

*Microcythæmia; a Morbid Condition of the Blood hitherto undescribed.*<sup>1</sup> By PROFESSORS VANLAIR and MASIUS.

IN this memoir the authors designate by the name of "microcythémie" a disease of which they believe the principal character to consist in a special alteration of the blood morphologically expressed by the presence of an enormous number of red corpuscles different from the ordinary red corpuscles. To these they assign the name "microcytes," from their small size, and the name *microcythæmia* is formed on the model of *leucocythæmia*. The observation of one case furnished the authors with the chief groundwork of their paper, and we shall follow them in prefixing a short relation of it to our summary of the memoir.

A young married lady, after the birth of a child, began to suffer from the following symptoms—pain in the splenic region, cardialgia, painful vomiting, general jaundice, and constipation. No gall-stones; fæces not pale. In addition great weakness and gradual enlargement of the spleen. Subsequently, aphonia without labial or laryngeal paralysis, followed by incomplete loss of power in, first upper, then lower, limbs. The jaundice gradually disappeared. The paralysis was more marked in upper than lower limbs, and was accompanied by atrophy, with occasional intense pain. There was no sign of want of co-ordinating power. The jaundice and most of the symptoms improved, but the paralysis and muscular atrophy increased.

The most remarkable change was, however, in the blood.

The blood was examined four times, once immediately after venesection, the other times some hours after, but having been carefully preserved in hermetically sealed tubes. A considerable quantity was obtained by deep incisions and scarifications.

The macroscopic appearance of blood was quite natural, as was also its coagulation.

Microscopically, it presented the following appearances:—The white corpuscles slightly less numerous than ordinarily the case, and none exceeding  $\cdot 01$  mm. in size. The red corpuscles also natural in colour, size ( $\cdot 006$  to  $\cdot 008$  mm.), and shape. They some of them formed rouleaux, others became spinous. The plasma was colourless. However, in the meshes of the irregular network formed by the rouleaux were seen a

<sup>1</sup> 'De la Microcythémie,' par MM. Vanlair et Masius, Professeurs à l'Université de Liège. Bruxelles, 1871.

large number of the bodies which the authors call "microcytes." They are characterised, not only by their small size, but also by certain peculiar properties.

Their *shape* is perfectly spherical, and their surface perfectly smooth, even when examined with very high powers. Their *diameter* is in the immense majority of cases  $\cdot 004$  mm., perhaps one in a hundred rather smaller, but they never fall below  $\cdot 003$  mm. The *colour* is the same as that of the red corpuscles, but, perhaps, a little darker. They are highly refracting, and thus contrast with the ordinary disks. They do not agglomerate like the ordinary corpuscles, but remain isolated between the masses of the latter. They are extremely mobile, being easily displaced by the smallest movement of the cover glass. As to their *nature*, these bodies are certainly not themselves nuclei, and do not contain nuclei. Their *number* was found in the earlier observations made to be at least equal to that of the ordinary red disks. In later observations the number of *microcytes* was greatly in excess. At the last examination, indeed, there were found to be not more than one or two normal red corpuscles to a hundred microcytes.

Besides the typical form of microcytes just described, there were found certain intermediate forms; for instance, some were as large as  $\cdot 005$  mm. in diameter, with some appearance of a central depression and without the brilliancy of the microcytes; these were seen especially at the commencement of the disease. Others, again, were as brilliant as the ordinary form, but measured  $\cdot 005$  mm. in diameter. These were chiefly seen at the last examination of the blood.

In general, no alteration was observed in the blood while under observation, but once only, on the last occasion when the blood was examined, the number of spherical globules visibly increased, but these spherical bodies formed out of the discoid were always rather larger than the previously existing microcytes. After maceration for two days no rouleaux are seen, and most of the discoid corpuscles become spherical, but they may still be distinguished from the microcytes. The action of heat on the microcytes is similar to the effect it produces on the red disks; in both cases segmentation occurs, but less readily in microcytes than in the ordinary disks. Distilled water has no effect on their form or size, but slowly decolourises them. Acetic acid and dilute solution of potash dissolve the spherical as they do the discoid corpuscles.

The urine showed no special abnormality, beyond a large quantity of uric acid.

The subsequent history of the patient is remarkable. About a year after the disease had reached its climax, nearly two years after its commencement, a marked improvement took place in all the symptoms, and on examination of the blood it was found to contain not a single microcyte, the red and white corpuscles being normal, and present in normal proportions, the only noticeable fact being that the red corpuscles were rather small.

Analysing the morbid phenomena presented by this case, the authors first discuss the *enlargement of the spleen*. This was clearly not due to amyloid degeneration, since this did not show itself in any other organ; nor was it the hypertrophy which is accompanied by leukæmia, the latter symptom being absent. It was equally distinct from the enlargement due to intermittent fever, and from the temporary swelling observed in typhoid or other febrile affections; in fact, it appeared to be an affection *sui generis*.

