obtained in MILLER's[1] mouse experiments. The value of immune response seems to have dropped in the 13-month group below that of the controls, owing also to the action of the old thymectomy, and this tendency remained perceptible even at the second measurement of the tertiary response (although the effect of the fresh thymectomy had disappeared by that time).

To sum up: (1) Results of the present experiments on rats support those of MILLER's mouse experiments. Total body irradiation of thymectomized adult rats reduced the immune response below that of the unimpaired controls, provided the antigenic stimulation was repeated. Such reduction was, however, neither durable nor did it occur in all age groups. (2) In general, the length of time elapsed since the removal of the thymus affected the immune response more than the age of the thymectomized animal. (3) Present results have substantiated the earlier observation that the primary immune response, instead of diminishing, becomes decidedly stronger if the time between thymectomy and immunization is long, a phenomenon presumably due to a liberation of another – immune substance producing – part of the lymphatic system from the inhibitory influence of the thymus. (4) The present results should be taken as a warning not to indulge in generalizations regarding the immunological role of the adult thymus. Although thymectomy performed on adult animals was followed by a diminution of immune response, the role of the adult thymus is still questionable and is not always effective, its effect was inhibitory rather than stimulatory and the role of the adult thymus by no means compares with the significance of this organ at the embryonic or neonatal stage.

Table II. Number of determinations (n) and the average critical tubes ($\bar{x}$)

Age of animals		Primary[a]	Secondary[b]	Secondary[c]	Tertiary[d]	Tertiary[e]
4 months						
	n	9	9	9	8	8
Controls	$\bar{x}$	5.89	5.56	4.44	6.00	4.25
Fresh thymectomy	n	8	7	6	6	5
	$\bar{x}$	6.25	5.57	5.00	4.50	4.40
9 months						
	n	8	6	4	4	4
Controls	$\bar{x}$	4.88	4.17	4.75	4.25	3.50
Fresh thymectomy	n	9	7	7	7	7
	$\bar{x}$	5.44	4.71	4.86	4.57	4.10
Thymectomy 6 months before	n	7	7	7	5	4
	$\bar{x}$	5.86	5.00	4.71	5.00	4.25
13 months						
	n	7	7	6	5	5
Controls	$\bar{x}$	5.29	5.43	5.17	6.00	5.20
Fresh thymectomy	n	9	7	6	5	4
	$\bar{x}$	4.44	4.86	5.00	4.20	5.25
Thymectomy 10 months before	n	5	5	5	5	5
	$\bar{x}$	6.20	5.40	4.60	5.00	4.00

Zusammenfassung. Röntgenbestrahlung thymectomisierter Ratten ergab eine abgeschwächte Immunreaktion. Für eine Immunreaktion adulter Tiere scheint jedoch der Thymus nicht notwendig zu sein. In Abhängigkeit von Zeit und Alter der Tiere zeigten sich Unterschiede in der Stärke der Immunreaktion.

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The Effect of Hyperthermia Applied in the Given Stages of Pregnancy on the Number and Form of Vertebrae in the Offspring of White Mice

In his former communication[1] the author has described the experiment which showed that in female white mice, hypothermia applied in the given stages of pregnancy caused inborn anomalies of the vertebral column, i.e. changes in the number of vertebrae in the given region, and occurrence of fused asymmetric or wedge-shaped vertebrae.

In 1964 the author started the second part of his experiment, which involved the investigation of the effect of hyperthermia applied in analogical stages of pregnancy; the material and methods of determining pregnancy, preservation, staining of skeletons and clearing being in both experiments identical[1]. The body temperature of the females was increased by 3–4 °C, ranging within 40–41 °C. For this purpose the females were put into a specially adapted thermostate for 20 h[2]. The experimental females were assigned to one of six groups (denoted by the letters A–F). In group A the body temperature was increased on day $7^1/_2$ of pregnancy, in group B on day $8^1/_2$ etc., until in group F hyperthermia was applied on day $12^1/_2$ of pregnancy. The total number of pregnant females amounted to 150, of which 53 died during the heat shock, and 75 gave birth to 372 youngsters (of which 22 were born dead).

So far 186 specimens have been examined, of which 48 showed inborn anomalies of the vertebral column. As in the former experiment, two kinds of malformation have been found: (1) Changes in the number of vertebrae in the given region; e.g. 6 instead of 7 cervical vertebrae, 12 (Figure 1) or sometimes 11 thoracic vertebrae instead of 13, 5 lumbar vertebrae (Figure 1) instead of 6. (2) Teratological changes consisting in fusion of the centra and arches of two or more neighbouring vertebrae, presence of split-out centra, and occurrence of wedge-shaped half-vertebrae (Figure 2) that caused scoliosis. Sometimes the

