

THE INFLUENCE OF THE THYROID GLAND ON THE ANAPHYLACTIC REACTIONS IN ANIMALS

VI. *Influence on Antibody Formation in Guinea pigs
Thyroidectomized and Immunized with S. typhi.*

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The influence of the thyroid gland on the anaphylactic response has been the subject of several papers published in this journal (1, 2, 3, 4, 5). From these studies it emerged, *inter alia*, that there was an appreciable decrease in the antibody content of the serum if thyroidectomy was performed prior to the sensitization with protein antigens. Guinea pigs were used as experimental animals.

In order to find out whether circulating antibodies to bacterial antigen were also affected by thyroidectomy, experiments with guinea pigs were carried out as follows.

MATERIALS AND METHODS

Guinea pigs of both sexes and with a weight of 200-250 g. at the start of the experiments were used in the present study. In one group the thyroid was surgically removed in one stage, and in another group the activity of the thyroid was destroyed by means of the isotope, I^{131} , the procedure being as previously described. In all animals the thyroid function was subsequently checked with tracer doses of I^{131} . If the thyroid function was

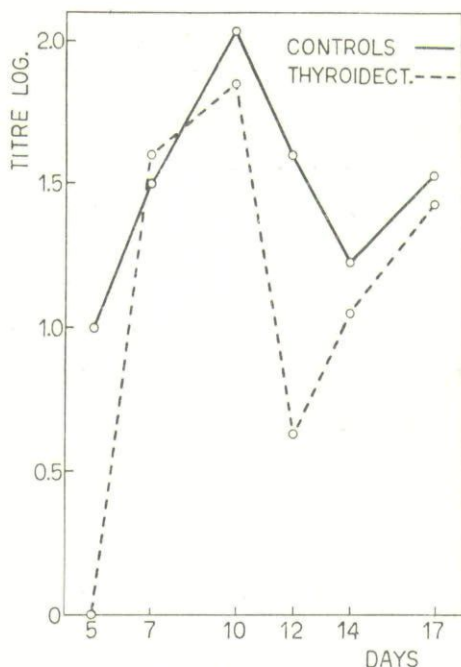


Fig. 1.

Demonstrates the changes in typhoid antibody titre from the 5th to the 17th day after the injection of typhoid antigen in controls and thyroidectomized guinea-pigs. Mean logarithmic values for each day of assay are given.

found to persist in the animals operated upon, even these were treated with I^{131} in a dosage sufficient to abolish the remaining activity. (In the following the term, thyroidectomy, will be used irrespective of whether the activity had been abolished by surgery or isotope treatment). When the thyroid function could be considered satisfactorily abolished, the animals were immunized with *S. typhi* antigen, 0.2 ml. of a suspension containing 10^9 bacteria per ml. being intradermally injected.

The guineapigs were divided into two groups, and from every animal serum was twice collected by cardiac puncture at intervals since the immunization as stated in the tables. Normal animals immunized at the same time served as controls.

The antibody content of serum was determined by agglu-

tionation in tubes¹. Serial twofold dilutions (starting serum dilution usually 1/5) of sera were mixed with equal volumes of a *S. typhi* H antigen containing (2.6×10^8 bacteria/ml.), and the mixtures were kept at 50° C. for one hour and at +4 overnight. The titre is recorded as the negative¹⁰ logarithm of the last serum dilution producing gross agglutination of the antigen. For convenience is then the first dilution (1/10) recorded as 1.

RESULTS

Fig. 1 demonstrates the changes in typhoid antibody titre from the 5th to the 17th day after the injection of typhoid antigen in controls and thyroidectomized animals. Mean logarithmic values (10 log titre) for each day of assay are given. Initially the titre values rise rapidly, as was to be expected. The highest values seem to occur on about the 10th day, then the titres decrease again. The 5, 7, 12 and 14-day assay groups comprise from 3 to 7 animals each, whereas the 10 and 17 day groups comprise 20–24 animals. In 20 controls and 20 thyroidectomies the assay was performed on both occasions in the same animals. In these cases a statistically significant decrease of titre from the 10th to the 17th day could be demonstrated, both in controls and thyroidectomies. (Controls, mean difference = 0.41 ± 0.06 log. units, $t = 6.9^{***}$; thyroidectomies, mean difference = 0.25 ± 0.09 log. units, $t = 2.7^*$).

