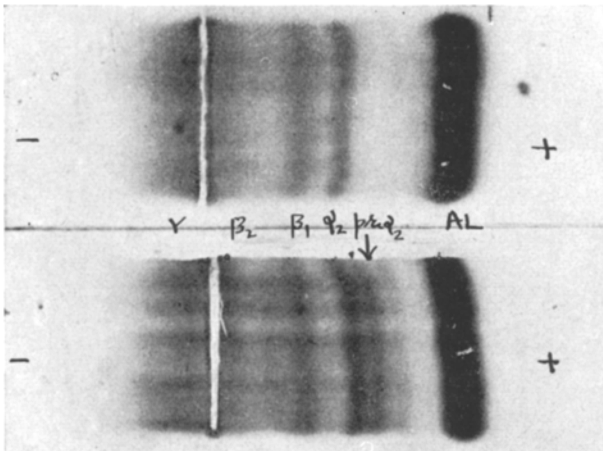

Fig. 1. Electrophoresis of horse serum proteins on agar gel at pH 8.6 before commencement of immunization (above) and after the very first dose of diphtheria toxoid (below).

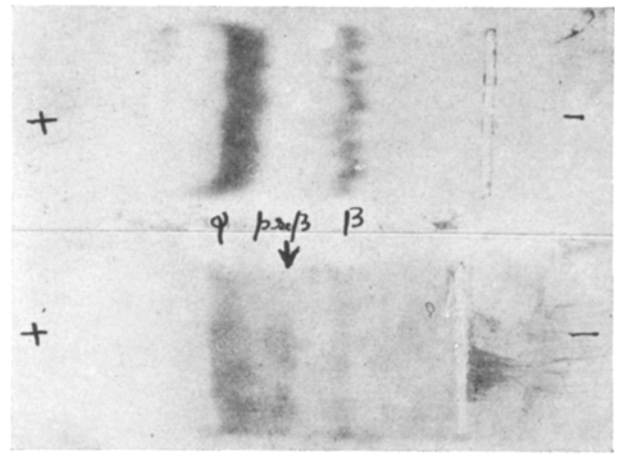

Fig. 2. Electrophoresis of horse serum lipoproteins on agar gel at pH 8.6 before commencement of immunization (above) and after the very first dose of diphtheria toxoid (below).

lipoprotein is found to be only a temporary change and the component disappeared as the hyperimmunization proceeded, whereas the pre-α_2-globulin, which appeared soon after the first dose, remained as a permanent feature throughout the hyperimmunization.

The significance of this pre-α_2-globulin and its function, if any, is not known. WAJCHENBERG[6] found that the sera of patients with diffuse massive necrosis were characterized by the appearance of pre-α_2-globulin. The appearance of pre-α_2-globulin after poisoning with carbon tetrachloride in rats has been reported recently[7]. Since carbon tetrachloride is known to damage the liver, the appearance of pre-α_2-globulin four days after the very first dose of diphtheria toxoid is probably an indication of disturbance in the liver function resulting in the excessive synthesis or secretion of the proteins of pre-α_2-globulin mobility.

Zusammenfassung. Der Immunisierungsvorgang durch Diphtherie-Toxoid wird beim Pferd elektrophoretisch im Agar-gel verfolgt. Das Auftreten eines Prä-α_2-Streifens wurde bald nach der ersten Toxoidgabe festgestellt.

U. S. V. ACHARYA and S. S. RAO

Department of Immunology, Haffkine Institute, Bombay (India), August 31, 1965.

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The Effect of Pinealectomy and Thymectomy on the Immune Capacity of the Rat

In earlier experiments[1] it was shown that mast cell production by the lymph nodes was stimulated by pinealectomy and cortisone treatment; PAS positive cells appeared in the spleen while mast cell production in the thymus was not altered. It was assumed that the pineal body was responsible for the inhibition of mast cell production by the lymph nodes, and that, after pinealectomy, activity would go on unhampered. Since the thymus-lymph node-spleen system seems to have a decisive role in antibody production[2-6], in the present experiments the effect of pinealectomy and thymectomy on the antibody production was studied in the rat.

Eighty adult rats of the Wistar strain were used in the experiment. Pinealectomy was performed without damaging the brain. The thymus was extirpated in toto, together with its capsule. If both operations were performed, pinealectomy followed the thymectomy (Table). 63 animals survived the intervention. They were immunized first with $150 \cdot 10^6$ sheep red blood cells and with $200 \cdot 10^6$ such cells as a secondary stimulus. For the hemagglutination test, blood was taken from the tail vein. The animals were studied in 2 groups, one 30 days and the other 240 days after the operations.

The Table shows the number of animals and the mean of the numbers of the last (critical) tubes showing macroscopical hemagglutination (these numbers are the logarithms to the base 2 of the reciprocals of the respective last dilutions). The standard deviation varied at about

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the 0.9 tube. This means that in the case of a comparison between 7 tubes, a difference of at least one tube was significant statistically.

