SCIENTIFIC PROCEEDINGS.

Peking Branch.

Peking Union Medical College, China, October 25, 1926.

3288

Relation of the Reticulo-Endothelial System to the Formation of Amyloid.

H. SMETANA. (Introduced by J. R. Cash.)

From the Department of Pathology of the Peking Union Medical College, Peking, China.

In a recent article Domagk[1] states that he succeeded in producing amyloid in the spleen and liver within 10 minutes, by intravenous injection of a large quantity of living cocci into a normal mouse. Furthermore, that he could produce amyloid within 2 minutes in the spleen and liver of a mouse, which had several injections of dead cocci previous to the final intravenous injection of living cocci. He also stated that this amyloid is formed by the phagocytic endothelial cells, and describes changes in these cells before and during the appearance of amyloid in their immediate neighborhood. This amyloid did not react to any of the specific stains (gentian violet or iodine), but showed metachromasia when stained with cresyl violet and giemsa.

In repeating these experiments we injected congo red intravenously shortly before killing the animals, in order to mark out the amyloid. In previous experiments this vital staining has proven to be the most delicate and reliable method for demonstrating the earliest traces of amyloid.[2]

We failed to find any traces of amyloid with this method in two series of animals, each consisting of 10 mice.

Many morphological pictures seen in experimental amyloidosis are inconsistent with the idea that amyloid is formed by the precipitation of a substance circulating in the blood stream. They sug-

gest rather its local formation. Experiments were therefore undertaken to find any possible relation between Reticulo-Endothelial Cells and amyloid.

Amyloid was produced in mice by daily injections of a 5 per cent solution of nutrose, as described by Kuczynski,[3] and the R. E. C.* were marked out by an intravenous injection of India ink before starting the daily injections of nutrose.

In studying the mutual relations between amyloid and R. E. C., this substance was found to be located exactly in those places where R. E. C. are most abundant: around the follicles of the spleen, around the periportal veins, and in the intermediate zone of the liver lobules, in the glomeruli, in the tissue between the tubules of the kidneys, and in the intestinal villi.

It also was found that amyloid invariably appears first in the form of small isolated patches, which suggests its local formation. This patchy formation of amyloid, and its presence in the immediate neighborhood of the R. E. C., marked out by India ink or trypan blue, supports the idea that it might be formed, actively, in some way, by these cells. Small patches of amyloid in the intermediate zone of the liver lobules are almost always surrounded by cells containing ink, which separate the amyloid from the liver cells, and which make these patches appear to be in the lumina of capillaries. Since R. E. C. are located in the capillaries, these pictures also support the idea that R. E. C. may in some way be responsible for the presence of amyloid. Otherwise amyloid, were its position outside the wall of capillaries, could not be surrounded by R. E. C., which contain ink injected several weeks previously.

Commonly one sees separate contiguous small patches of amyloid surrounded by liver cells. Cells which contain ink granules separate these patches from the liver cells and from each other. This seems to indicate the mechanism by which contiguous streaks of this material are formed. This contiguity is seen in advanced cases.

Certain morphological changes in R. E. C., before and during periods of amyloid, suggest severe damage of these cells. It is possible that amyloid is formed only by damaged or altered cells.

Organs of mice, in which India ink was injected intravenously, after amyloid was already developed, showed a marked decrease, and even absence of ink-containing cells in areas where amyloid was present. Identical pictures were seen in organs of mice injected repeatedly with trypan blue after the development of amyloid.

These findings indicate that there are either no R. E. C. in these

* Reticulo Endothelial Cells.

areas, or that these cells have been markedly altered physiologically. Other parts of the liver and spleen, where there was no amyloid present, showed the usual amount of phagocytic cells loaded with India ink.

There is no evidence that R. E. C. are primarily converted into amyloid. Were this true, the patches of amyloid would constantly contain large numbers of ink granules. This, however, is not the case. R. E. C. are secondarily involved in this process; they become partly and completely surrounded by amyloid and are found embedded in this substance. Finally, they die leaving only their phagocytized ink granules in their places.

In order to determine whether it is possible to influence the time of the appearance of amyloid by blocking the R. E. C. with India ink, series of mice were repeatedly injected intravenously with India ink, while amyloid was produced by subcutaneous injections of nutrose. Control animals were injected with nutrose only. In 5 out of 6 series the appearance of amyloid was markedly delayed in mice whose R. E. C. were filled with India ink. In one series, animals with and without ink showed amyloid at the same time; in this series the animals had received only one intravenous injection of India ink.

It is true that these experiments have only limited value. In the first place it is impossible to block the R. E. C. completely; secondly, there is considerable irregularity in the time necessary for the experimental production of amyloid, even with standardized injections of nutrose. But since the attempted blockade of R. E. C. did result in delay of the appearance of amyloid, this fact, though in itself inconclusive, at least supports the other observations leading to the idea that R. E. C. are in some way concerned in the formation of amyloid.

---

[1] Domagk, G., *Virchows. Arch. Path. Anat.*, 1924, cclii, 594.

[2] Smetana, H., *Johns Hopkins Bull.*, 1925, xxxvii, No. 6, 383.

[3] Kuczynski, M., *Virchows. Arch. Path. Anat.*, 1922, ccxxix, 185.

[4] Benhold, *Dtsch. Arch. klin. Med.*, cxlii, 32.