

Careful observation of this rule in treating trauma to the head will save many patients who are now killed by too precipitate operating while they are still in a badly shocked condition.

An increase in intracranial pressure, then, is of paramount importance as an indication for operation in injuries involving the brain. From the foregoing we learn that there is a normal intracranial pressure of from 6 to 10 mm. Hg., depending upon the existence of a normal relationship between the secretion and absorption of the cerebrospinal fluid. The cerebrospinal fluid is secreted by the choroid plexus, and distributed for absorption throughout the spinal and cerebral subarachnoid space. From this space it is chiefly—in fact almost wholly—absorbed into the venous circulation. A rise in intracranial pressure occurs when either the rate of secretion is increased, or the rate of absorption interfered with. A rise in the pressure of the cerebral venous circulation interferes with the rate of absorption of the cerebrospinal fluid. This rise may be produced in a variety of ways varying from a more or less temporary congestion of the meninges, to large extra or intra-dural blood clots, and subarachnoid, subpial, or intra-cortical hemorrhages. Depending upon the location and extent of these hemorrhages, localizing symptoms, such as reflex changes, paralyses, etc., may be produced. Depending on the amount of increase of the cerebrospinal pressure systemic symptoms involving the pulse and respiratory rates, blood pressure, changes in the eye grounds, and mental state may be produced. All of these objective symptoms are inconstant and variable, and the determination of their degree cannot be carried out with any accuracy. The degree of rise of intracranial pressure, on the other hand, can be measured with absolute accuracy, and the amount of the increase above the normal gives a constant and invariable indication as to what operative procedure must be undertaken to correct the intracranial pathology. Intracranial pressure as measured by the Landon Spinal Manometer, reading above 10 and below 16 mm. Hg. calls for repeated lumbar puncture with drainage of sufficient cerebrospinal fluid to reduce the pressure to normal. Readings above 16 mm. Hg. call for decompression, preferably subtemporal. No individual suffering from an injury to the brain should be either treated or examined while in a state of surgical shock, and no such patient who can be demonstrated to have reached the final stage of intracranial hypertension—namely oedema of the medulla—should be operated upon, as the mortality in this latter class of case is 100% regardless of the treatment instituted. It is dangerous and often fatal to postpone treatment on a patient suffering from intracranial hypertension until X-rays of the skull are available. They can give no pertinent information that is not already at hand, and have no bearing on the operative indications of the case.

#### CONCLUSIONS.

1. The indications for operation in injuries involving the brain are three: compound fracture of the skull, depressed fracture of the skull, and a rise in the intracranial cerebrospinal fluid pressure.
2. The intracranial cerebrospinal fluid pressure depends on the relation between the secretory powers of the choroid plexus and the absorptive powers of the cerebral venous circulation.
3. Intracranial hypertension may and often does cause death in the absence of any injury to the bony coverings of the skull.
4. All cases that have received or that are suspected of having received an injury to the brain, no matter how slight, should, as soon as they have recovered from their surgical shock, have the pressure of their cerebrospinal fluid measured, and the treatment should be based primarily upon this finding alone.

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#### CONCERNING THE TYPE OF INJURY TO RENAL EPITHELIAL CELLS WHICH INCREASES THE SUSCEPTIBILITY OF THE CELLS TO THE ACTION OF THE GENERAL ANESTHETICS.

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SEVERAL years ago certain studies<sup>1, 2</sup> were made concerning the relative toxicity of uranium nitrate in animals of different age periods. The observation was made that uranium nitrate, when given in a constant quantity per kilogram, was more toxic for old animals than for young animals and puppies. There occurred in

the old animals a more marked disturbance in the animals' metabolism and, furthermore, the kidney injury in the old animals was of a severer type than could be demonstrated in the kidneys of young animals and puppies. The characteristic difference in the pathology of the kidney in these animals of different ages was the amount of stainable lipid material which appeared in the renal epithelium. The puppies and young dogs showed stainable lipid material in the form of dust-like particles and small droplets in the epithelial cells of the loops of Henle, while the older animals showed large droplets and fused masses of such material in this location and also much stainable lipid in the highly specialized secretory cells of the convoluted tubules.

