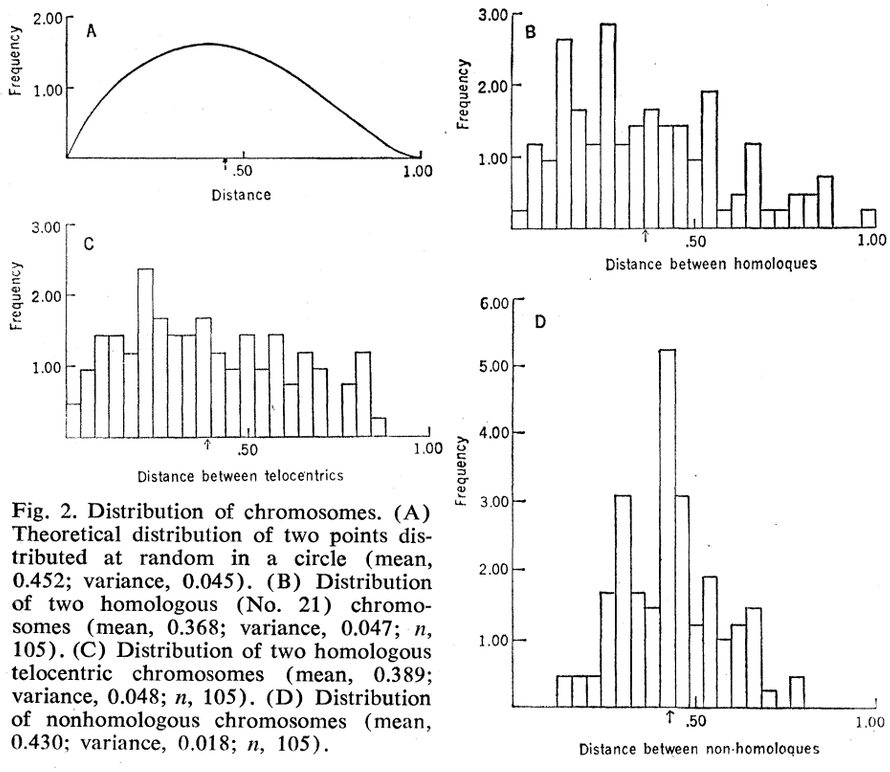

Fig. 2. Distribution of chromosomes. (A) Theoretical distribution of two points distributed at random in a circle (mean, 0.452; variance, 0.045). (B) Distribution of two homologous (No. 21) chromosomes (mean, 0.368; variance, 0.047; n, 105). (C) Distribution of two homologous telocentric chromosomes (mean, 0.389; variance, 0.048; n, 105). (D) Distribution of nonhomologous chromosomes (mean, 0.430; variance, 0.018; n, 105).

mize the differences due to squashing.

If we consider the nonhomologous chromosomes as two points distributed at random in an area, the expected frequency distribution can be calculated by the substitution of a series of values from 0 to 1 in Hemmersley's formula (Fig. 2A). The mean and variance of such an expected distribution were 0.452 and 0.045, respectively. The Wilcoxon matched pairs signed-ranks test was used for the statistical comparisons of these distributions of homologous and nonhomologous chromosomes (*4*).

The frequency distribution for nonhomologous chromosomes was not significantly different from the expected frequency distribution ($P < .05$). The mean and variance were 0.430 and 0.018, respectively. The close fit to the theoretical curve verifies the assumption that the nonhomologous chromosomes were distributed at random in the flattened cell.

The homologous chromosomes were not distributed at random (Fig. 2, B and C). The frequency distributions obtained for the telocentrics (Fig. 2C) and the pair of chromosomes 21 (Fig. 2B) were skewed to the right, resulting in a lower mean value. The mean and variance were 0.368 and 0.047 and 0.389 and 0.048, respectively, for the homologs of chromosome 21 and the telocentrics. The frequency distributions for homologs were significantly different from the frequency distribution for nonhomologous chromosomes ($P < .05$). Furthermore, the frequency distribution for homologous chromosomes 21 did not differ significantly from the frequency distribution of the pair of telocentrics.

There is association of the homologs of chromosome 21 and of the telocentrics in somatic cells of *Avena sativa*. It is probable that such attractions apply to all the homologous chromosomes of the oat complement. Somatic association appears to be a more widespread phenomenon in plants and animals than previously thought although its cytological and physiological significance is still obscure.

