

For the synthetic valuation (FISHER) of several experimental series we have used the χ^2 test of PEARSON:

$$\chi^2 = \sum \chi_i^2 = -2 \cdot 2,3026 \sum \log P_i;$$

P_i being the respective probabilities of finding a value of t equal or higher than the calculated one.

We have used the modification of COCHRAN and COX of test t when the variances of the two samples were significantly different.

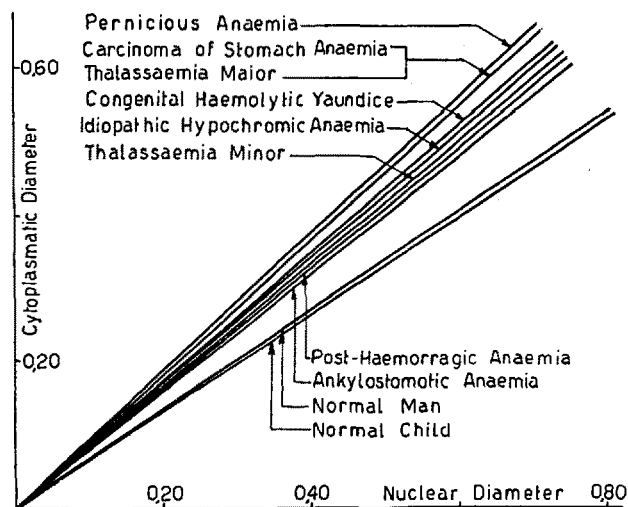
M_1, M_2, S_1, S_2 being the respective averages and sums of the squares of the deviations of the two samples, we calculate

$$\frac{(M_1 - M_2)}{\sqrt{\frac{S_1}{n_1(n_1-1)} + \frac{S_2}{n_2(n_2-1)}}}$$

and compare the result with the level 5% (or 1%) given by

$$\frac{\frac{S_1}{n_1(n_1-1)} \sqrt{t'_{0,05}} + \frac{S_2}{n_2(n_2-1)} \sqrt{t'_{0,05}}}{\frac{S_1}{n_1(n_1-1)} + \frac{S_2}{n_2(n_2-1)}}$$

where n_1 and n_2 are the respective numbers of observations of the first and of the second sample, and $t_{0,05}$ and $t'_{0,05}$ the respective 5% significant t of the first sample (with degrees of freedom = $n_1 - 1$) and of the second sample (with degrees of freedom = $n_2 - 1$).



The figure shows the slopes of the interpolating lines of the cytoplasmic diameter against the nuclear one. Each straight line indicates the average value in one condition studied. The straight lines are made to start from the origin of cartesian axis, i. e. as if the known terms of their equation were null: this was done to make more evident the slope of the straight lines.

Results, reported in the table and in the figure, show that:

(1) The average correlation coefficients (r) of thalassaemia major and minor, congenital haemolytic jaundice, idiopathic hypochromic anaemia, gastric carcinoma anaemia and post-haemorrhagic anaemia show a significant increase as compared with the normal one. On the contrary there is no significant difference between the normal average correlation coefficient (r) and the corresponding ones of pernicious anaemia and ankylostomiasis anaemia.

(2) The average slopes (a) of pernicious anaemia, thalassaemia major and minor, congenital haemolytic jaundice, idiopathic hypochromic anaemia and gastric carcinoma anaemia show a significant increase when compared with the normal one. On the contrary no significant difference is to be found between the normal average slope and the corresponding ones of ankylostomiasis and post-haemorrhagic anaemia.

These results taken as a whole show us that both dimensional nucleo-cytoplasmic correlation and growth of erythroblast are disharmonious not only when the erythropoiesis is induced in an abnormal erythroblastic type, such as the megaloblast of pernicious anaemia, but also when an active erythropoiesis occurs through normoblastic differentiation. For instance, in the case of thalassaemia major and minor, of congenital haemolytic jaundice, of idiopathic hypochromic anaemia, of gastric carcinoma anaemia. Instead in other erythropathies, although the erythropoiesis is altered, an abnormal growth of the erythroblast is not sufficiently demonstrated, as, for instance, in the case of post-haemorrhagic anaemia.

