continued on the diet until exitus, were noteworthy during the last 2 weeks of the experiment in that there was a precipitous drop in both the erythrocyte and hemoglobin levels. The final red blood-cell counts were 4,260,000 (No. 473) and 3,900,000 (No. 393) cells per cu.mm., and the hemoglobin determinations were 52 (7.4 gm.) and 36 (5 gm.) % respectively. It is to be emphasized that, throughout the experiment, the color indices remained between 0.5 and 0.7 and the cell-volume less than normal. The anemia, therefore, continued to be hypochromic and microcytic in character.

In these 2 dogs parenteral injections of liver extract† failed to alleviate symptoms, or to alter the progress of the anemia.

The third dog (No. 161) showed a reduction in the number of erythrocytes after 75 days of restricted diet. Progress of the anemia stopped, however, with the daily feeding of raw beef which is rich in vitamin B_2 (G), and subsequently there was a rise in the erythrocyte level.

Conclusion. A diet restricted in vitamin B_2 (G) when fed to dogs with an artificial achylia gastrica did not produce macrocytic anemia.

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Cortico-Adrenal Insufficiency in Rats Under Reduced Pressure.

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This report concerns one of the aspects of a broader research project in which a fairly comprehensive study was made of the response of rats to reduced pressure, inclusive of the relation of such response to some pathological conditions both in rats and other animals. By experiments carried out under a variety of standardized levels of low pressure and for a series of standardized periods of exposure to such pressures, it has been shown that various functional factors respond in a uniform and typical manner to these environments. On this evidence 3 stages could be distinguished with respect to the total exposure period of a rat to the low pressure environment: (a) a pre-adaptive stage during which most deviations of values indicate an unfavorable effect, (b) an adaptive stage during which deviations occur in the opposite direction and are indicative of adaptive adjustments, and (c) a post-adaptive stage during

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which functional shifts occur again in a direction suggesting pathological changes. The third of these stages was found to occur mainly when the animals were exposed for extended periods to very low levels of pressure and was considered to be an expression of an exhausted adaptive function.

It was considered also that the functional changes occurring during this third stage would be the most promising material for suggesting the nature of the general functional state which is produced by artificial and possibly also natural altitude conditions. For this purpose the total picture of physiological effects found during this stage was compared with the syndromes of various pathological conditions of known etiology. It was discovered that the functional alterations under these particular low pressure conditions are identical with the functional alterations resulting from cortico-adrenal insufficiency in adrenalectomized animals. Some earlier observations, *viz.*, the sudden and unexpected deaths of apparently normal rats and the finding of intestinal hemorrhages in many of these rats, supported the assumption that the adrenal activity is involved in the deterioration of animals in this abnormal "climate." It was reasoned that if some direct proof could be obtained for the correctness of this assumption it would become useful later for relating acclimatization to altitude with the function of the adrenal cortex. It was the purpose of this particular investigation to furnish such experimental proof.

If a deficiency of the cortical hormone is the direct cause of the abnormal functional effects during the post-adaptive stage it could be predicted that administration of such hormone would ameliorate the condition of the rats. This prediction was proven to be correct. The rats which received charcoal adsorbate of the cortical hormone with the food lived much longer than low pressure rats without cortin. Moreover, the administration of cortical extract had a definite normalizing effect on the various functional levels in the former group of rats.

If the cortico-adrenal activity is inhibited at later stages under reduced pressure it would be expected that some structural damage of the gland could be demonstrated to have occurred previously. Such histological evidence for adrenal damage was obtained. In cases in which this damage was not easily detectable from cellular necrosis and hemorrhages, it consisted of a confluence of lipoid droplets which Zwemer has postulated as a sign of cortico-adrenal insufficiency.

Of the several causes which could be suggested for this structural and functional damage an exhaustion due to overwork appeared

a priori to be the most likely. In order to substantiate this hypothesis it was necessary to provide a reasonable explanation for an initial stimulation of the cortical activity under reduced pressure. A greater demand for cortical hormone by the body under diminished pressure appeared as the most reasonable explanation. Attempts to obtain some evidence for an increase of the cortin requirements of low pressure rats constituted the third step in this investigation.

The cortin requirements of adrenalectomized rats were first carefully determined with respect to atmospheric conditions. This procedure was repeated with respect to a series of graded low pressure environments. The amounts of assayed charcoal adsorbates of cortical hormone needed to maintain the adrenalectomized low pressure rats alive increased progressively with the lowering of the pressure gradient. Moreover, the increment in rat units per 100 mm. decrease in pressure underwent a gradual and quite considerable rise with the lowering of the pressure. The minimum dose was more than 20 times higher at a pressure of 300 mm. than normally. It may be inferred that rats with intact adrenals under a similar pressure require an equal amount of cortical hormone and that their cortical apparatus may not be able to supply all of this demand without finally becoming exhausted.

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Relation of Certain Bile Acids to Absorption of β-Carotene in the Rat.*

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In previous work from this laboratory[1] it has been shown that deoxycholic acid acts as a carrier of irradiated ergosterol and of β-carotene across the intestinal tract of the rat. This is probably

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