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Cerebral Hemorrhage in Relation to Birth Asphyxia

Abstract. *The brains of monkeys and guinea pigs asphyxiated at birth, completely resuscitated, and killed at various times thereafter revealed no petechial hemorrhages. However, when postnatal distress and other factors leading to a moribund state occurred, the brains revealed petechial hemorrhages.*

Postmortem examinations of human infants who die soon after birth sometimes reveal petechial cerebral hemorrhages. Pathologists generally believe that asphyxia is the cause of these hemorrhages. Some medical examiners, especially in France, entertain the possibility of homicide by suffocation when an infant is discovered dead in its crib with its face up and its brain contains petechial hemorrhages. Whether asphyxia at birth is actually the cause of cerebral hemorrhages cannot be established in human subjects, but experiments in animals have shed light on the question.

The subjects of the present research were guinea pig and monkey (*Macaca mulatta*) fetuses of known gestational age and newly born infant monkeys. Cesarean sections were performed under local anesthesia, usually near term. Either the fetus with its placenta and membranes was removed intact or the fetal membranes were opened, a small rubber bag containing saline solution was slipped over the fetal head, and the umbilical cord was clamped. These techniques induced asphyxia, the duration of which was varied from less than 5 minutes to more than 21 minutes, resuscitation becoming necessary in monkeys asphyxiated for 8.5 minutes or more.

Events accompanying asphyxia at birth are as follows: The blood Po_2 quickly approaches zero, Pco_2 rises, and pH declines. Initially there is a brief tachycardia and a few rhythmical respiratory movements following which the fetus executes some mass movements and then enters into primary apnea which, in the absence of anesthesia, lasts less than a minute. The heart rate promptly slows, but blood pressure at first increases and then gradually declines. With exhaustion of oxygen from the blood, glycogen stores are called upon for tissue respiration and the fetus begins to gasp at two to four gasps per minute, which end, on the average, 8.5 minutes after the start of asphyxiation. Secondary, or termi-

nal, apnea leads to death in 8 or 9 minutes more unless resuscitation is successfully applied. If oxygen under positive pressure is admitted to the lungs in time, the heart action improves promptly, but a state of areflexia persists for about twice the length of time of the asphyxiation. The course of events in the guinea pig fetus is similar, although the time to last gasp is shorter (4 to 6 minutes).

The effects of birth asphyxia were much the same in the two species. The neuropathology has been described and illustrated (*1*). The lesions were remarkable for their focal character, bilateral symmetry, and absence of hemorrhages. In no instance was a hemorrhagic lesion encountered in the brain of a monkey asphyxiated during delivery, successfully resuscitated, and deliberately killed later on. This statement is based on a survey of serial sections of brains of 73 monkeys, killed from a few days to 10 years after resuscitation. Nonhemorrhagic focal lesions likewise were encountered in brains of asphyxiated and resuscitated guinea pigs that were deliberately killed at various times after birth (*2*). Additional degenerative changes and brain atrophy developed in the course of time, but signs of hemorrhage were absent (*3*). Furthermore, fetuses asphyxiated to death had no hemorrhages in their brains.

Asphyxia at birth did not produce petechial cerebral hemorrhages. Then what does do so? How can we account for the little hemorrhages in the brain of human infants that had been asphyxiated?

Petechial hemorrhages were encountered in brains of some asphyxiated newborn animals that had been resuscitated and managed to live for a little while (even weeks or months) but then for various reasons failed to survive or were killed just before they would have died (*4*). These were encountered in both species. Six infant monkeys that became depressed and moribund 1 day to more than 4 months after they had been resuscitated following asphyxiation for 10 to 16 minutes at birth were found to have petechial hemorrhages of recent origin with blood corpuscles outside the vessels (Fig. 1). Since no phagocytic reaction to the hemorrhages had set in, I doubt that these hemorrhages had been produced by the immediate events of asphyxiation but believe that they had come just before death. Another monkey survived 10 days, and petechial hemorrhages had formed early enough to permit a reaction to develop; many darkly stained nuclei of microglia or phagocytes appeared around the hemorrhagic foci.

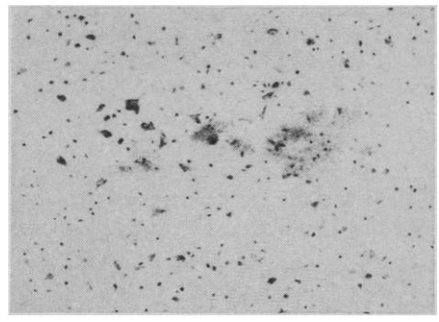

Fig. 1. Petechial cerebral hemorrhages in a monkey that had been asphyxiated for 11 minutes at birth and developed status epilepticus on day 3, at which time it was killed.

