corticoids without a corresponding increase in either testoids or folliculoids.

*Summary.* In gonadectomized animals treated with 10% formalin solution there occurred a marked hypertrophy of the adrenal glands, but no significant change in the size of the accessory sex organs (vaginal smear and preputial glands in the female; seminal vesicles and prostate in the male). It is concluded that the adrenal cortical hypertrophy, so characteristic of the alarm reaction, is not accompanied by increased sex hormone production.

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## 13901

## Effects of Anoxia at Birth on Central Nervous System of the Guinea Pig.

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Studies on intrauterine respiration, respiratory changes at birth and tolerance by the newly born of anoxia have been reviewed elsewhere.[1] It has been observed that manifestations or cerebral pathology and impairment of the intellect are frequently associated with histories of cyanosis and apnea at birth.[2,3] Some investigators have cautioned that nerve cells of the young may be even more susceptible to damage by anoxia than those of the adult. These and similar clinical studies have been questioned because they were based on selected cases, and fully adequate controls were not available.[4] In the present experiments in guinea pigs with litter-mate controls, the thesis that asphyxia neonatorum can elicit irreparable destructive changes in the central nervous system has been tested.

The abdomen of the animal at or near term was anesthetized with 1 cc of a 1% solution of procain hydrochloride. No other anesthetic was employed. One fetus was delivered immediately through a midline incision to serve as a control. The uterine vessels were then clamped or the umbilical cords of the remaining fetuses were compressed through small incisions in the uterus.

Varying degrees of anoxia were induced in 103 animals. Fifty-eight of them were delivered just before or just after intrauterine respiratory movements, induced by the anoxia, had ceased. Survivors (38%) were those which suffered no anoxial apnea and required no resuscitation. Forty-five guinea pigs were delivered after 6 to 21 min of anoxia, after the fetal heart had become slow and often after it could no longer be palpated. Resuscitation was accomplished in 71% of them by inflating the lungs with oxygen or oxygen containing 10% carbon dioxide. The gases were administered from small rubber bags attached to hypodermic needles which were inserted into the trachea. Respiration was simulated by compressing and releasing the trachea above the needle. Resuscitation was accomplished in a few minutes to more than an hour; the time required was not consistently related to the duration of anoxia. These animals exhibited characteristic symptoms of asphyxia pallida; namely, apnea, atonia, bradycardia, relaxation of anal sphincters, and cold pale skin.

*Results.* All experimental animals, including those in which anoxial apnea had not

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1 Windle, W. F., *Ann. Rev. Physiol.*, 1943, **5**, in press.

2 Schreiber, F., *J. A. M. A.*, 1938, **111**, 1263.

3 Clifford, S. H., *J. Pediat.*, 1941, **18**, 567.

4 Galaway, C. E., in discussion of Schreiber's paper.[2]

been reached, exhibited symptoms of central nervous system damage lasting from a few hours to more than a month. All showed motor weakness and tremors, were unable to get onto their feet during the first hour or more after respiration had been established, and when they did right themselves, usually held the head to one side tending to fall in that direction. They rarely cried and did not respond to bright flashes of light or loud sounds. In contrast, the 90 controls were alert, cried and righted themselves in a few minutes although many were slightly tremorous and weak for a few minutes to an hour.

Pronounced and persistent symptoms resulted in 40 animals. Partial flaccid paralysis was more commonly observed in the hind than in the forelimbs. In one instance, a picture of complete spinal transection was seen. Decerebrate states were observed in many animals after respiration had been established. The spasticity was more marked in the fore- than in the hind limbs and was sometimes accompanied by opisthotonus. Recovery was more rapid than in cases of flaccid paralysis and was usually complete within 24 hr. In some animals it lasted more than a week. Persistent tremors and fortuitous convulsive movements were commonly encountered. The facial as well as the limb muscles were involved in some animals. Rhythmical running movements often occurred in the early phase of recovering from anoxia. Incoördination of muscular effort was observed in nearly all experiments. Ataxia frequently persisted for several days and occasionally persisted a week or longer. Recovery from motor impairment was highly variable, but usually seemed to be complete in a few days. Some animals remained partially paralyzed until they died or were killed a week to 10 days after birth. Most of them showed no evidence of motor disturbances after two weeks.

Sensory functions appeared to be affected in varying degree after anoxia at birth. During the early hours after resuscitation, many animals were hyperirritable. Touching the nose, limbs or body often led to convulsions or fits of running movements. Irritability usually subsided in an hour or 2 and by the second day the guinea pigs exhibited impairment of sensation. They were less responsive to tactile and painful stimuli than their normal litter-mates and some appeared to have lost cutaneous sensations to a marked degree. Most animals lost the startle response to sharp sounds.

