Döhle Bodies Associated with Uncomplicated Pregnancy

By Max R. Abernathy

The appearance of Döhle bodies within the leukocytes of normal pregnant women has recently been described. Döhle bodies, found in the late stages of granulocyte maturation, are presently considered vestiges of basophilic cytoplasm of the progranulocyte, not true cytoplasmic inclusions. Döhle bodies stain blue with Wright's stain and are readily visible in the pinkish cytoplasm of the mature granulocyte (Fig. 1). They stain red with pyronin methyl-green because of their RNA content. Döhle bodies are usually 1 to 2 microns in diameter but may be as large as 5 microns, round or oval, irregular in shape, and most often lie near the periphery of the cell. The present report comprises (1) a careful study by light microscopy of serial blood films from 15 uncomplicated gravid women, (2) screening of blood films from 500 uncomplicated pregnancies, and (3) a review of the literature of Döhle bodies.

Materials and Methods

Fifteen pregnant women without complications, except iron deficiency, were selected for study and were closely followed as outpatients. These 15 patients included 5 primiparas and 10 multiparas. Complete blood counts (hemoglobin, hematocrit, total leukocyte count, and 100 cell differential) were obtained at frequent intervals during pregnancy. The hemoglobin and hematocrit did not prove to be pertinent and will not be discussed. The number of Döhle bodies present per 100 granulocytes was recorded. A total leukocyte count and 100 cell differential was performed on each woman during active labor, at 30 minutes postpartum, at 4 days postpartum and again 6 to 8 weeks later. The total leukocyte count was performed on blood anticoagulated with EDTA. Unanticoagulated blood was used exclusively for the Wright-stained blood films; stained films from blood anticoagulated with EDTA, heparin and potassium oxalate were unsatisfactory. Single blood films from 500 uncomplicated pregnant women were stained with Wright's stain and examined. In some instances, blood films were stained with pyronin methyl-green and examined. These 500 women were representative of all stages of pregnancy and up to 6 weeks postpartum. A control study was performed on 500 clinically normal nonpregnant women.

Results

In blood films of the 15 patients followed throughout pregnancy, Döhle bodies were evident at the time of the first examination at approximately 2 months gestation, throughout pregnancy and as long as 6 to 8 weeks postpartum. The number per 100 granulocytes increased in parallel with the antepartum and postpartum leukocytosis (Fig. 2). Persistent neutrophilia was present in all stages. Of the 500 random blood films examined from pregnant women, all but 9 revealed the presence of Döhle bodies in from 2 to 5 per
cent of granulocytes counted. In over 500 clinically normal nonpregnant women used as a control, no Döhle bodies were seen within the granulocytes on fresh blood films.

The use of anticoagulants for the study of Döhle bodies was contraindicated. Döhle bodies in blood films made from anticoagulated blood were less distinct and not as sharply outlined as opposed to their usually sharp definition in unanticoagulated blood. All anticoagulants studied tended to give a “smudged” or “faded” appearance to the Döhle bodies. The number of Döhle bodies seen in anticoagulated blood seemed to be less than the number seen in unanticoagulated blood. The presence of Döhle bodies seen with Wright stain was confirmed by staining with pyronin methyl-green, which showed the nucleus green and the Döhle bodies red.

**DISCUSSION**

Döhle in 1911 described the inclusion bodies in the granulocytes of 30 cases of scarlet fever. Similar inclusions had been described previously by Wechselmann and Hirschfeld in a patient with myeloid leukemia and by May in 1909 in a young woman with an anemia. The early investigators described the Döhle bodies as blue inclusions seen in mature granulocytes stained with Wright's stain. Rheder in 1944 proved, by using ultraviolet photographic techniques, that Döhle bodies were not true cytoplasmic inclusions but integral parts of the cytoplasm representing a disorder of the maturation of myeloid cells.

There have been scattered reports of the presence of Döhle bodies in various infections. They have been observed transiently in erysipelas, diph-
Fig. 1B.—Döhle bodies in neutrophilic leukocyte accompanied by toxic granulation. Wright stain, magnification × 1250.