Analysis of the hemagglutination measured in the critical tubes was performed by 2-way analyses of variance. Evaluation was done by analysis of variance of such effects of thymectomy or pinealectomy which showed a uniform tendency among the 4 groups as a whole. If no such tendency was found, those pairs of treatment which could be expected to yield significant differences were examined by Student's *t*-test. In the case of a primary antibody response, a 2-way analysis of variance was carried out of the effect of pinealectomy and of the time elapsed until the first immunization.

Results. Early effects: Pinealectomy induced significant decrease in the primary response. Thymectomy also reduced the response as compared to the control. Thymectomy followed by pinealectomy evoked no significant change as compared to the effect of pinealectomy itself. In the secondary response at the first measuring, the double operation yielded a significantly higher level than any of the operations done separately. Thymectomy by itself significantly reduced the response, while the diminishing effect of pinealectomy was not significant statistically. At the second measuring of the secondary response, the increasing effect of pinealectomy was significant, while thymectomy seemed to be ineffective.

Late effects: Thymectomy resulted in a significant increase, while pinealectomy significantly reduced the response. Pinealectomy in thymectomized animals induced a smaller yet significant decrease. Consequently, the increasing effect of thymectomy was inhibited by pinealectomy, although the increase was significant as compared to the effect of pinealectomy alone. At the first measuring of the secondary response, the combined operation caused a significant but smaller increase than any of the operations done separately. At the second measuring of the secondary response, pinealectomy caused significantly higher values than the other operations; all these were completely prevented by thymectomy.

As to the relations between the two main groups, the effect of pinealectomy in the early and late groups seemed to be identical, thus it was not time-dependent. The effect of thymectomy was a significant decrease in the early group and a significant increase in the late one. The effect of pinealectomy was not influenced by thymectomy in the early group, while it caused a significantly increasing tendency in the late group.

At the first measuring of the secondary response, the operations by themselves, or their combination, caused a smaller difference as compared to the control in the early group than it did in the late one. The effects of the single operations, as well as the antagonism in the case of their combination, which was statistically significant according to a 4-sample *t*-test, showed different directions in the early and the late group. At the second measuring of the secondary response, the values were much more balanced but, under the effect of pinealectomy, a significant increase could be observed in the late group. In the early group, the same operation caused an increase at the boundary of significance only. In the case of double operation, this increase was unchanged in the early group, while it fell to the control level in the late one.

Conclusions. (1) Pinealectomy exerts an influence on antibody production in two phases. It diminishes the primary response early and late after the operation, and it increases the secondary response. This effect takes long to appear but it is intense and durable. (2) Thymectomy inhibited antibody production only for a short time. The late effect consisted in a highly significant increase of antibody production. (3) The pineal gland and the thymus mutually influence each other concerning their effect on antibody production. (4) Time is a very important factor in the effects of thymectomy and/or pinealectomy. (5) For the increasing effect of pinealectomy on the secondary response, the presence of the thymus is necessary.

Numbers of determinations (n) and average critical tubes ($\bar{x}$)

		Primary	Secondary 1	Secondary 2
Early effect[a]				
Control	n	8	8	8
	$\bar{x}$	5.8	4.6	3.5
Thymectomy	n	8	9	10
	$\bar{x}$	4.0	3.4	3.8
Pinealectomy	n	8	5	6
	$\bar{x}$	3.4	3.8	4.5
Pinealectomy-thymectomy	n	8	7	6
	$\bar{x}$	3.6	5.0	4.5
Late effect[b]				
Control	n	4	5	5
	$\bar{x}$	5.5	3.2	3.8
Thymectomy	n	10	9	9
	$\bar{x}$	8.1	7.6	3.4
Pinealectomy	n	7	7	7
	$\bar{x}$	3.1	7.1	8.0
Pinealectomy-thymectomy	n	7	7	6
	$\bar{x}$	4.4	5.1	3.8

[a] Thymectomy 95 days and pinealectomy 30 days before the first immunization. [b] Thymectomy 285 days and pinealectomy 245 days before the first immunization. Primary: response one week after the first immunization. Secondary 1: response one week after the second and three weeks after the first immunization. Secondary 2: response two weeks after the second immunization.

Zusammenfassung. Kurze Zeit nach Exstirpation des Corpus pineale wird eine abgeschwächte primäre, längere Zeit danach eine verstärkte sekundäre Immunreaktion festgestellt. Nach Thymectomie kommt es zuerst zu einer Hemmung, später zu einer Förderung der Immunreaktion. Corpus pineale und Thymus beeinflussen sich gegenseitig immunologisch.

G. Csaba, M. Bodoky,
J. Fischer, and T. Ács

Institute of Histology and Embryology, University Medical School and Department of Biometry, Mathematical Institute of the Hungarian Academy of Sciences, Budapest (Hungary), November 22, 1965.