poietin production, it appears important that the length of stimulation, the size and place of the lesion, age difference, species, etc. be as nearly comparable as possible before any ultimate evaluation can be made[13,14].

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Zusammenfassung. Es wurde die Wirkung von künstlichen, bilateralen, elektrolytisch gesetzten Läsionen in verschiedenen Bezirken des Hypothalamus auf die Bildung von Erythropoietin untersucht: Jugendliche (entwöhnte) Ratten reagieren nicht gleich wie erwachsene Ratten, und die verschiedenen Kerne des Hypothalamus beeinflussen die Erythropoietin-Bildung verschieden.

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Variation of the Fine Structure in Granulocytes of Great Apes

As part of a continuous study on comparative primate hematology, the leucocyte ultrastructure of the Great Apes was investigated with the electron microscope. The studies were performed on peripheral blood obtained from chimpanzees, gorillas and orangutans. Investigations by light microscopy have shown that white cell morphology of the Great Apes is very similar to, and almost indistinguishable from, morphology of human leucocytes, although certain typical morphological characteristics have been found[1]. On the other hand, different histochemical properties have been demonstrated in neutrophilic leucocytes of man, gorilla, chimpanzee and orangutan[2]. The present study showed the presence of characteristic differences in the ultrastructure of gorilla and orangutan granulocytes.

Blood was obtained from 3 animals of each species (*Gorilla gorilla, Pan troglodytes, Pongo pygmaeus*) from the femoral vein by free flow through plastic tubing into a heparinized, siliconized centrifuge tube. Cells were prepared for electron microscopic study by routine methods[3] with some modifications. Osmium tetroxide or glutaraldehyde were used for fixation and sections were stained in saturated uranyl acetate solution in 20% alcohol and lead citrate. Examination of sections was made in a Siemens Elmiscop I, electron microscope.

At least 1000 cells were examined from each species, and the following number of pictures were taken for further examination: gorilla, 109 pictures from 105 different cells; chimpanzee, 242 pictures from 200 different cells; orangutan, 106 pictures from 95 different cells. The final magnifications varied from × 4000 to × 45,000.

The *neutrophilic* leucocytes from gorilla and chimpanzee were indistinguishable from each other and similar to human neutrophils, as described by LOW and FREEMAN[3] and others[4]. The cytoplasm was well filled with specific granules which had a limiting membrane. 2 kinds of granules were consistently present: larger, round or ovoid granules with a very dense content and smaller, elongated rod-like granules of somewhat lower density. The orangutan neutrophils showed the same characteristics. However, in addition to the 2 kinds of specific granules, a third type of granule was consistently present. These granules measured up to 0.7 μ were rod-like or spindle shaped and were surrounded by a membrane. Characteristically, their content was not homogenous; as in the other types of specific granules, but consisted of numerous fibers or needles running parallel to each other from end to end in the long axis of the granules. Occasionally these fibers were densely packed, forming crystal-like densities located centrally in the granule (Figure 1). This type of granulation seems to be a morphological characteristic of the orangutan neutrophil, as it has not been found in neutrophils of other Great Apes, nor has it been found in neutrophils of selected Old World monkeys (Cercopithecideae) or in neutrophils of New World monkeys (Ceboideae)[5]. The granules can also be demonstrated after glutaraldehyde fixation. On morphological grounds alone it can be said that they are distinctly different from the oval azurophilic and the specific elongated granules characterized in neutrophils by previous authors[6–8]. Since these 2 types of granules are equally present in orangutan neutrophils further histochemical studies may reveal additional differences and characteristics.

The *eosinophilic* leucocytes of the orangutan were indistinguishable from human eosinophils. In addition, however, the cells of this species usually showed one or more dark inclusions of irregular shape with lipid-like staining characteristics. In light microscopy, the orangutan eosinophils show characteristic vacuoles if fixed in methanol and stained with Wright-Giemsa stain. These vacuoles are conceivably lipid, and identical or related to the lipid-like bodies found in electron microscopy. These structures are not seen in human eosinophils nor are they commonly present in eosinophils from other primate species. The gorilla eosinophil differs from all other eosinophils in the structure of the specific eosinophilic granules. The matrix of the granules is darker than in eosinophilic granules of

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other species, and crystal-like inclusions are often absent or not discernable. The typical needle-like structure was present in only 25 out of 453 granules (Figure 2). Chimpanzee eosinophils showed considerable variation in presence or absence of crystals, but some crystal-like inclusions were usually discernable. For the Great Apes, the almost consistent absence of crystal-like inclusions in eosinophilic granules seems to be a characteristic of the gorilla eosinophil.