Conditions conducive to formation of hemorrhages over the surface of the brain or within it include elevating the intrauterine pressure experimentally. Oxytocin was given to pregnant monkeys restrained in the supine position near term. This did not lead to vaginal birth, so delivery was completed by cesarean section. Congestion of superficial vessels of the brain and hemorrhages from these vessels were found in two fetuses that were examined postmortem. In another, that lived for 1 day after oxytocin had been used, there were hemorrhages in the globus pallidus on either side (Fig. 2).

Hemorrhages thought to have been caused by trauma were observed in a monkey that had a spontaneous breech delivery during which the head had been retained and required manual extraction. There were superficial gross hemorrhages as well as microscopic hemorrhages in the brain.

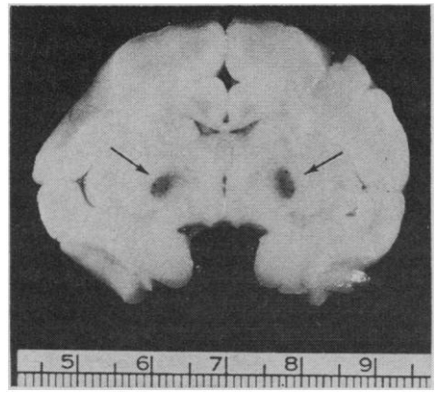

Fig. 2. Sections through the brain showing hemorrhages (arrows) in the globus pallidus of a 1-day-old monkey delivered by cesarean section after oxytocin had been administered to the mother to induce uterine contractions.

Finally, small, recent, superficial cerebral hemorrhages of unexplained causes were encountered in three monkeys that had been asphyxiated for 15 minutes at birth and resuscitated without incident. One died at 18 months of age while an electroencephalogram was being recorded during photic stimulation (*5*). The other two were killed at 8.5 months of age while in apparently good health. Thus, the hemorrhages could hardly have been due to the initial birth asphyxia.

There was another unexplained case in which the infant monkey was thought to have fallen some time before it was killed at 8 days of age. It had an extradural hemorrhage. Possibly the other hemorrhages of unknown etiology also came about from head injuries inflicted when the brain-damaged animals had tried to run, for nearly all the monkeys were unsteady and lacked coordination of extremities in locomotion (*6*).

The hemorrhages of traumatic origin in monkeys were similar to those sometimes encountered in human infants delivered with forceps through a narrow birth canal, but neither injury of the monkey's falx cerebri nor bleeding below the foramen magnum were seen. Apparently only in those monkeys receiving oxytocin and in the breech delivery were pressures on the fetal head great enough to do harm.

These studies lead me to conclude that asphyxia neonatorum is not the direct cause of hemorrhages in the brain of the newborn infant. An explanation of the presence of hemorrhages in infant animals and human subjects following moribund states and their absence in brains of animals deliberately killed while in good health following resuscitation is not immediately forthcoming. However, theoretical explanations have been proposed. Cammermeyer (*7*) some time ago discussed the agonal nature of cerebral ring hemorrhages, employing the term "agonal nature" in its broadest sense, including the entire period of dying. He suggested that poor oxygenation with ischemia when the blood pressure fell during the moribund state had a deleterious effect on the walls of small blood vessels which could then no longer sustain the increased pressure due to the shift of blood from arteries to veins at the moment of heart arrest.

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6 October 1969

Neutrophils: Their Role in the Formation of a Tick Feeding Lesion

Abstract. *Dogs infested with adult* Rhipicephalus sanguineus *were given nitrogen mustard to reduce leukocyte numbers. In the treated animals the tick lesions were insignificant, lacking the collagen destruction found in untreated hosts, but the ticks engorged normally. Feeding results from tick secretions causing vascular trauma and is independent of tissue damage associated with inflammatory responses.*

Some authors have suggested that the feeding lesions of ticks result from extra-oral digestion through the action of cytolysins in their salivary secretions (*1*). However, a study of the development of the feeding lesions caused by *Boophilus microplus* suggested that "specific vascular damage results from the saliva of the tick while tissue damage is caused by the host response" (*2*). This hypothesis was based on the finding that collagen destruction beneath the mouthparts of the tick was preceded by an intense infiltration of polymorphonuclear neutrophil leukocytes (PMN), a finding also noted with other Ixodidae. This infiltration is similar to that of the Arthus and Schwartzman reactions (*3*) where it is accepted that the intense infiltration of the involved tissues by PMN's leads to necrosis. Under conditions of polymorphonuclear leukopenia, necrosis does not occur (*3*).

