main stem branches, and lobar and lobular subdivisions of the pulmonary artery, which indicates that the site of increased vascular resistance is distal to large pulmonary arteries. It thus seems clear that PACS produces vasoconstriction of small, precapillary (arteriolar) branches of the pulmonary artery.

The relationship of PACS to other substances capable of pulmonary pressor activity is of importance. Preliminary studies on the isolation of the pressor material indicate that full activity is retained after filtration through 5-μ Millipore filters and therefore the active principle of PACS must be smaller than 5 μ in diameter. Treatment of the washings in an ultrafiltration apparatus results in essentially all of the activity being retained on the inside of the filtration membrane. Apparently the diameter of active material is greater than 50 Å. From these studies it is clear that the substance involved is not any previously described species of relatively small molecular weight. Likewise, the mode of action of PACS differs from that of other agents previously investigated for pulmonary pressor activity (histamine, serotonin, bradykinin, adenosine triphosphate, epinephrine, and norepinephrine) in its relatively slow onset of action, its prolonged effect, and its ability to produce brisk pulmonary hypertension without profound effect on cardiac output, blood oxygen tensions, heart rate, or systolic blood pressure.

The ability of PACS to evoke pulmonary vasoconstriction in the calf as well as in the dog is likewise of importance. This observation indicates that the pressor activity does not result from an unusual allergic response produced by the injection of PACS. It likewise suggests that PACS may be of broad comparative physiologic importance, since it is active in species of two different orders of mammals.

It may be of interest to speculate on a possible relationship between hypoxia and the elaboration of PACS. It is generally accepted that hypoxia does produce pulmonary vasoconstriction (*1, 2*). Hypoxemic pulmonary vasoconstriction occurs in the isolated lung, and is evoked in the face of high oxygen tension, by agents such as CN^- and dinitrophenol which disrupt oxidative metabolism (*1, 9*). Both findings are consistent with a humoral mechanism for hypoxic pulmonary vasoconstriction. Although not universally accepted, the bulk of evidence favors a precapillary location as the likely site of hypoxic pulmonary vasoconstriction (*1*).

There are several lines of indirect evidence that the elaboration of PACS might be related to local pulmonary hypoxia. The demonstration of PACS in the young calf, an animal with a brisk vasoconstrictive response to hypoxia, is suggestive. The fact that the experimental conditions under which PACS is obtained were invariably associated with hypoxemia and pulmonary hypertension is likewise suggestive. The ability of PACS to produce specific precapillary pulmonary vasoconstriction resembles the pattern of pulmonary vasoconstriction produced by hypoxia. The saline solution used to obtain PACS was equilibrated with approximately 100 percent N_2. This was done as a possible approach to increasing the yield of PACS should it prove that the elaboration of PACS was directly related to hypoxemia. Since filling the lung with saline in vivo is associated with deficient O_2 exchange, it is not possible to state in absolute fashion that PACS was elaborated in response to hypoxemia. Nor was the question answered by studies in which the saline was equilibrated with 100 percent O_2 rather than 100 percent N_2. Even with the saline at a pO_2 of 760 mm-Hg, arterial hypoxia and pulmonary hypertension developed. The precise relationship between hypoxia and PACS may possibly be clarified by studies of the elaboration of PACS under hyperbaric conditions.

The precise role of PACS in the physiological regulation of the pulmonary circulation and its relationship to hypoxia will require chemical isolation of the substance involved.

EUGENE D. ROBIN
CARROLL E. CROSS
J. EUGENE MILLEN
H. VICTOR MURDAUGH, JR.
Department of Medicine, University of Pittsburgh Medical School, Pittsburgh, Pennsylvania 15213