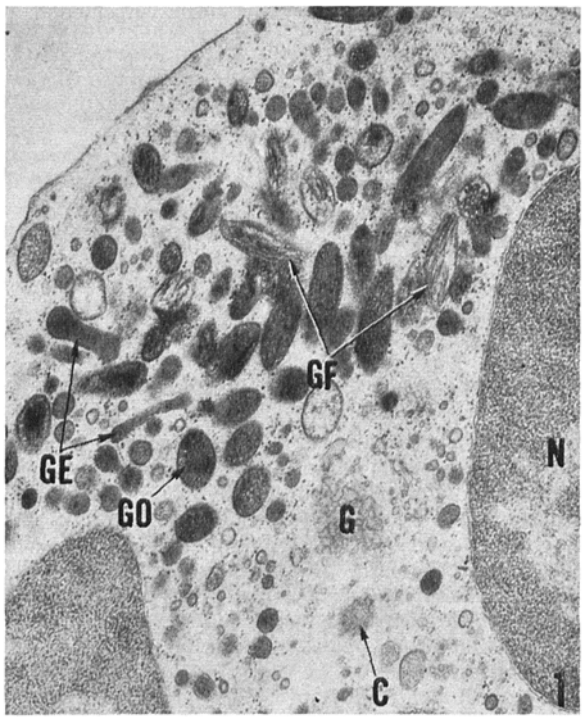

Fig. 1. Orangutan: neutrophil leucocyte with specific granules. GE, elongates granules; GO, oval granule; GF, 'fiber granules' (not seen in other species); G, Golgi apparatus; C, centriole; N nucleus. × 21,000.

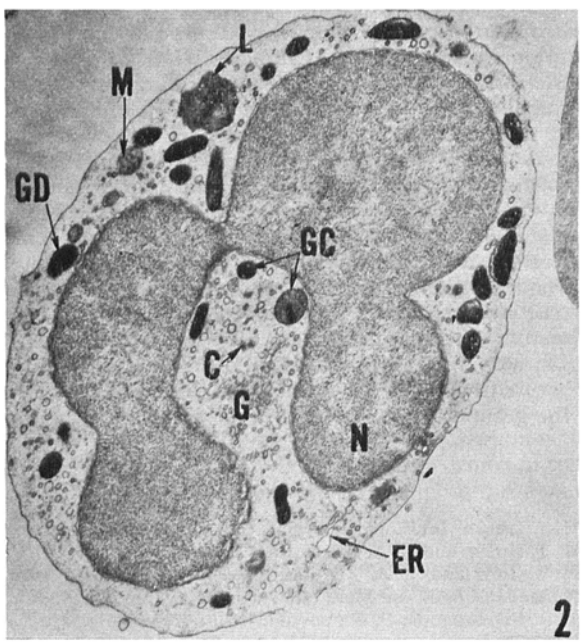

Fig. 2. Gorilla: eosinophil leucocytes with specific granules. GD, dense eosinophilic granule (predominant type of granulation in gorilla, 95%); GC, eosinophilic granules with crystal-like inclusions (5% in the gorilla, predominant type of granulation in other species); G, Golgi apparatus; C, centriole; ER, endoplasmic reticulum; M, mitochondrium; L, lipid-like substance; N, nucleus. × 10,500.

Basophilic leucocytes were not found in this study and the structure of lymphocytes, monocytes and platelets of these species will be described separately[5].

The interpretation of these findings is not obvious at the present time. Variation in fine structure of eosinophilic granules such as seen in gorilla eosinophils is not uncommon and has been observed in other primate species[5]. On the other hand, the fibrillar granules of the orangutan neutrophil are unique and have not been described in other species. Orangutan neutrophils differ from other Great Apes' neutrophils in that they show a very high alkaline phosphatase activity[2]. Whether the histochemical differences are related to the differences in ultrastructure needs further evaluation.

The ultrastructure of the 'fiber' granules in orangutans is somewhat reminiscent of the ultrastructure of 'Auer bodies' found in acute forms of myelogenous leukemia[9]. It has been claimed that the formation of Auer bodies occurs parallel with changes from the usual acid pH of the granules[10]. Consequently, it may be speculated that some of the orangutan granules present pH conditions predisposing the formation of these structures. It is likely that these granules may eventually find a place within the lysosomal concept. Further histochemical studies are needed to elucidate this question and to decide whether the granules may be considered as primary lysosomes or whether they represent very special forms of secondary lysosomes[11,12]. The presence, however, of these structurally very differentiated granules in the orangutan and their absence in other species is of phylogenetic significance. The findings indicate that the orangutan falls outside of the generalized pattern observed in the fine structure of neutrophil leucocytes of other species and it may suggest increased specialization of the orangutan out of the mainline of phylogeny[13,14].

Zusammenfassung. Elektronenmikroskopische Untersuchungen der Granulocyten anthropoider Affen ergaben Unterschiede in der Struktur der eosinophilen Granula und eine bisher unbekannte fibrilläre Granulationsform in Orangutan Neutrophilen.

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