A comparison between the mean values of controls and thyroidectomies on corresponding days after the antigen injection was performed by means of an ordinary t-analysis. On the 10th and the 12th day the mean values of the thyroidectomized animals could be shown to represent lower values than the controls'. (10th day, Difference = 0.21 ± 0.07 log. units, $t = 2.9^{**}$, d.f. = 44; 12th day, Difference = $0.82 \pm$

¹ Dr. Astrid Fagraeus has kindly performed the antibody determinations, for which I am very grateful, and I am greatly indebted to Dr. A. Sollberger who carried out the t-analysis.

TABLE 1
Agglutination in Immunized Thyroidectomized Guinea-pigs.

Animal no.	Date of thyroidectomy	Date of injection of 10^{11}	Tracer iodine		Date of typhoid injection	Agglutination	
			Date	Uptake		Day after antigen in.	Titre $10 \log$.
12	Oct. 15.1954	Dec. 11	Nov. 17.54 March 21.55	+ o	April 13.55	5 12	< 1 1.3
14	March 23.1955		March 30.55	+	April 13.55	5 12	< 1 1.0
15	Sept. 8.1954	Dec. 11	Oct. 13.54 March 30.55	+ o	April 13.55	5 12	< 1 1
20	Aug. 18.1954	Sept. 9	March 30.55	o	April 13.55	5	< 1
21	Sept. 8.1954	Dec. 11	Oct. 13.54 March 30.55	+ (+)	April 13.55	5 12	< 1 < 1
22a	March 23.1955		Oct. 13.54	+	April 13.55	7 14	1.9 1.3
24	Sept. 8.1954	Dec. 11	Oct. 13.54 March 21.55	+ o	April 13.55	7 14	1.6 1.3
51	Sept. 14.1954	Dec. 11	Oct. 13.54 March 21.55	+ o	April 13.55	7 14	1.0 1.9
70	Sept. 3.1954	Sept. 9	March 30.55	o	April 13.55	14	1.9
5		July 21			Sept. 17.54	10 17	1.9 1.9

13	Sept. 8, 1954			Sept. 17, 54	10	1.6
34a	May 29, 1954	July 21		Sept. 17, 54	17	< 1
23		July 21	Sept. 22, 54	Sept. 27, 54	10	2.2
25		July 21	Sept. 22, 54	Sept. 27, 54	12	1.9
31		July 21	Sept. 22, 54	Sept. 27, 54	17	1.9
50	May 29, 1954		Sept. 22, 54	Sept. 27, 54	12	1.9
4	Sept. 21, 1954		Oct. 2, 54	Sept. 27, 54	17	2.2
16	March 26, 1954	May 16	Aug. 9, 54 Aug. 22, 54 Oct. 15, 54	Oct. 18, 54	12	1.9
			Oct. 13, 54	Oct. 18, 54	17	1.6
32		July 21	Oct. 13, 54	Oct. 18, 54	10	2.5
33	March 15, 1954	July 21	Oct. 13, 54	Oct. 18, 54	17	1.9
65	Sept. 28, 1954		Oct. 13, 54	Oct. 18, 54	10	2.2
34		Aug. 25	Nov. 17, 54	Nov. 26, 54	17	2.2
35a		Aug. 25	Nov. 17, 54	Nov. 26, 54	10	2.5
50a		Aug. 25		Nov. 26, 54	17	1.9
54		Aug. 25		Nov. 26, 54	10	5
					17	4
					10	4
					17	5
					10	6
					10	1.9
					17	1.9

TABLE 1 (cont.)

