LETTERS TO THE EDITORS

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Plasma Cellular Reaction and its Relation to the Formation of Antibodies *in vitro*

DURING secondary response, elicited in sensitized rabbits by means of intravenous injections of the homologous antigen, the number of plasma cells in the spleen increased considerably, simultaneously with the formation of antibodies[1]. The cellular reaction was localized almost exclusively to the red pulp, especially after the injection of living *Salmonella typhi* (about 500 millions/kgm.). The spleen was investigated by means of biopsies at intervals during antibody formation; differential counts of imprints were made and histological sections were examined. The stain used was methyl green pyronine (Unna–Pappenheim). In the earliest stages of the reaction, in the first phase of antibody formation, large reticulum cells of characteristic appearance (called transitional cells) presented themselves. One or two days later, immature plasma cells appeared at the places where transitional cells were previously found, and after a further few days mature plasma cells were seen in increasing numbers. There were numerous transitions between the different stages of development. No plasma cells were usually seen in the lymph follicles.

Antibody formation in vitro. Small pieces of spleen tissue, partly from the red pulp, partly from the lymph follicles, were excised in different phases of antibody formation, and their capacity for forming antibodies *in vitro* was investigated. In each tube, containing 300 mgm. of fluid, one or two pieces were cultured. Their weight (wet) was about 0·2 mgm. The culture fluid consisted of normal rabbit serum (3 parts), tyrode solution (2 parts) and isotonic sodium bicarbonate (1 part). A gas mixture, consisting of 80 per cent oxygen, 4·5 per cent carbon dioxide and the remainder nitrogen, was passed into the tubes[2]. The tubes were incubated at 37° for 5–12 hours. The capacity for antibody formation *in vitro* of the red pulp rich in plasma cells proved to be considerably superior to that of the lymph follicles (see Table 1). By serial investigations on the same animal, it was found that the tissue pieces were most active in forming antibodies when the immature plasma cells predominated. The transition from immature to mature cell coincided with a decline in the capacity to form antibodies *in vitro*. Pieces of the same size were excised from other organs rich in R.E.S. Their capacity for antibody formation *in vitro* was investigated and proved to be very much inferior to that of the red pulp of the spleen (see Table 2). Experiments were also made to trace the antigen (living *Salm. typhi*) after intravenous injection. The greatest number of bacteria was found in spleen and liver, less in bone-marrow, and very few bacteria could be demonstrated in lymph glands and thymus. In the spleen the bacteria were found in large numbers in the red pulp, and only small numbers in the follicles.

It is concluded that plasma cells appear in connexion with great antigen stimulation. The antigen incites a conversion and an intensification of the protein production in the reticulo-endothelial cell. From the functional point of view, development culminates in the formation of the immature plasma cell. The further differentiation of the cell, when mature plasma cells appear, marks the transition to a less active state, and the mature plasma cell then becomes the final link in a chain of development, a cell which has already passed its greatest functional activity.

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TABLE 1. COMPARISON BETWEEN THE CAPACITY OF THE RED AND THE WHITE PULP TO FORM ANTIBODIES *in vitro*. THE SPLENIC TISSUE EXAMINED AT DIFFERENT STAGES OF ANTIBODY FORMATION IN THE RABBIT

No.	Days after re-inject.	Serum titre		Duration of culture (hr.)	No. of plasma cells in each tube (1 cell about 0·2 mgm.)	No. of tubes containing 300 mgm. cult. fluid		Geom. mean of titres *in vitro*	
		Day of culture	Preceding day			Red pulp	Lymph follicles	Red pulp	Lymph follicles
S 167	4	1/10,240	1/1,280	12	1	12	12	1/12	0
	7	1/40,960	1/40,960	12	1	12	12	1/3·6	0
S 173	4	1/10,240	1/1,280	12	1	6	7	1/4·8	1/0·3
	7	1/81,920	1/81,920	12	1	7	7	1/3·6	1/0·4
S 186	4	1/5,120	1/640	8	1	10	10	1/4·6	1/0·3
				12	1	13	8	1/8·6	1/0·4
	10	81,920	81,920	12	1	6	6	1/2·8	0
S 175	4	1/640	1/160	8	1	10	10	1/3·7	1/0·8
				12	1	10	10	1/7·5	1/1·6
	8	1/10,240	1/10,240	12	1	11	10	1/0·5	1/0·1
S 190	4	1/1,280	1/80	5½	1	20	10	1/3·3	1/0·4
					2	10	8	1/5·5	1/1·3
S 203	5	1/20,480	1/2,560	8	1	27	20	1/19·7	1/1·4

TABLE 2. THE ANTIBODY FORMATION CAPACITY *in vitro* OF VARIOUS ORGANS RICH IN R.E.S.

No.	Duration of culture	Tissue in each tube (mgm.)	Geom. mean of titres of culture fluids				
			Splenic red pulp	Lymph gland	Thymus	Bone marrow	Liver
S 182	12 hours	0·4	1/30·0	0	0	0	0
No. of tubes			10	10	5	10	10
				L. axill. 1/2·7*			
S 206	5 hours	0·8	1/72·7	L. popl. 0	0	1/1·0	1/1·0
No. of tubes			12	6 each	12	12	12

* Lymph. gland. axill., regional to the subcutaneous agar focus containing antigen, through which the rabbit was sensitized.

[1] Fagraeus, *Nord. Med.*, **30**, 1381 (1946).
[2] Cf. Parker, "Methods of Tis ue Culture" (New York, 1938).