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Riassunto

Sono state condotte ricerche sulla auxologia dell'eritroblasto basofilo del midollo osseo umano normale e di varie eritroblastosi. In particolare si è indagato, durante il periodo dell'intercinesi cellulare, sulla quantità di cui cresce il citoplasma rispetto al crescere di una quantità unitaria del nucleo, valutata in base al coefficiente angolare dell'interpolante lineare del diametro citoplasmatico rispetto a quello nucleare. È stato inoltre indagato sulla correlazione dimensionale nucleo-citoplasmatica.

Le ricerche hanno dimostrato anomalie auxologiche dell'eritroblasto non solo quando l'eritropoiesi segue una linea eritropoietica anormale, quale ad esempio quella megaloblastica dell'anemia perniciosa, ma anche in molte eritroblastosi dove l'eritropoiesi si svolge lungo la differenziazione normoblastica.

Effect of the Reticulo-Endothelial Blockade by Thorotrast on the Development of Normal Heterohemagglutinins in Fowl

The origin of normal antibodies has been the subject of much controversy. LANDSTEINER¹ and HIRSZFELD *et al.*² developed the theory of "serogenesis". According to them, the main factors in the development of normal antibodies are genetic inheritance and age. On the other hand, there are some evidences which suggest that "normal" immune body production may be due to antigenic stimuli and may be from heterologous antibodies. E. g. FORSSMAN³ and BAILEY⁴ demonstrated that intake of certain foods or some infections may provoke production of antishape hemolysins in rabbits. Furthermore,

¹ K. LANDSTEINER, *The Specificity of Serological reactions* (Harvard U. Press, 1945).

² H. HIRSZFELD, L. HIRSZFELD, H. BROKMAN, W. HALBER, and M. MAYZNER, *J. Immunol.* 9, 571 (1924); *Ergebn. d. Hyg.* 8, 367 (1926); *Z. Immunitätsforsch.* 53, 391 (1927).

³ J. FORSSMAN, *Acta path. microbiol. Scand.* 23, 45 (1946).

⁴ H. H. BAILEY, *Amer. J. Hyg.* 8, 398 (1928).

Week	Group No								
	1			2			3		
	Animals alive	Mean Titer	SE of Mean	Animals alive	Mean Titer	SE of Mean	Animals alive	Mean Titer	SE of Mean
Hatching	25	0	0.00	25	0	0.00	25	0	0.00
1	22	0	0.59	20	1	0.94	12	0	0.08
2	20	1	0.33	14	2	0.88	10	1	0.33
3	19	4	1.63	12	3	1.35	8	1	0.38
4	18	16	7.52	11	8	2.97	3	6	2.00
5	16	64	12.25	9	64	17.45	0	—	—
6	12	70	14.1	9	65	17.1	0	—	—
7	12	80	13.2	8	70	14.15	0	—	—
8	11	80	12.4	6	72	18.9	0	—	—
9	11	75	14.0	6	72	18.9	0	—	—

the site of immune body production has recently become the subject of much debate¹.

The aim of the present study was to investigate the effect of reticulo-endothelial blockade by Thorotrast on the development of normal rabbit-heterohemagglutinins in chicks.

The effect of reticulo-endothelial blockade on immunological reactions, immune body production and natural resistance to infections was reviewed by JUNGENBLUT² and JAFFÉ³. Recently GOTH and HOLMAN⁴ described prevention of anaphylactic shock in dogs by Thorotrast. These authors consider this substance as the most powerful reticulo-endothelial blocking agent available.

Rywosch⁵ observed that newly hatched chicks possess no rabbit-hemagglutinins, but these develop gradually within a few weeks.