References and Notes

1. A. Fishman, *Physiol. Rev.* **41**, 214 (1961).
2. D. Aviado, *Pharmacol. Rev.* **12**, 159 (1960).
3. The term "agent," as used in the title and abstract, is convenient and is used in a descriptive and not a chemical sense. Until the chemical species involved is isolated it is not possible to be certain that one is dealing with a single agent. For similar reasons, the term "PACS" is employed to describe what is essentially the physiological activity of a saline washing which undoubtedly contains many different chemical species. However, there is an acceptable scientific precedent for such terminology. The term "renin" was used prior to chemical characterization to describe a pressor substance obtained from kidney tissue.
4. H. Hellems, F. Haynes, L. Dexter, *J. Appl. Physiol.* **2**, 24 (1949).
5. We are grateful to Dr. Klaus M. Bron, University of Pittsburgh Medical School, for performing the angiographic studies.
6. Pulmonary vascular resistance (PVR) is actually equal to [PAP (mean) minus left atrial pressure (mean)] ÷ cardiac output. In the present studies measurements of left atrial pressure were not obtained and pulmonary capillary ("PC") pressures were not measured in all animals. Therefore, PVR was approximated as the ratio of PAP (mean) to cardiac output. Since there was no significant change in "PC' pressure, this approximation appears to be acceptable.
7. We are grateful to Dr. Robert S. Totten, University of Pittsburgh Medical School, for performing the pathological studies.
8. D. F. J. Halmagyi, B. Starzecki, J. McRae, G. J. Horner, *J. Surg. Res.* **3**, 418 (1963); S. M. Sabesin, *Amer. J. Pathol.* **44**, 889 (1964).
9. E. Bergofsky, B. Bass, R. Ferretti, A. Fishman, *J. Clin. Invest.* **42**, 1201 (1963); T. Lloyd, *J. Appl. Physiol.* **20**, 488 (1965).
10. Supported in part by PHS grant H-0559 and in part by a grant from the Tuberculosis League of Pittsburgh.

20 March 1967

Geochemical Evidence of Present-Day Serpentinization

Abstract. *Ultrabasic (pH > 11) water issues from some fresh ultramafic bodies. The properties of the ultrabasic solutions are believed to be due to current reactions yielding serpentine from primary olivines and pyroxenes. The low concentrations of divalent iron, divalent magnesium, and dissolved silica from the serpentinization require an increase in rock volume.*

Structural relations and the absence of metamorphic aureoles indicate that many ultramafic bodies of the alpine type have reached their present positions through cold intrusion in tectonically mobile belts. The ubiquitous alteration of the original olivine and pyroxene to minerals of the serpentine group, however, is generally considered to have occurred at elevated temperatures, early in the history of an ultramafic body. We present evidence from studies of natural water that, in addition to the conventional interpretation, serpentinization may also be occurring locally at comparatively shallow depth and low temperatures at the present time. We do not know how much of the serpentine in the geologic record has been formed by the process we describe.

Waters of two chemically distinctive types are found in springs issuing from ultramafic rocks in California and Oregon. Most abundant is a moderately alkaline (*p*H range 8.3 to 8.6) magnesium bicarbonate water of meteoric origin. Less abundant, but of great potential significance, is a previously

unreported type of ultrabasic (*p*H range 11.2 to 11.8) calcium hydroxide water that may be related to serpentinization of pyroxene and olivine. The chemical characteristics of the moderately alkaline waters are given in Table 1, and those of the ultrabasic waters are shown in Table 2. Field determinations were made of *p*H and bicarbonate ion (HCO_3^-) concentrations. Further chemical analyses of preserved samples were made later. All samples were filtered (0.45-μ filter) at the time of collection and were split into acidified (*p*H 2) and raw fractions for the appropriate chemical analyses.

The magnesium bicarbonate springs are typically associated with surficial features such as shallow topographic depressions, landslides, and bedrock sills in the stream beds. Thus, they apparently represent the discharge of shallow groundwater of meteoric origin (*1*). The high Mg^{+2} concentrations reflect the weathering of magnesium-bearing phases, possibly within the soil (*2*). In spite of the high HCO_3^- concentrations, the partial pressure of CO_2 is low, probably due to the sparse vegetation that characterizes ultramafic terrane (*3*). The moderately alkaline springs emerge from completely serpentinized ultramafic bodies such as that at Table Mountain, California (*4*), as well as from localities within the bodies of fresh or incompletely serpentinized rocks (Tables 1 and 2). Thus, the chemical characteristics of this presumably shallow, moderately alkaline groundwater seem to be related to the weathering of serpentine minerals and other magnesium-bearing phases.

