pressure. The recovered samples were studied by a powder x-ray diffraction technique with a modified 57.3-mm Debye-Scherrer camera. Details of the experimental procedure have been described elsewhere (*9*).

In the pressure region between 100 and 240 kbar (inclusive), the glass crystallized completely to pyrope garnet. However, at 250 kbar, the x-ray diffraction film showed the presence of about 30 percent of a new phase possessing the ilmenite-type structure, the remaining 70 percent consisting of pyrope. At 290 kbar, a nearly pure ilmenite-type phase of $MgSiO_3 \cdot \frac{1}{3}Al_2O_3$ or $(Mg_{.75}Al_{.25})(Si_{.75}Al_{.25})O_3$ has been observed. The aluminum is probably distributed between the magnesium and the silicon sites equally, unless there is magnesium silicon disorder, which seems unlikely. The x-ray diffraction data for the ilmenite phase of $MgSiO_3 \cdot \frac{1}{3}Al_2O_3$ obtained at about 300 kbar are listed in Table 1. A least-squares fit of *d*-spacings yields lattice parameters of $a_0 = 4.755 \pm 0.002$ and $c_0 = 13.360 \pm 0.005$ Å for the hexagonal cell of the ilmenite structure. The relative intensities listed in Table 1 are very similar to those of the ilmenite-type phase of $MgSiO_3$ and Al_2O_3, and the characteristics of reflection extinctions are consistent with the space group ($R\bar{3}$) of the ilmenite structure. The molar volume for the ilmenite phase is thus calculated to be 26.26 ± 0.03 cm^3/mole. It is inferred that the garnet-ilmenite transition of $Mg_3Al_2Si_3O_{12}$ occurs at loading pressures between 240 and 250 kbar and at 1000° to 1400°C. The zero-pressure volume change associated with the garnet-ilmenite transition of $3MgSiO_3 \cdot Al_2O_3$ is -8.08 cm^3/mole, or -7.1 percent.

It would be of great interest to compare the observed lattice parameters and the molar volume of the ilmenite-type phase of $MgSiO_3 \cdot \frac{1}{3}Al_2O_3$ with those of the ilmenite-type phase of $MgSiO_3$ and Al_2O_3. The *a*-axis for the ilmenite-type phase in this work is 0.47 percent greater than the value for an ideal solid solution between $MgSiO_3$ (ilmenite) and Al_2O_3 (corundum), the *c*-axis is 0.45 percent smaller than ideal, and the volume is 0.48 percent greater than ideal.

From Table 1, it is also seen that the orthorhombic perovskite modification of pyrope-garnet starts to appear at a loading pressure of about 300 kbar. In an earlier study (*6*), I have reported that pyrope-garnet disproportionates into a mixture of $MgSiO_3$ (perovskite modification) plus Al_2O_3 (corundum) at pressures greater than 300 kbar. In view of the similarity between the x-ray diffraction patterns of Al_2O_3 (corundum) and $MgSiO_3 \cdot \frac{1}{3}Al_2O_3$ (ilmenite), the previously observed Al_2O_3 (corundum) in pyrope-garnet might be residual ilmenite ($MgSiO_3 \cdot \frac{1}{3}Al_2O_3$) reported in this work. The evidence that the *d*-spacings and the characteristics of reflection extinctions for the perovskite phase observed in pyrope-garnet differ from those for the pure $MgSiO_3$ (*10*) supports the conclusion that a substantial amount of Al_2O_3, if not all of that of the pyrope composition, is accommodated in the orthorhombic perovskite lattice. The synthesis of the orthorhombic perovskite phase of $ScAlO_3$ at high pressure (*11*) also lends considerable support to the above conclusion. Thus, the ilmenite phase of $MgSiO_3 \cdot \frac{1}{3}Al_2O_3$ may transform directly to a single phase possessing the orthorhombic perovskite structure, instead of a mixture of $MgSiO_3$ (perovskite modification) plus Al_2O_3 (corundum).

Recovered samples from shock-wave studies on iron-rich garnets have been reported to be an orthorhombic modification of the ilmenite structure (*12*). However, the x-ray diffraction pattern of that work was interpreted by me (*13*) as a mixture of several intermediate high-pressure phases of iron-rich garnets on the basis of static high-pressure studies. Furthermore, the ilmenite-like phase for iron-rich silicates has not yet been observed in any of the static high-pressure experiments (*14*).

Results of this study indicate that pyrope garnet in the upper mantle would persist through the transition zone (400 to 650 km), and then transform to the ilmenite structure in the upper part of the lower mantle, and ultimately transform to the orthorhombic perovskite phase. In conjunction with the orthorhombic perovskite phases developed by olivine and pyroxene (*10*, *15*) these results strongly suggest that the earth's lower mantle comprises mainly perovskite phases of ferromagnesian silicates.

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Reduced Warfarin Binding of Albumin Variants

Abstract. *Binding studies of albumins A/A and A/Me from human plasma and isolated albumin revealed small, but statistically significant, reductions in warfarin binding of albumin A/Me compared to albumin A/A. Such differences in binding in vitro could result in altered pharmacological responses to warfarin administered to individuals possessing albumin A/Me. To determine if clinically significant differences in warfarin distribution exist, observations should be made in vivo on patients of different albumin phenotype who are receiving warfarin therapeutically.*

Normal subjects exhibit large interindividual variations in the disposition of several commonly used drugs, due mainly to genetically controlled differences in rates of drug metabolism (*1*). This conclusion, based on twin and family studies performed under basal conditions, revealed that environmental factors contribute surprisingly little to the maintenance of these large variations between individuals that range in magnitude from 3- to 30-fold, depending on the drug and the population. However, basal rates of drug disposition are readily altered by nu-