Seventy-five white leghorn chicks were used for this study. One day after hatching, and thereafter weekly during 9 weeks, 0.2–0.5 ml blood was obtained by heart puncture. Group 2 received 6 ml/kg thorotrast intra-

cardially after each heart puncture. Group 3 received the same amount at intervals of three days, group 1 received corresponding amounts of normal saline. The animals were maintained on Purina Startena mash and water *ad libitum*. The number of chicks alive at each bleeding is shown in the table. Microagglutination was performed by the hanging drop method on micro culture slides and read under the low power of the microscope. Rabbit red blood cells in 2% suspension (always obtained from the same rabbit) were mixed in the relation of 1:1 with the corresponding dilution of chick serum.

The average hemagglutinin titers of all animals alive at each bleeding are shown in the figure and in the table. From these data it is evident that the maximum amount of Thorotrast which may be given without killing the animals has no significant effect on the development of normal heterohemagglutinins.

These results seem to support the theory of "serogenesis" of normal antibody formation. However, because of certain contradictions in reported results of the effect of reticulo endothelial blocking agents on the formation of immune bodies by antigenic stimuli⁴, it is not possible, on the basis of the present study, to conclude that the reticulo-endothelial system plays no role in normal antibody formation.

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Zusammenfassung

Der Kaninchen-Heterohämagglutinin-Titer im Serum von weißen Leghorn-Küken wurde einen Tag, nachdem die Küken ausgebrütet waren, bestimmt. Danach wurde der Titer wöchentlich, während neun Wochen, ermittelt. Wöchentliche intrakardiale Verabreichung von 6 cm³/kg Thorotrast hatte keinen Einfluß auf die Entwicklung von normalen Kaninchen-Heterohämagglutininen. Die gleiche Dosis von Thorotrast erwies sich bei Verabreichung an jedem dritten Tag als toxisch. Die maximal erreichbare retikulo-endotheliale Blockade durch Thorotrast scheint die Entwicklung normaler Heterohämagglutinine nicht zu beeinflussen.

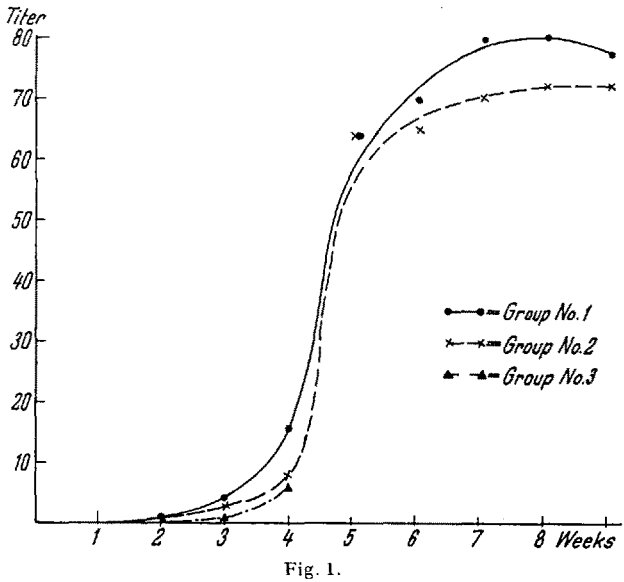


Fig. 1.

¹ A. FAGRAEUS, Acta. med. Scand. Suppl. 204, 1 (1948).
² C. W. JUNGENBLUT, Erg. Hyg. Bakt. Immunitätsforsch. u. Exp. Therap. 11, 1 (1930).
³ R. H. JAFFÉ, Physiol. Rev. 11, 8, 277 (1931).
⁴ A. GOTH and J. HOLMAN, J. Pharm. Exp. Therap. 89, 379 (1947).
⁵ M. RYWOSCH, Zbl. Bakt. 44, 468 (1907).

¹ C. W. JUNGENBLUT, Erg. Hyg. Bakt. Immunitätsforsch. u. Exp. Therap. 11, 1 (1930). – R. H. JAFFÉ, Physiol. Rev. 11, 8, 277 (1931).