The ultrabasic, calcium hydroxide water has thus far been found only in areas underlain by fresh or partially serpentinized peridotite and dunite. Such springs often occur in linear groups (as many as 15 springs in a group) and are almost invariably found along the bottoms of the deeper canyons. Although this mode of occurrence indicates that the ultrabasic water is emerging from a deep source along faults or shear zones, it cannot be readily classified as a deep-seated water of magmatic, metamorphic, volcanic, or connate origin by the criteria of White (*1*). The low temperatures and low concentrations of Li^+, F^-, $SiO_{2(aq)}$, B, CO_2, and sulfides indicate a nonmagmatic source. The absence of CO_2 and the low B concentrations seem to preclude a metamorphic origin. The low temperatures, the low concentrations of $SiO_{2(aq)}$, Na^+, Cl^-, F^-, and the absence of nearby volcanism probably rule out a volcanic origin; the very high Cl^- concentration of a connate water is also lacking. The close association with unserpentinized ultramafic rocks in three widely separated localities suggests that the distinctive chemical characteristics of the ultrabasic waters can be tentatively explained as the result of local processes involving reactions between olivine and pyroxene and deeply circulating ground water. For olivine, the chemical reaction, written for convenience in terms of MgO end-members, is:

$$2Mg_2SiO_4 + 3H_2O = Mg_3Si_2O_5(OH)_4 + Mg^{+2} + 2OH^-$$

Taking as an example a reaction of the enstatite component of pyroxene,

$$H_2O + MgSiO_3 = Mg^{+2} + SiO_{2(aq)} + 2OH^-$$

the solution would be equimolar in Mg^{+2} and $SiO_{2(aq)}$. A rise in *p*H is required by the reaction and might lead to supersaturation and precipitation of Mg carbonates (*5*) (if any carbonate species were initially present in solution) and brucite. The result would be a solution rich in silica with respect to Mg^{+2}, but not necessarily silica-rich in the absolute sense suggested by others (*6*). Possibly some confusion has been caused by writing the serpentinization reaction

$$3MgSiO_3 + 2H_2O = Mg_3Si_2O_5(OH)_4 + SiO_{2(aq)}$$

which, again, shows only that the solutions are silica-rich in comparison to Mg^{+2}. This reaction might yield the high *p*H values observed in the ultrabasic water. The ultrabasic solutions are all supersaturated with the major components (*7*) of the brucite that has been recognized as an accessory mineral in a number of alpine serpentinites (*8*). The ultrabasic water contains little Mg^{+2} and no carbonate species. If the ultrabasic waters are locally derived from the shallow meteoric water, then these constituents must have been removed. The high *p*H apparently yielded by the above serpentinization reaction would foster precipitation of magnesium carbonates in addition to brucite. Hydromagnesite has been found in veins at Red Mountain, California, but we have no evidence that widespread carbonate precipitation has taken place during serpentinization.

The rise in *p*H of waters reacting with either olivine or pyroxene may well be the cause for the very low concentrations of Fe^{+2}, Mg^{+2}, and CO_3^{-2}, but the *p*H rise does not cause supersaturation with respect to $Ca(OH)_2$ (*9*). The Ca^{+2} in the aqueous solution from the solution of pyroxene will remain in solution unless precipitated as a carbonate mineral. Thus, the result of the serpentinization that we must postulate to explain the ultrabasic waters is the removal of CaO, and little else, from the original rock;

Table 1. Chemical properties of meteoric water; *p*H data from field measurements. Sample D: Red Mountain, Stanislaus County, California, SE¼ sec. 15, T. 6 S., R. 5 E., *p*H 8.71, 15.6°C; sample E: John Day, Grant County, Oregon, SW¼ sec. 20, T. 14 S., R. 33 E., *p*H 7.27, 8.0°C; sample F: Cazadero, Sonoma County, California, NE¼ sec. 13, T. 9 N., R. 12 W., *p*H 8.87, 23.5°C.

Constituents	Concentrations (parts per million)		
	Sample D	Sample E	Sample F
Ca^{+2}	3.4	0.50	5.4
Mg^{+2}	101	16	40
Na^{+1}	6.4	0.5	3.6
K^{+1}	0.3	.2	0.2
Cl^{-1}	6.3	0	5.8
SO_4^{-2}	20	0.4	0.4
HCO_3^{-1}	489.6	85.8	195
CO_3^{-2}	13.4	0.06	8.1
Fe^{+2}	0.03	.03	0
Mn^{+2}	.02	.03	0.04
$SiO_{2(aq)}$	4.6	20	5.4
F^{-1}	0.1	0	0.1
NO_3^{-1}	2.5	0	0.20
NO_2^{-1}	0	0.01	0.01
NH_4^{+1}	0.09	.01	0
B	0	.03	0.02
Cr (total)	0	.02	
Li^{+1}	0	.02	0.01
Sr^{+2}	0	0	0.01

Table 2. Chemical properties of ultrabasic solutions; *p*H data from field measurements. Sample A: Red Mountain, Stanislaus County, California, SE¼ sec. 15, T. 6 S., R. 5 E., p*H* 11.78, 15.6°C; sample B: John Day, Grant County, Oregon, NW¼ sec. 10, T. 14 S., R. 33 E., *p*H 11.25, 31.0°C; sample C: Cazadero, Sonoma County, California, NE¼ sec. 13, T. 9 N., R. 12 W., *p*H 11.72, 18.0°C.