Döhle bodies have been observed in severe thermal burns; they are present about the second day in cases affecting greater than 13 per cent full thickness skin loss, but their appearance is rare in patients with less than 2 per cent full thickness skin loss. Cytotoxic agents have been reported to produce high percentages of Döhle bodies which persisted during long term chemotherapy.

Laszlo has been unsuccessful in demonstrating Döhle bodies by electron microscopy. He surmises that they represent a type of developmental anomaly that can be produced by many causes. He has observed that Döhle bodies often accompany toxic granulation of neutrophils, and occasionally he has observed Döhle bodies in immature granulocytes and in monocytes. Jordan and Larsen recently reported Döhle bodies by electron microscopy in ultrastructural studies of the leukocytic inclusion bodies in the May-Hegglin anomaly. They state that a given section for electron microscopy samples only about 3 per cent of the total volume of a leukocyte. This may explain the negative electron microscopy findings by Laszlo and us.

Oski et al. have shown that Döhle bodies contain no lipid, glycogen, mucopolysaccharide or DNA. Their further studies showed that they were not phagocytized thrombocytes or were not related to a plasma component. Disappearance after incubation with ribonuclease substantiated their RNA content.

The presence of Döhle bodies in the neutrophils of patients with the May-
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Fig. 2.—Ratio of Döhle bodies per 100 granulocytes to total leukocyte and granulocyte counts. Each point represents the mean determined from 15 uncomplicated pregnancies.

Hegglin anomaly\textsuperscript{15,16} and also in their nonsymptomatic relatives, represents a characteristic finding in this condition. The appearance of Döhle bodies in pseudo Pelger-Huet cells aids in differentiating these cells from true Pelger-Huet cells.\textsuperscript{17} Döhle bodies have been observed in mature neutrophils in the Chediak-Higashi anomaly.\textsuperscript{18}

Other leukocytic inclusions that are seen in leukocytes are the Snapper-Schneid bodies.\textsuperscript{19,20} The Snapper-Schneid bodies are observed after therapy with amidine drugs, used in the treatment of multiple myeloma or plasmacytoma. They may be differentiated from Döhle bodies in that they appear only in peripheral and marrow plasmacytes; they contain amidine plus ribose nucleic acid and are presented as multiple inclusions.

It is extremely difficult to explain the appearance of Döhle bodies in normal pregnant women. If we accept the theory that these cytoplasmic inclusions are products of a granulocytic maturation defect, then their incidence may be related to the increased granulopoiesis of pregnancy.\textsuperscript{21}

**SUMMARY**

Döhle bodies have been described in the neutrophilic leukocytes of uncomplicated gravid women. Of 500 blood films screened from uncomplicated pregnancies, all but 9 exhibited Döhle bodies. Serial studies of 15 uncomplicated pregnancies, followed throughout all 3 trimesters and for 6 to 8 weeks post-
partum, repeatedly showed Döhle bodies. No Döhle bodies were found in the leukocytes of the 500 normal nonpregnant women used as a control.

The appearance of Döhle bodies in uncomplicated pregnancy and their relationship with the inclusions found in various states are unexplained.

**SUMMARIO IN INTERLINGUA**

Corpores de Döhle es describite, occurrente in le leucocytos neutrophilic de feminas in pregnantia noncomplicate. In 500 frottis de sanguine examinate ab subjectos in pregnantia noncomplicate, omnes exhibiva corpores de Döhle, con 9 exceptiones. Studios serial de 15 pregnantias noncomplicate, continuante a transverso omne le 3 trimestres e durante 6 e 8 septimanas post parto, monstrava reptetitement le presentia de corpores de Döhle. Nulle corpores de Döhle esseva trovate in le leucocytos de 500 normal feminas nonpregnante qui esseva usate como grouppo de controlo.

Le appariation de corpores de Döhle in pregnantias noncomplicate e lor relation con le inclusiones trovate in varie status clinic remane sin explication.

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