environment. On the basis of the present results it might be supposed that the injected lipid and protein fractions from bursa, thymus and liver act as an adjuvant. However, the failure of bursa lipid and thymus protein to reconstitute and increase the antibody production in bursaless birds, and the inability of all the materials used to induce a higher elaboration of hemagglutinins in unoperated chickens does not support this assumption. The simplest construction which can be placed upon these results suggests that the multiple injections of some tissue constituents to a certain degree stimulate, in an unknown way, the 'quiescent' antibody-producing machinery of bursectomized birds, while being inactive in unoperated chickens whose antibody-forming apparatus is functioning normally. It is pertinent to mention here that we have put forward a hypothesis, in connection with the antibody response of hyperimmunized bursaless chickens[6], that the antibody response threshold is elevated in those birds and that cumulative exposure to antigens may trigger a response[7,8].

The most striking finding revealed by this study deals with the restorative activity of lipid and protein fractions from liver, the liver protein being particularly effective in reconstituting the formation of ME-resistant antibody. One might be tempted to infer that the liver per se is capable of exerting an immunological function or interfering in immune affairs. Bearing in mind the high functional and biochemical complexity of the liver, this possibility cannot be ruled out, although it requires more experimental support than that offered here[9].

*Zusammenfassung.* Neugeborene bursaektomierte Küken wurden mit aus der Thymus, Bursa fabricii und Leber isolierten Lipid- und Protein-Fraktionen behandelt und hernach durch menschliche Erythrocyten immunisiert. Einige dieser Fraktionen, einschliesslich der Leberproteine und Leberlipide, führen zu einer Erhöhung der Hämagglutinin-Produktion.

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## Mechanism of Decreased Erythropoiesis in Thyroidectomized Rats

The thyroid clearly exerts an effect on red cell production, as is evidenced by the anaemia which develops in experimental animals and human subjects after thyroidectomy[1-5]. When the total circulating red cell volume reaches its new steady-state after thyroid ablation, the red cell survival has been found to be normal[4,5]. Therefore, anaemia develops as the result of a decreased red cell production.

Theoretically, a decrease in red cell production could result from several causes: such as a decrease in the number of erythrogenic elements in the blood-forming tissues, an increase in intramedullary time, or an increase in intramedullary death. Clarification of the mechanism by which red cell production is reduced in the thyroidectomized rat was the object of this study. For this purpose an iron kinetic study was done as well as determinations of number of erythroid cells in normal rats and rats of the same age injected with $I^{131}$ 8 months prior to the onset of the study.

Male rats of the Wistar strain, weighing approximately 300 g were used throughout these studies. One half of the group was injected with 700 $\mu$C of $I^{131}$ i.p. and the remainder served as normal controls.

The total circulating red cell volume was determined by the $Fe^{59}$ labelled cell dilution method[6]. The results obtained at the time of autopsy are shown in the Table. Following thyroidectomy the circulating red cell volume decreased 24% below normal. Plasma volume showed an increase of 7%. Quantitative measurements of the fraction of the total erythropoietic marrow present in a femur obtained by in vivo labelling with $Fe^{59}$ and isolation of the entire skeleton[7] showed that one femur contained 7.5% of the total erythroid marrow in normal rats, whereas this value was 6.3% in thyroidectomized rats.

For iron kinetic studies the rats were given 1.0 $\mu$C of $Fe^{59}$ i.v. and at various times thereafter were anaesthetized with ether and as much blood as possible was drawn from the abdominal aorta. Through the same needle the rat was thoroughly perfused with saline (the jugular vein was cut to allow outflow of blood and perfusate) until the heart stopped beating. The detailed method has been published elsewhere[7].

After thyroid ablation, as it is shown in the Table, the plasma iron concentration decreased 15%. The rate of erythropoiesis as measured by the red cell iron turnover rate[8] decreased after thyroid destruction. The magnitude of the decrease in the hemoglobin synthesis rate was about 20% of the control value. A comparable decrease in the plasma iron turnover rate was found. The clearance half time of radioiron from the plasma was prolonged in the thyroidectomized group when compared to the normal one. The fractional decrease in the hemoglobin synthesis rate after thyroidectomy was similar to the decrease

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observed in total red cell volume. This probably reflected steady-state conditions at the time of autopsy. Total number of erythroid cells in the bone marrow of the thyroidectomized rats/100 g of body weight was 46% of the number in the normal controls. The calculated mean erythron life span and the mean time of iron fixed in red cell precursors were approximately the same for both normal and thyroidectomized rats.