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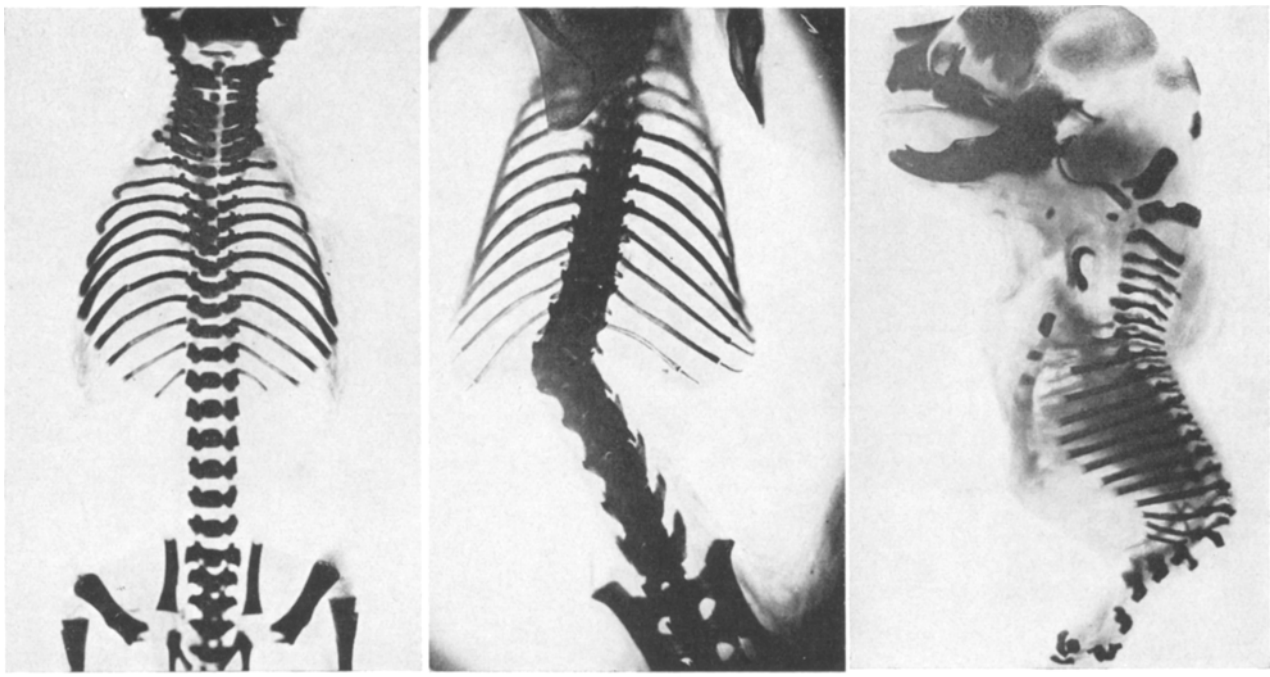

1 2 3

Fig. 1. The offspring of a female, group C. Reduction in the number of vertebrae: in thoracic region 12 instead of 13, in lumbar region 5 instead of 6. Fig. 2. The offspring of a female, group B. The first lumbar vertebra is wedge-shaped (half-vertebra) and causes a distinct scoliosis. Fig. 3. The offspring of a female, grou B. Very distinct teratological changes of the vertebral column and inhibition of the development of its farther portions (such individuals were born dead).

teratological changes were very distinct. In extreme cases they led to inhibition of the development of farther portions of the vertebral column (Figure 3); in such cases, death of the offspring has been observed.

The control series consisted of 300 skeletons of newly born specimens belonging to the same colony, of which only 12 showed anomalies in the structure of the vertebral column. These anomalies consisted of the occurrence of 6 cervical vertebrae in 3 specimens, 12 thoracic vertebrae in 2 specimens, 5 lumbar vertebrae in 4 specimens, and some anomalies in sacral vertebrae in 3 specimens. It may be easily seen that the number of anomalies of the vertebral column found in the control series did not exceed 4%. On the other hand, the anomalies of the vertebral column induced by hyperthermia observed in 25.9% of the animals investigated seem to be sufficient to draw a conclusion that in pregnant mice an increased body temperature induces inborn anomalies of the vertebral column.

The results obtained confirm the hypothesis assumed in the former communication[1]; namely, that in mammals there is a rather close relation between the temperature of the body during the development and the number and arrangement of somites analogous to that reported in fishes and amphibians[3,4].

The anomalies in the structure of the vertebral column induced experimentally resemble some inborn malformations of the vertebral column encountered in man (scoliosis, half-vertebrae etc.[5,6]). Hence, bearing in mind that in pregnant mammalian females an increase of temperature[7–9] may induce some inborn anomalies of brain, eyes, palate, limbs etc., it seems that the increased body temperature during certain stages of pregnancy could be one of the reasons for the anomalies just described.

Zusammenfassung. Trächtige Mäuseweibchen wurden in der Zeit zwischen dem $7^1/_2$ten und $12^1/_2$ten Tag der Gravidität im Hyperthermieverfahren während 20 h auf einer Körpertemperatur von 40–41 °C gehalten. Bis jetzt wurden von 75 Versuchstieren insgesamt 372 Junge erhalten und 186 untersucht. 48 Jungtiere zeigten angeborene Missbildungen der Wirbelsäule: Reduktion der Wirbelzahl, Anomalien der Wirbelkörper, Wirbelbogen sowie der Rippen.

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