In later publications,<sup>3, 4, 5</sup> there has been shown to occur a marked difference in the ability of the animals of the two age groups to form urine and to respond to various diuretic solutions when the animals of the different age periods had been poisoned by uranium nitrate and anesthetized by ether, chloroform or by Gréhan's anesthetic. The young animals and puppies, during a period of anesthesia which lasted from one hour to two hours and forty-five minutes, formed urine and, furthermore, the kidneys of these animals remained responsive to the stimulation of various diuretic solutions as caffeine, theobromine and theocin. The group of old animals, on the contrary, during a similar period of anesthesia, either formed less urine per minute or urine formation ceased. In such animals the urine-forming value of the above-mentioned diuretic solutions was negative. That part of the kidney mechanism on which these substances act failed to respond to the stimulation. This lack of response on the part of the kidney is not due to any failure in the systemic blood pressure, of the anuric and non-responsive animals, nor is it due to any lack of response on the part of the peripheral vascular mechanism of the kidney to these solutions. The pathological changes in the kidneys of the anuric animals, which differentiates them from the kidneys of the young animals that form urine and respond to diuretic solutions, is found in the renal epithelium. In the former group of animals, in which the use of uranium had led to a marked accumulation of stainable lipid material in the epithelium, the anesthetic has induced changes leading to the death of these cells. In the puppies and young animals in which, following the use of uranium, there was less accumulation of stainable lipid in the epithelium, the changes of degeneration following the anesthetic are either absent or slight in extent. Death of the cells does not occur.

In more recent investigations<sup>6, 7, 8</sup> studies have been made of the amount and distribution of stainable lipid material in the renal epithelium of naturally nephropathic dogs, and of the susceptibility of the kidneys of these animals

to the general anesthetics. These studies have shown that the primary injury to the kidney in such animals takes place in the glomeruli, the tuft of capillaries located at the site of origin of each uriniferous tubule. The injury to these structures results in the formation of connective tissue between the capillary loops, the walls of which become thickened and finally obliterated. The earliest evidence of injury which can be detected in the renal epithelial cells lining these tubules is an accumulation of stainable lipid material in the cells of the loops of Henle and, especially, in the secretory cells of the convoluted tubules. When kidney tissue from such animals, stained for lipid material, is compared with kidney tissue from normal animals that serve as controls, the difference in the amount and location of the stainable lipid material is striking. In the kidneys of normal animals such material is only found as dust-like particles and droplets in the loops of Henle. It has not been demonstrated in the convoluted tubule epithelium. In the naturally nephropathic animals stainable lipid material is found in the loops of Henle as large masses, which may be of such size as to obscure the structure of these cells, and such material is, furthermore, found as granular particles and droplets in the convoluted tubule epithelium. Following the establishment of this difference in the amount and location of stainable lipid material in the renal epithelium of naturally nephropathic animals, as contrasted with the stainable lipid content of renal epithelial cells in normal animals, both types of animals were anesthetized by ether or chloroform in order to ascertain if any relationship existed between the amount of lipid material in the renal epithelium of the kidney and the susceptibility of these cells to the action of the anesthetics. The normal control animals of these experiments have continued to form urine during the period of anesthesia, and when the kidneys were subjected to the action of such diuretic solutions as caffeine, theobromine, 5. per cent. glucose and 0.9 per cent. sodium chloride solutions, there developed an increase in urine formation.