To study the possible role of PMN in tick feeding, a leukopenia was induced by the administration of nitrogen mustard in four dogs infested with *Rhipicephalus sanguineus*.

Intravenous injections of mustine hydrochloride (Boots Pure Drug Co.) in distilled water (1 mg/ml) were given to two dogs at a rate of 1.75 mg/kg, while two other dogs received 2.0 mg/

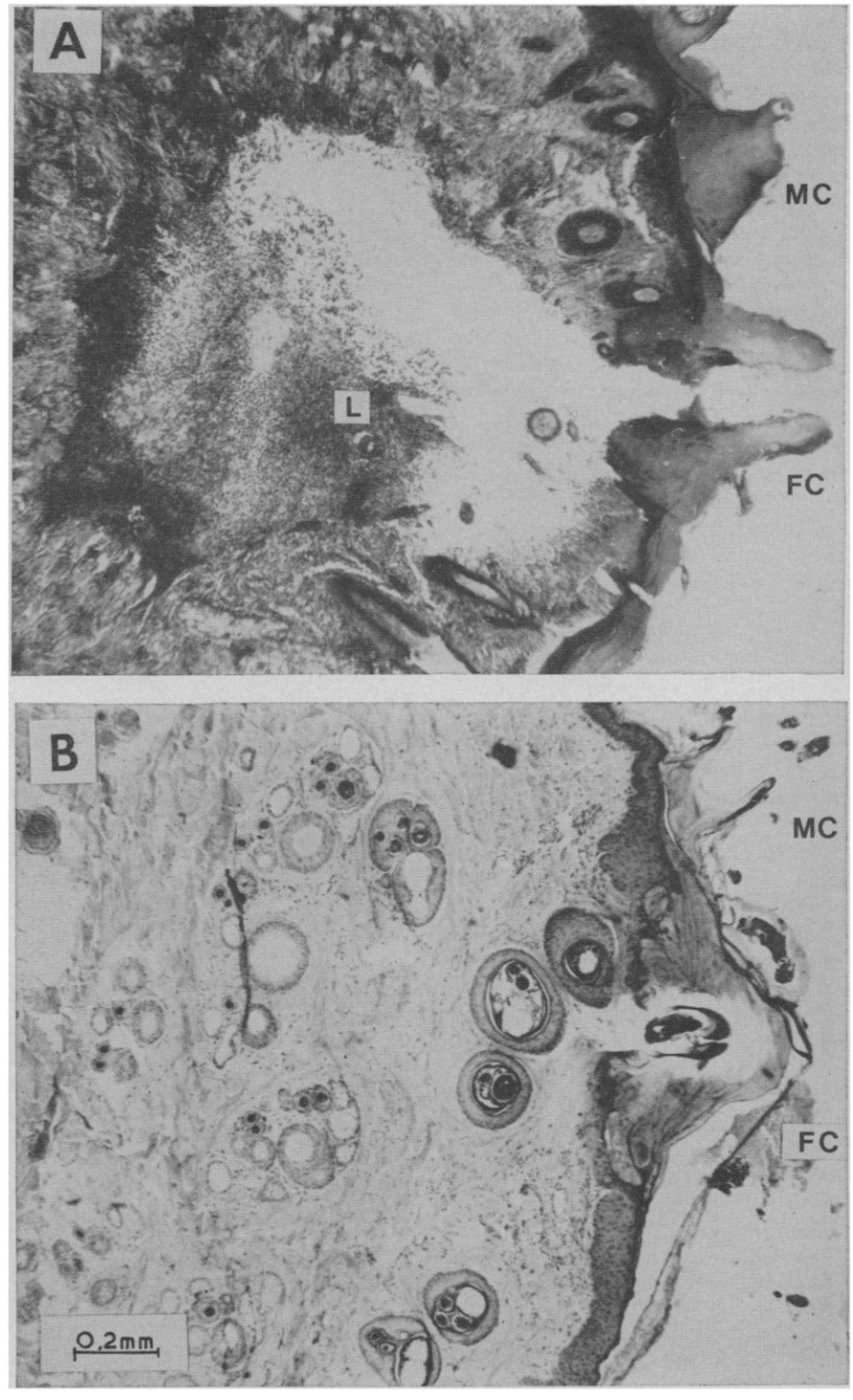

Fig. 1. Sections through the skin of dogs at sites of attachment of engorged females with associated males of *Rhipicephalus sanguineus*. (A) On a normal untreated dog. (B) On a dog treated with nitrogen mustard. *MC*, Cement of male tick; *FC*, cement of female; *L*, lesion.