Animal no.	Date of thyroidectomy	Date of injection of 1st	Tracer iodine		Date of typhoid injection	Agglutination	
			Date	Uptake (%)		Day after antigen inj	Titre 10log.
76	Nov. 26.1954		Jan. 25.55	+	Nov. 26.54	10	1.9
						17	1.9
75a	Nov. 26.1954		Jan. 25.55	o	Nov. 26.54	10	1.9
						17	1.9
80	Nov. 26.1954		Jan. 25.55	+	Nov. 26.54	10	2.2
						17	2.2
72		Aug. 25			Nov. 26.54	10	1.9
						17	1.6
84	Nov. 26.1954				Nov. 26.54	10	1.9
						17	1.6
86	Nov. 26.1954				Nov. 26.54	10	1.9
						17	1.6
22		July 21	Sept. 4.54	o	Sept. 7.54	10	1.9
						10	1.3
10	Aug. 18.1954		Sept. 4.54	o	Sept. 7.54	17	1.3
35		July 21	Sept. 4.54	o	Sept. 7.54	10	1.3
75	Sept. 3.1954		Sept. 4.54		Sept. 7.54	10	1.6
						10	1.0
44	Sept. 4.1954				Sept. 7.54	17	1.0
						10	1.9
61	June 11.1954	July 21	Sept. 4.54	o	Sept. 7.54	17	1.9

TABLE 2
Agglutination in Immunized Normal Guinea pigs.

Animal no.	Date of typhoid. injection	Day after antigen inj.	Titre 10 _{log} .
2	April 13.1955	5	1.9
		12	1.6
4	April 13.1955	5	1
		12	1.6
5	April 13.1955	5	< 1
		12	1.6
20	April 13.1955	5	1.6
30	April 13.1955	7	2.2
		14	1.9
40	April 13.1955	7	< 1
		14	< 1
60	April 13.1955	7	2.2
		14	1.9
3	Sept. 8.1954	10	1.9
4	Sept. 8.1954	17	2.2
		10	1.9
5	Sept. 8.1954	10	1.9
		17	1.6
11	Sept. 17.1954	10	1.9
80	Sept. 27.1954	12	2.5
		17	2.2
81	Sept. 27.1954	12	2.2
		17	1.9
82	Sept. 27.1954	12	2.5
		12	1.9
83	Sept. 27.1954	17	1.6
		10	2.5
70	Oct. 18.1954	17	2.2
		10	2.2
71	Oct. 18.1954	17	1.9
		10	1.9
72	Oct. 18. 1954	17	1.9
		10	2.2
73	Oct. 18.1954	17	1.6
		10	2.5
40	Nov. 26.1954	10	2.2
42	Nov. 26.1954	12	2.5
		17	1.9

TABLE 2 (cont.)

Animal no.	Date of typhoid. injection	Day after antigen inj.	Titre $10_{\log}$.
43	Nov. 26.1954	12	2.8
		17	1.9
44	Nov. 26.1954	12	2.2
		17	1.6
46	Nov. 26.1954	12	2.2
		17	1.9
51	Nov. 26.1954	12	2.2
52	Nov. 26.1954	12	2.2
		17	1.6
53	Nov. 26.1954	12	2.5
		17	2.2
55	Nov. 26.1954	12	2.8
		17	2.2
56	Nov. 26.1954	12	1.9
		17	1.9
60	Nov. 26.1954	12	2.2
		17	1.6
61	Nov. 26.1954	12	2.2
		17	2.2
62	Nov. 26.1954	12	1.9
		17	1.9
12	Sept. 17.1954	12	2.2
13	Sept. 17.1954	17	1.9
6	Sept. 8.1954	12	1.6
		17	1.9
10	Sept. 17.1954	12	1.3
		17	2.5
1	Sept. 8.1954	12	1.9
		17	2.2
2	Sept. 8.1954	12	2.2
		17	2.2

0.30 log. units, $t = 2.7$, d.f. = 9). On the 17th day no difference could be shown to exist in spite of the relatively large number of data. As regards the 5th day, the analysis is difficult owing to the great number of zero values in the thyroidectomy group. However, a simple comparison between

the frequency of zero values in the controls and in the thyroidectomies makes the existence of a difference almost statistically significant ($p = 0.05$).

SUMMARY AND CONCLUSIONS

It might be stated that in both controls and thyroidectomized guineapigs the antibody titre shows an initial rise, culminates about the 10th day after the antigen injection, and is then decreasing. In the thyroidectomized animals the initial rise seems to be somewhat smaller, but the culmination is found roughly to coincide with that of the controls. Also during the following drop it is likely that the values for the thyroidectomized animals are on a somewhat lower level, but towards the end of this stage, when the values for controls and thyroidectomized animals are converging, no difference between them can be established.

Hence, the thyroidectomized animals seem to be somewhat less capable of producing immune antibodies than normal animals, at least for a certain period of the experiment.

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