The same might be said to be true of the enlargement and subsequent atrophy of the liver, this being not referable to any of the ordinary causes of atrophy of this gland.

As to the small globules seen in the blood of this patient, they were decidedly different from the ordinary red globules—first, in their smaller size; secondly, in their spherical shape. Bodies somewhat similar have been seen by various observers. Lehmann first noticed that the red globules of the portal vein were smaller and more spherical than those of other parts of the circulatory system, and unusually resistant to the action of water and acetic acid. Funke saw similar globules in the splenic vein. Max Schultze described red globules smaller than the ordinary ones, and of spherical shape, either crenated or granular, from the blood of several persons; and this observation was confirmed by Klebs, who described also some small spherical globules having a uniform surface; none of these observations, however, precisely accords with that of the author's. Schultze was unable to decide with perfect certainty whether the globules observed by him were pre-existent in the blood, or altered after removal from the vessels. The authors have, however, been able to determine positively that their "microcytes" existed as such in the blood.

The distinctive characters of microcytes are summed up as follows:—Perfectly spherical form, remarkable permanence of shape, power of resistance to reagents, constant isolation in the field of the microscope, excessive refractive power, smallness and uniformity of size. In attempting to define their physiological nature two suggestions are made—that

they may be transitional forms between the white and the red globules, or that they may be a stage in the retrograde metamorphosis of the red globules. The former supposition is obviously untenable, since forms intermediate between white and red corpuscles are known, and are different from microcytes; and it seems, therefore, more probable that microcytes are atrophic forms, that is to say, red corpuscles which are in course of destruction, the more so as the artificial destruction of red corpuscles by heat, pressure, or desiccation, produces very analogous forms. Thus, the white corpuscles would come to represent the infancy of the blood-elements, the red corpuscles their adult stage, and microcytes the period of old age.

The cause of so grave an alteration of the red corpuscles remains still obscure, but the spleen and liver both suggest themselves as possible seats of the change. Among many conflicting opinions as to the function of the spleen, several authorities agree in attributing to it a destructive action on the red globules, while a more general consensus of opinion ascribes the same function to the liver. The theory which the authors found upon the case observed by them is as follows:—That the spleen, though not destroying the red corpuscles, alters them and prepares them for destruction, converts them, that is to say, into microcytes, which are further destroyed in the liver, though in neither place does the change affect more than a small proportion of the corpuscles.

Supposing that the spleen should undergo hypertrophy, and its action on the blood-corpuscles be proportionally intensified, the number of microcytes sent into the circulation by the splenic vein will be proportionally increased; and this increase will be greater still if there should be a simultaneous atrophy, that is to say, diminished action of the liver, which would thus destroy a smaller number of microcytes. The proportion of these in the blood might then become quite enormous. This theory is thought to explain more simply than any other the fact that the composition of the blood remains almost unaltered after the extirpation of the spleen. If, normally, the only action of the spleen on the blood is to produce *microcytes*, and the normal function of the liver be to destroy them, while the latter organ remains sound the blood will not betray by its composition whether the number of microcytes formed be large, small, or actually none at all, that is to say, whether the action of the spleen be vigorous, feeble, or *nil*.

The authors have made numerous researches on the blood of men and animals to test the truth of their views.

In human blood they find that a very small number of microcytes are often present in a state of health, but that their existence is not constant.

In various diseases they have found a few microcytes, as, for instance, in typhoid fever, in puerperal fever of a pyæmic character, in one case of acute rheumatism, and in acute pneumonia; among chronic diseases, in cirrhosis of the liver and constitutional syphilis; but the number was always inconsiderable.

Observations on the blood of animals showed that, while birds and frogs had no microcytes, they were found normally in mammalia (especially the rabbit and the guinea-pig), in the blood of the splenic vein, except when the animal was killed fasting, while they were constantly absent in the blood of the hepatic vein. These facts are the main support of the theory that microcytes are formed in the spleen and destroyed in the liver.

The authors further analyse the remaining symptoms presented by the case which form the groundwork of their treatise. The jaundice they believe to have been hæmatogenic, only owing to the presence in the blood, not of bile-pigment, but of a substance derived from the blood—the *hæmapheic* icterus of Gübler. The urine was also found to contain in excess various substances which might be derived from retrograde metamorphosis or oxidation of blood-corpuscles. The paralysis they believe to have been due to affection of the nerve centres.

The simultaneous occurrence of these various symptoms the authors believe to be attributable to no known disease, and hence they feel themselves justified in regarding *microcythæmia* as a true morbid entity. Further, they have the record of a precisely similar train of symptoms having occurred previously to a sister of their patient, although in that case, which was fatal, nothing was known of the state of the blood.