Constituents	Concentrations (parts per million)		
	Sample A	Sample B	Sample C
Ca^{+2}	48	35	53
Mg^{+2}	0.4	0.1	0.3
Na^{+1}	40	33	50
K^{+1}	1.1	2.3	1.2
Cl^{-1}	32.0	19	55
SO_4^{-2}	1.4	0.0	0.0
CO_3^{-2}	0.0	0.0	0.0
Fe^{+2}	.03	0.0	0.01
Mn^{+2}	.02	.01	.05
$SiO_{2(aq)}$	5.2	5.9	.3
Al^{+3}	0.4	0.7	0.0
Sr^{+2}	.03	.1	.06
Li^{+1}	.03	.02	.02
Cr (total)	0.0	.02	
F^{-1}	0.00	.1	0.0
NO_3^{-1}	0.2	.4	1.0
B	.1	.08	0.01
NH_4^{+1}	.2	.2	.1
NO_2^{-1}	.01	0.00	

MgO, FeO, Mn_2O_3, Cr_2O_3, and most of the SiO_2 remain behind.

Other serpentinization processes apparently lead to the same result as the process we propose. The conclusion is supported by comparison of chemical analyses of bulk rock samples from fresh peridotites and pyroxenites (from California) with analyses made of serpentinites (*10*). The fresh peridotites and pyroxenites (*10*) contain 0.037 to 16.9 percent of CaO by weight, whereas the serpentinites by analysis contain CaO in amounts ranging from "not detectable" to 2.49 percent by weight; the comparison shows a probable removal of CaO upon serpentinization. Twelve analyses of serpentine-group minerals (*11*) show a maximum CaO content of 0.3 percent by weight, indicating that CaO is not readily incorporated into serpentine-group minerals. A study of fresh and serpentinized ultramafic rocks in California and elsewhere (*12*) also has shown that the CaO component is selectively removed upon serpentinization.

In some serpentinization, the transformation of olivine and pyroxene must be accompanied by an increase in rock volume. The increase in volume at depth could result in serpentinite extrusion (*4*). Continued rising due to expansion may also explain why so many ultramafic bodies are topographically high, despite their apparently rapid reduction by slumps, landslides, and stream erosion.

IVAN BARNES
V. C. LAMARCHE, JR.
GLEN HIMMELBERG
U.S. Geological Survey,
Menlo Park, California 94025

References

1. D. E. White, *Geol. Soc. Amer. Bull.* **68**, 1637 (1957); *ibid.*, p. 1659.
2. W. Wildman, M. Jackson, L. Whittig, in *Agronomy Abstracts* (American Society of Agronomy, 1966), p. 67.
3. R. H. Whittaker *et al.*, *Ecology* **35**, 259 (1954).
4. W. R. Dickinson, *Geol. Soc. Amer. Bull.* **77**, 451 (1966).
5. F. A. Mumpton, H. W. Jaffe, C. S. Thompson, *Amer. Mineral.* **50**, 1893 (1965).
6. T. P. Thayer, *ibid.* **51**, 68 (1966).
7. W. M. Latimer, *Oxidation Potentials* (Prentice-Hall, New York, ed. 2, 1952), pp. 222 and 236; P. B. Hostetler, *Amer. J. Sci.* **261**, 238 (1963).
8. P. B. Hostetler, R. G. Coleman, F. A. Mumpton, B. W. Evans, *Amer. Mineral.* **51**, 75 (1966).
9. R. G. Bates, V. E. Bower, E. R. Smith, *J. Res. Nat. Bur. Stand.* **56**, 305 (1956).
10. E. H. Bailey, W. P. Irwin, D. L. Jones, *Calif. Dept. Natur. Resources Div. Mines Bull.* **183**, 84 (1964).
11. W. A. Deer, R. A. Howie, J. Zussman, *Rock Forming Minerals* (Wiley, New York, 1962), vol. 3, pp. 176 and 177.
12. N. J. Page, thesis, Univ. of California, Berkeley (1966).

