matured and ovulation took place, vagina, cervix and uterus behaving in accordance with the stage of the sexual cycle. These were the effects in guinea pigs in which there was considerable gain in weight, and in which the thyroid showed no hypertrophy. (b) In the animals which did not gain in weight or gained little, the thyroid gland (with one possible exception) showed hypertrophy. The ovaries were hypotypical, contained much interstitial gland and, in one case also a pseudolutein body. Vagina, uterus, and mammary gland were in a resting condition. (c) There was an intermediate group in which the guinea pigs gained much in weight, but less than in Group A. The thyroid showed no or only a trace of hypertrophy. The follicles developed well in the ovaries and proestrus as well as ovulation could occur, but at the same time interstitial gland and pseudolutein bodies or the latter alone formed. The other sex organs behaved normally, except that we found a quiescent vagina in a case in which both interstitial gland and pseudolutein tissue were present. Hypertrophy of the thyroid and the resulting deficiency in weight caused a hypotypical condition of the ovaries; in addition the acid extract was responsible more directly for the formation of interstitial gland and pseudolutein bodies.

We may conclude that after a long continued series of injections of acid extract of cattle anterior pituitary a gradual adaptation, partial or even complete, to the effects of the injections may take place in young guinea pigs and that there seems to exist a considerable difference in the ability of individual animals to acquire this increased tolerance. We may attribute the hypotypical condition of the ovaries largely to the relative undernourishment caused by the induced hypertrophy of the thyroid gland.

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Production of Experimental Polycythemia with Cobalt.

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During a continuation of our studies on nutritional anemia, a polycythemia was observed in rats receiving a certain mixture of metals with Cu as a supplement to a milk-Fe diet, whereas the same

mixture of metals without Cu failed to produce this condition. The data are reported together with those from a study of the metals or combination of metals responsible for the polycythemia.

Male albino rats, 26 days old, were placed in glass cages and fed whole milk for 4 days. A mixture of Mn, Co, Ni, Zn, Cu, and Fe salts was then added as a supplement to the milk diet 6 days a week. All metals were fed as the same preparations, and at the lower levels, used in our previous work.[1]

Weekly hemoglobin determinations showed normal values until the animals were 7 to 9 weeks of age, when a definite increase in hemoglobin occurred. The rats presented an extremely ruddy appearance, and their eyes, ears, and paws became deep red. When it was evident that this was not a transitory condition, hematological studies were made on the animals of this group, as well as on 2 control groups—one receiving the milk diet supplemented by Cu and Fe only, and the other, a normal stock diet. The group averages, based upon 3 determinations at weekly intervals on each rat, may be summarized as follows:

TABLE I.

Diet	No. of Rats in Group	Hemoglobin (gm. per 100 cc.)	Erythrocytes (per cu. mm.)	Cell Volume %
Stock	6	13.5	9,436,945	53.6
Milk-Fe-Cu	6	12.2	8,547,778	48.6
Milk-Fe-Cu + Mn, Co, Ni, Zn	5	19.4	14,599,000	76.5

The table shows that the animals on the entire mixture of metals exhibited a marked polycythemia, whereas the rats of either control group showed none. The animals showing polycythemia are now 275 days old and the condition has persisted for 30 to 32 weeks. Another group of rats, not reported here, received the mixture of metals without Cu and developed a progressive anemia rather than a polycythemia. Thus, it is apparent that one of the metals—Mn, Co, Ni, or Zn—or some combination of these metals, acts with Cu to produce a polycythemia in rats on a milk-Fe diet.

To determine which one or what combination of the 4 metals mentioned above was responsible for the polycythemia, 2 rats were placed on each of the 15 possible combinations of the 4 metals—Mn, Co, Ni, and Zn—as a supplement to a milk-Fe-Cu diet. Three animals on this basal diet and 7 on a stock diet were maintained as controls. In every one of the 16 animals that received *cobalt,* there

[1] Underhill, F. A., Orten, J. M., and Lewis, R. C., *J. Biol. Chem.*, 1931, **91**, 13.

appeared the same marked increase in hemoglobin, erythrocytes, and cell volume as was previously observed, whereas none of the other 24 animals showed any increase above normal values. The total and differential leucocyte counts in this and in the previous experiments showed similarity between the different groups of animals. Further work of a preliminary nature with $CoSO_4$, used in place of the $CoCl_2$, has shown that it is also effective in producing a polycythemia. Thus, it is definitely established that Co acting with Cu as a supplement to a milk-Fe diet is the causal agent in producing the polycythemia observed in our rats.

In a study of the toxicity of metals, Waltner and Waltner[2] have reported a polycythemia in the rat after feeding metallic cobalt and after the injection of Co salts in significantly larger doses than those given in our experiments.

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Grafting of Larval and Adult Eyes in Amblystoma Punctatum.

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Replanted and transplanted eyes of *Amblystoma punctatum* were studied daily for many months in 193 larval grafts on larval hosts around 21 mm. in length and in 102 adult grafts on adult hosts varying in age from 1 to 2 years and in length from 6 to 18 cm. Since no striking differences exist based merely on replantation and transplantation, a comparison is given based on the age of the graft. Return of circulation after operation was obtained in 40% of old adults, where sloughing or partial resorption was high, against 80% of young adults. Its earliest appearance was on the first day in young adults and on the third day in old adults. The earliest in larvae was 18 hours. Although in adults it had occurred earlier in the younger specimens than in older ones it was present in half of the cases in 10 days. By the fourth day it was observed in one-half of the larvae. About one-third of adult grafts and most of the larval eyes showed no corneal or lenticular opacity. In a few cases of adult and larval grafts the opacity was transient but in any case of excessive trauma sloughing of the bulb was subsequent to a

[2] Waltner, K., and Waltner, K., *Klin. Wochenschr.*, 1929, **8**, 313.