

## THERAPEUTIC VALUES IN SOME RARE ELEMENT COMPOUNDS.

### Preliminary Report.

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The therapeutic value of germanium as an erythropoietic agent was first advocated by Hammitt, Nowrey, and Müller (1), several articles appearing in the medical journals by these authors in the years 1922-5. However, their work was largely discredited by the published reports of work done by Minot and Sampson (2), by Bodansky and Hartman (3), by Alexander (4), by Kast, Kroll and Schmitz (5), and by Whipple and Robbins (6).

A review of the published articles shows (a) that experimentation was largely done upon healthy animals, or on animals made anemic by simple bleeding, (b) that only two types of germanium compounds were tried, (c) that the modes of administration to patients and to animals were quite limited whereas many modifications are possible, (d) that very little account was taken of the diet used at the time of treatment and (e) that the possibility of a germanium compound acting catalytically upon physiologic processes is suggested in only one article where it is given the rôle of an oxygen carrier (7).

Lenker (8) reports some success in the use of germanium compounds for severe anemia but, unfortunately, he found it necessary to use unsterilized solutions for injections and he gave no account of accompanying treatment or of diet. The solution was given by injection, never by mouth. He concludes that in cases of pernicious anemia  $\text{GeO}_2$  has some value in that it prolongs life and makes the patient more comfortable.

The writer has worked upon the assumption that different compounds of germanium may differ in physiological properties and that a small dosage may produce a contrasting effect to a large one. Similar examples of such action may be noted in the use of alcohol, ether, and other drugs. Furthermore, a new drug may be expected to react differently upon a healthy animal than it will upon one that is ill.

A series of preliminary experiments were run on guinea pigs

rendered anemic by disease, but in the process of recovery, and on albino rats in which anemic condition was produced by deficient diet. The medicinal values of several compounds of germanium thus tested showed marked variation. Germanium dioxide in water or in sodium hydroxide solution was given to anemic animals by mouth, or by subcutaneous injections in dosage of 1 to 2 milligrams  $\text{GeO}_2$  per kilo body weight twice a week. Some of the compounds used were toxic to the anemic animals the treatment being followed by a decrease in red blood cells, a large increase in the white cells, and the final death of the animals. Other of the compounds given to the same type of anemic animals in dosage not to exceed 1 milligram per kilo body weight at intervals of five or seven days were found to yield a steady increase in red blood cells and the animals returned to health more rapidly than the controls. It is evident that germanium, according to its state of combination, and its method of administration to anemic animals, may act as a toxic agent injurious to the animals, or as an efficient remedial agent that aids recovery.

Some of the more beneficial compounds were tested upon anemic animals kept upon deficient diet. These showed a definite increase in red blood cells but the increase was much larger in animals on a complete diet. It is quite logical that the blood will build up more rapidly when all materials for repair are supplied. This constructive work was found to take place with greater speed in the treated animals given complete diet than in the controls given a complete diet.

Therapeutic values of arsenic have been shown to vary with diet. (9) The related compounds of germanium apparently vary in reaction in a similar way.

The fact that the blood coagulates rapidly where animals have received several large doses of germanium compound indicates some relation to the thrombin equilibrium. This in turn is dependent upon the calcium balance. It is suggested that germanium in its efficient compounds has to do with the calcium metabolism within the blood stream and the blood-forming organs. That it acts catalytically is evidenced by the small quantities necessary to bring about results. As in the case of other drugs there is a probability that several reactions take place as the result of its administration. Administered in large quantities other reactions appear paramount and the mild catalytic action obscured.

A germanium compound showing large efficiency in ani-

mals was supplied from our laboratory to several physicians for patients suffering from severe anemia. Both the secondary and the primary types of anemia were found to respond to this treatment as reported by these physicians. Several cases of pernicious anemia have been materially benefitted as shown in the following records taken from case histories. Practically all cases of secondary anemia were discharged from the hospital in normal health.

Case No. 1 is remarkable in that the patient recovered rapidly, was able to go about the house in three weeks, was driving his car in a month following the treatment and has had no relapse in two and a half years. He cannot be convinced that further laboratory tests are necessary, and says he enjoys the best health he has had in years.

Case No. 2 went back to work in July, had a short relapse in August, returned to work in September (1926), and has worked continuously to the present time.

Case No. 4 had just returned home from the hospital when first taken by the physician reporting. Liver treatment prescribed by some physicians was continued while germanium treatment was added. It may be noted that whereas the highest point attained in red blood corpuscles under liver treatment alone was less than four and a half million, with the addition of germanium compound an increase of one and a half million was produced which gives confirmatory evidence of the catalytic action of the compound in anabolic processes where all necessary components are supplied.

A simple increase in red blood corpuscles in itself may not indicate a better state of health but when this is combined with other favorable symptoms recorded in practically all reports received it does give evidence of a positive value for certain compounds of germanium. The composition of these compounds provides a topic to be discussed in a later paper.

#### Citations.

1. Hammitt, Nowrey, and Müller. *J. Exper. Med.* 35, (1922). Nowrey, *Bull. J. H. Hosp.* 35, (1924).
2. Minot and Sampson. *Boston Med. and Surg. J.* Nov., 1923.
3. Bodansky and Hartman. *J. Metab. Res.* 4, 595, (1923).
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6. Whipple and Robscheit-Robbins. *Am. J. Physiol.* Jan., 1927.
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CONDENSED CHART SHOWING INCREASE IN RED BLOOD CORPUSCLES AND HEMOGLOBIN IN CASES OF PRIMARY ANEMIA AFTER TREATMENT WITH A GERMANIUM COMPOUND.

Case No.	Date treatment began	RBC	Hemo-globin	Date of report on case	RBC	Hemo-globin	Comment
1.	Dec. 1, 1925	700,000	..	Feb. 21, 1927	.....	..	"Best health in years,"
2.	May 27, 1926	2,960,000	48	Feb. 3, 1927	4,520,000	83	"Works continuously,"
3.	Feb. 17, 1927	2,560,000	28	April 5, 1927	4,160,000	40	"Heart action became normal,"
4.	May 18, 1927	4,370,000	70	June 11, 1927	6,020,000	85	} April 23, 1928 "These patients reported to be getting along nicely;"
5.	Nov. 8, 1927	2,700,000	65	Nov. 28, 1927	4,180,000	85	
6.	Nov. 8, 1927	2,640,000	65	Nov. 28, 1927	4,200,000	80	
7.	Nov. 27, 1927	1,460,000	28	Dec. 31, 1927	2,710,000	58	