27 March 1967

Virus-Induced Erythropoiesis in Hypertransfused-Polycythemic Mice

Abstract. *Friend, Rauscher, and polycythemic viruses produce a marked erythrocytopoiesis in the spleens of infected mice. The erythrocytopoiesis induced by the Friend and Rauscher viruses can be inhibited in a hypertransfused-polycythemic state. Like erythropoietin, the polycythemic virus can initiate erythropoiesis in this state. However, the mechanism by which the polycythemic virus initiates erythropoiesis in this state is not understood. These studies also show similarity of the Friend and Rauscher viruses in their erythropoietic response.*

Viruses, such as Friend (*1*), Rauscher (*2*, *3*), and the polycythemic virus (*4*), produce marked erythrocytopoiesis in the spleen of mice; for this reason they have been referred to as erythropoietic viruses. This report deals with the erythropoietic responses induced by these three erythropoietic viruses in mice in a hypertransfused-polycythemic state (*5*, *6*).

Swiss male mice (Ha/ICR, 5 to 6 weeks old) were used, and a hypertransfused-polycythemic (HP) state (*5*) was induced by intraperitoneal injections of 0.5 ml of washed, packed, homologous red blood cells on 3 consecutive days and again on day 5. This resulted in hematocrits on the order of 70 to 75 percent. The viruses were then given to each group when the HP state was achieved. This state in virus-infected mice was prolonged by giving red-cell transfusions twice a week to maintain the hematocrits above 70 percent.

The polycythemic virus (*4*), first detected in our laboratory, has been passed since 1961, and it is now in its 96th passage generation. This virus could be a variant of Friend virus or a passenger virus present in filtrates prepared originally from Friend virus-infected spleens of Taconic Swiss mice. The erythropoietic patterns induced by Friend and Rauscher viruses are similar, but the polycythemic virus induces an erythrocythemia and increases in granulocytes and platelets (*4*). The mice in each group were inoculated intraperitoneally with 0.2 ml of a splenic filtrate. The titers (infectious dose, 50 percent effective, ID_{50}) of the respective splenic filtrates (per milliliter) used in this study were: $10^{5.0}$ for the Rauscher virus, $10^{4.2}$ for the Friend virus, and $10^{4.5}$ for the polycythemic virus.

Erythropoietic parameters used were the uptake of Fe^{59} (*7*) and reticulocyte counts. All mice were injected intravenously with 0.5 μc of Fe^{59} on the 13th day of virus infection; the uptake of Fe^{59} in the femur, blood, and spleen was determined 24 hours later (the 14th day of virus infection).

In a HP state, erythropoietic production and morphological evidence of erythropoiesis are drastically depressed (*5*, *6*) (Table 1). So far, erythropoiesis has only been initiated in a HP state by the administration of erythropoietin or substances that influence erythropoietin production (*8*). Consequently, this has been used as a reliable assay for the detection of erythropoietin activity in plasma, urine, and other body fluids (*9*). However, as early as the first week, HP mice infected with the polycythemic virus showed resump-

Table 1. Response of polycythemic, Friend, and Rauscher viruses in hypertransfused-polycythemic (HP) Ha/ICR Swiss mice 14 days after infection. ±, Standard deviation.

Mice and treatment	Response to virus					
	Spleen weight (g)	Average 24-hour Fe^{59} uptake* (%)			Reticulocytes (%)	Hematocrit (%)
		Femur	Blood	Spleen		
Normal	0.15 ± .04	0.49 ± .05	24.8 ± 2.8	1.2 ± .08	0.5 ± .03	42 ± 1.2
HP	.24 ± .02	.09 ± .02	0.41 ± .09	0.07 ± .03	0.0	75 ± 3.4
HP + ESF†	.16 ± .03	.54 ± .09	19.8 ± 3.4	5.8 ± 1.2	3.8 ± 1.0	73 ± 2.8
HP + polycythemic virus	.98 ± .12	.10 ± .02	22.8 ± 1.5	15.3 ± 2.1	3.5 ± 1.2	79 ± 5.4
HP + Friend virus	.18 ± .03	.07 ± .01	0.45 ± .08	0.19 ± .02	0.0	70 ± 5.0
HP + Rauscher virus	.21 ± .02	.17 ± .01	.40 ± .06	.5 ± .07	0.0	73 ± 6.0

* Average from minimum of five mice per group. † One unit of erythropoietin was administered subcutaneously on 3 successive days, and 0.5 μc of Fe^{59} was injected intravenously on the 4th day. Uptake of Fe^{59} was determined on the 5th day.