Somnolence was observed in some of the experiments. The animals which had been anoxemic closed their eyes and lay quietly in the cage for many minutes at a time during the first one to 3 days. They would go to sleep while standing, the head would drop, and they would topple over before awakening. Reduced activity levels were encountered even 3 to 4 weeks after birth when animals were tested in a simple maze.

The behavior of all experimental and control animals was observed daily from birth until they died or were killed 1 day to 8 weeks later. Even after motor symptoms were no longer evident it was possible to observe behavior differences by critically comparing the animals which had been asphyxiated with their litter-mates. The experimental guinea pigs were less irritable, more docile and less aware of changes in the environment than the controls. The experimental animals were undisturbed by new situations, *e.g.*, a maze or problem box, in contrast to their litter-mates which often showed marked frustration.

The brains of all specimens were preserved and are being studied histologically. Great variation in histological changes have been encountered in 17 specimens compared with their normal litter-mates. Histopathology was questionable or slight in 6 animals subjected to less than 8 min of anoxia. Definite, often marked, changes were present in all others. Generalized necrosis of brain and spinal cord with chromatolysis, edema, small hemorrhages and ventricular enlargement appeared during the period from 2 to 5 days after birth. Glial proliferation and loss of nerve cells, especially in pyramidal layers of the cerebral cortex, was observed between 5 and 9 days; and generalized atrophy together with glial scars marked the older specimens (14-43 days). The most severe pathology

was not encountered in those specimens subjected to the longest periods of anoxia. The sites of damage varied widely from experiment to experiment.

Comparison of the present results with those in adult animals[5,6] reveals points of difference which are attributable to characteristics of the young animal. The nerve cells of the newly born appear to be much less vulnerable than those of the adult and withstand anoxia for greater lengths of time. There seems to be less specificity in respect to anoxial damage in the newborn than in the adult.[7]

[5] Weinberger, L. H., Gibbon, M. H., and Gibbon, J. H., Jr., *Arch. Neur. and Psychiat.*, 1940, **43**, 961.

[6] Thorner, M. W., and Levy, F. H., *J. A. M. A.*, 1940, **115**, 1595.

[7] Kabat, H., and Grenell, R. S., *Anat. Rec.*, 1942, **82**, Sup. p. 33.

*Summary.* Anoxia induced at birth invariably produced symptoms of neural damage. Transient shock, tremors, ataxia, and incoördination were not usually associated with impaired behavior or brain pathology. More than 8 min of anoxia lead to such symptoms as decerebrate states, marked ataxia, convulsions, paralysis, hyper- and hypoesthesia and somnolence, correlated in some cases with behavioral changes. Highly variable nonspecific devastation of brain and cord tissues, occasional hemorrhages, gliosis and generalized atrophy were encountered.

All experiments were controlled with healthy litter-mates and permit the conclusion that neonatal asphyxia (asphyxia pallida) may induce irreparable fortuitous destruction of large or small regions of the brain.

## 13902 P

## Response to Murine Poliomyelitis Virus (Lansing Strain) of Mice on Different Levels of Thiamin Intake.*

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The following is a preliminary report on the relation of thiamin intake to the response of mice inoculated with the Lansing strain of murine poliomyelitis virus.[1] This investigation is part of a long-range program for the study of the relation of diet to resistance to infection.

In each of the 4 experiments summarized here, litters varying from 21 to 31 days of age were split among the groups being compared. Each mouse (except one uninjected group in Experiment I) was injected intracerebrally with 0.03 ml of a 0.5% suspension of mouse brain in saline. Normal mouse brain was used for the controls. Mouse brain infected with the Lansing strain of mouse-adapted poliomyelitis virus served as the virus inoculum. This amount of virus corresponded to between 10 and 100 fifty-percent-mortality doses.

Previous experience had shown that 100 $\mu$g of thiamin per 100 g of diet (called diet 100) cover the needs of the growing mouse and that 10 $\mu$g per 100 g of diet (called diet 10) lead to signs of deficiency within 15 days.

The first 3 experiments, totaling 646 mice, failed to show any significant difference between mortality of groups on diet 100 inoculated with virus and those on diet 10 inoculated with virus, injected with normal brain, or uninjected. The incidence of paralysis, on the other hand, was markedly greater in the high-thiamin than in the low-thiamin groups inoculated with virus.

Averaging the 3 experiments (each of

* Aided by a grant from The National Foundation for Infantile Paralysis, Inc.

[1] Armstrong, C., *Pub. Health Rep.*, 1939, **54**, 2302.