Therefore, we have only the decrease in the number of erythroid precursors to explain the 'thyroidectomy anaemia' in the long term postoperative rat. This finding, in the absence of any significant difference in ferrokinetics, leads to the conclusion that erythropoiesis is decreased in the chronically thyroidectomized rat because of a decrease in the number of erythrogenic elements in the bone marrow. If the erythroid responsiveness of erythropoietic tissue to erythropoietin is the same in thyroidectomized as in normal rats, then the decrease in bone marrow erythroid precursors found in the former would result from a decrease in the erythropoietin production rate in these animals. Work is in progress to test this possibility[9].

Hematologic data from normal and thyroidectomized rats

| | Normal | Thyroid-ectomized |
|---|---|---|
| Body weight, g | 453.4 | 300.5 |
| Hemoglobin, g/100 ml | 13.2 (0.31)[a] | 11.9 (0.26) |
| Hematocrit, % | 45.5 (1.24) | 38.9 (1.18) |
| Blood volume, ml/100 g body weight | 4.72 (0.05) | 4.39 (0.10) |
| Red cell volume, ml/100 g body weight | 2.17 (0.03) | 1.79 (0.06) |
| Plasma volume, ml/100 g body weight | 2.54 (0.02) | 2.60 (0.20) |
| % of total erythropoietic marrow present in right femur | 7.50 (0.80) | 6.30 (0.90) |
| Nucleated erythroid cells/100 g body weight ($\times 10^9$) | 0.43 (0.11) | 0.20 (0.09) |
| Plasma iron, $\mu$g/100 ml | 123.70 (0.41) | 105.50 (0.21) |
| Plasma $Fe^{59}$ half time, min. | 57 | 70 |
| Plasma iron turnover rate, $\mu$g/day/100 g | 47 | 39 |
| Red cell iron utilization, % | 66 | 64 |
| Hemoglobin synthesis rate, $\mu$g/day/100 g | 914.7 | 735.3 |
| Mean erythron life span, days | 57 | 58 |
| Mean time of iron fixed in red cell precursors, h | 27 | 26 |

[a] Standard error of the mean.

*Resumen.* El volumen de la masa roja circulante descendió en un 24% en ratas radioyodotiroidectomizadas después de 8 meses de administrado et $I^{131}$. Hubo un descenso similar en la sintesis diaria de hemoglobina/100 g de peso corporal. Los estudios de la cinética del hierro fueron semejantes en ambos grupos. No hubo aumento de la eritropoyesis inefectiva ni del periodo intermitótico medular. El número de células eritroides en la médula ósea de las ratas atiroideas mostró una disminución significativa con respecto a los animales controles, hecho que seria el responsable de la anemia post-tiroidectomia.

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## Altered Wound Healing in X-Irradiated Rats: The Effect of Bone Marrow Shielding

The effect of total-body irradiation on wound healing has been the subject of recent investigation[1-4]. Studies in this and other laboratories[4] have demonstrated that the temporal relationship between the wound and the exposure to irradiation is of importance in the response to this combined injury. Our prior studies have shown that when the rat is wounded 4 days following irradiation there is an increase in mortality of the wounded irradiated animal and wound contracture is markedly delayed. The explanation for this phenomenon is unclear. The purpose of the present study was to determine the effect of bone marrow shielding on wound contracture following irradiation.

Female Walter Reed rats, 10–12 weeks of age were fed a standard pellet diet, allowed water ad libitum, randomly assorted and individually housed. 800 R in air was delivered by means of a 250 KVP X-ray machine at a dose rate of 64.3 R/min. Shielding was provided by open-ended lead cylinders of 1.5 cm thickness measuring 6.5 cm in diameter and 8 cm in length. A 20 cm long perforated plastic cylinder was fashioned so as to fit snugly over the lead cylinder, and was utilized to restrain the animal during irradiation. Following light ether anesthesia, the

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