The naturally nephropathic animals that were anesthetized by the same anesthetics for the same length of time have shown a marked decrease in urine formation as compared with the control animals or they have ceased to form urine. When such animals are given the above-mentioned diuretic solutions, the solutions are found to have less effect than they have in normal animals. In those naturally nephropathic animals that were rendered anuric by the anesthetics these solutions are ineffective. No urine formation occurs. A histological study of kidney tissue obtained from the two groups of animals shows that the renal epithelium in the normal control animals has been unaffected by the anesthetics. The cells show no distinct evidence of degeneration. The renal epithelium

in the naturally nephropathic animals, which was shown to contain a great increase in the amount of stainable lipid in comparison with the normal epithelium, has shown, following the period of anesthesia, marked degeneration characterized by edema, vacuolation and death.

From the foregoing analysis of the experimental data presented in this paper, the following summary appears allowable.

The earliest evidence of injury to renal epithelium which is induced by uranium nitrate consists in an increase in the amount of stainable lipid material in these cells. The amount of such material that accumulates in the epithelium is influenced by the age of the animal. In old animals there is a greater accumulation of such material in renal epithelial cells than occurs in young animals and puppies. When animals from these age groups are anesthetized by chloroform, ether or by Gréhant's anesthetic, the severity of the action of the anesthetic on the renal epithelium shows a parallel with the amount of stainable lipid material that can be demonstrated in such cells prior to the use of an anesthetic. The kidneys of old animals, in which the use of uranium has resulted in a marked accumulation of stainable lipid, show very marked changes of degeneration from the use of the anesthetics. The kidneys of the young animals and puppies, in which less stainable lipid has accumulated in the epithelium, show little or no injury from the anesthetics.

A study of the kidneys of naturally nephropathic dogs indicates that the primary injury to the kidney develops in the glomeruli. The earliest evidence of the secondary injury to the renal epithelium consists in a marked accumulation of stainable lipid material in these cells and, especially, the secretory cells of the convoluted tubules. When such naturally nephropathic animals are anesthetized by chloroform or ether, and the effect of these anesthetics on the kidney is contrasted with the effect of the same anesthetics on the kidneys of normal control animals, a parallel is found between the toxic action of the anesthetics for the two groups of animals and the amount of stainable lipid that can be demonstrated in the renal epithelium. In the kidneys of the naturally nephropathic animals, in which the amount of stainable lipid has greatly increased in the renal epithelium secondary to the glomerular injury, the anesthetics induce an early degeneration and death of these cells, and urine formation is arrested. In the normal control animals, in which only a small amount of stainable lipid can be demonstrated in the loops of Henle, such degenerative changes do not occur, and these animals form urine during the period of anesthesia.

Some twenty years ago Hans Meyer<sup>9, 10</sup> and Overton<sup>11</sup>, working independently, developed a theory, the so-called Meyer-Overton Law,

which is used to explain the entrance of certain narcotic and anesthetic substances into the cells of the central nervous system. These investigators were able to show that the affinity which the methane group of anesthetic substances possessed for the central nervous system was dependent upon the partition coefficient of these substances between the watery blood plasma and the lipoids of these cells. As the solubility of the anesthetic substance increased for the lipid material of the cell it became of greater anesthetic value.

From the observations which have been made in the present study concerning the stainable lipid content of renal epithelial cells, the Meyer-Overton Law would appear to apply to cells in this location as well as in the central nervous system. The investigation indicates that, following the accumulation of lipid material in the renal epithelium, these cells, on account of their increased lipid content, take up more of the anesthetic substance than do normal cells and, as a result of more of the anesthetic substance entering the cells, degenerative changes develop which impair or suspend the function of these cells. A definite relationship exists between the amount of stainable lipid material in renal epithelial cells and the susceptibility of the kidney to the toxic effect of the methane group of anesthetic substances.

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## ACUTE PUERPERAL INVERSION WITH THE REPORT OF A CASE.\*

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IN perusing the statistics of the incidence of acute puerperal inversion in the literature, the casual reader may be led to believe that it need only be given academic thought. But the one bit of enlightenment these figures should afford

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