diagnosis when certain symptoms characteristic of early plumbism manifest themselves, more particularly when a history of exposure to contact with lead can be obtained.

The history of exposure is the all-important aid in the diagnosis, and careful inquiry should be made by the physician as to the details of the patient's work, and he should not be satisfied with a general designation which may not give any indication of exposure to lead.

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THE EFFECT OF INTRASPINAL INJECTIONS OF SERUMS WITH AND WITHOUT PRESERVATIVES *

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It is an established fact that the administration of antimeningitis serum by intraspinal injection has practically turned the former 70 per cent. mortality from epidemic meningitis into 70 per cent. recoveries. Accumulated experience, however, has apparently shown that the injection of the serum itself may have been the cause of death in a very small number of cases. These deaths have been explained in a variety of ways, and of these I shall mention here only the statement of S. P. Kramer that they were caused by the trikresol which had been added as a preservative to the serum, a contention which has recently been supported by Hale[1] on the basis of experimental work on dogs and cats.

EXPERIMENTS WITH TRIKRESOL

Because of the importance of this matter I have carried out during the last few months a series of experiments not only with dogs, but also with monkeys, in order to determine what effects are produced when serums containing 0.3 trikresol, 0.3 per cent. chloroform or 0.3 per cent. ether are injected subdurally. As control injections, horse-serum without any preservative, and Ringer solution were employed. In all animals the blood-pressure was recorded either from the carotid artery (dogs) or from the femoral artery (monkeys); the respiration was registered in all by means of a pleural cannula. The intraspinal injections in the dog were made after a laminectomy had been performed, for the results without this were very uncertain; in monkeys, however, the subarachnoidean space was tapped exactly as in human beings by introducing a needle into the second to the fourth lumbar space. The dogs were maintained at a constant level of ether anesthesia by intratracheal insufflation, a procedure which absolutely prevents death from central respiratory causes. The monkeys were kept under ether anesthesia by means of an ordinary ether cone and received no respiratory aid whatsoever, but always breathed spontaneously. The chloroform and ether serums were not warmed before injection.

The results of these experiments are briefly as follows:

Dogs are much more sensitive to the intraspinal injection of 0.3 per cent. trikresol serum than monkeys, but dogs nevertheless tolerate up to 6 c.c. and more per kilogram without danger as a rule, provided that an efficient artificial respiration is maintained. In the dog, stoppage or impairment of the respiration is the great danger; the drop in blood-pressure, though often pronounced after larger doses, does not persist if the respiration is efficient.

ACTION IN MONKEYS

Monkeys, on the other hand, are relatively extremely resistant to 0.3 per cent. trikresol antimeningitis serum, and tolerate injections aggregating more than 6 c.c. per kilogram usually without any dangerous effect on spontaneous respiration. The blood-pressure generally shows a more or less decided drop, but the normal level is regained within some minutes. To illustrate the enormous quantities which a monkey can tolerate, the following experiment may be mentioned: A monkey of 2,835 gm. received intraspinally 21 c.c. of 0.3 per cent. trikresol antimeningitis serum (New York Board of Health), 23 c.c. 0.3 per cent. chloroform antimeningitis serum (Massachusetts Board of Health) and 10 c.c. of Ringer solution, and was in excellent condition at the end of the experiment. It is of interest that the same animal had received the previous day 6 c.c. trikresol serum and 15 c.c. chloroform serum intraspinally, and that on both days the respiration and blood-pressure were registered; moreover, on the second day the injections (usually 3 c.c. per dose, sometimes 5 c.c., at seven-minute intervals) were made while the animal had a full left-sided pneumothorax and was therefore not a normal animal.

Both in the monkey and in the dog the effects obtained on the blood-pressure and respiration by trikresol seem partly dependent on an increased intraspinal pressure: local applications of 0.3 per cent. trikresol in saline on the medulla of dogs does not give the same quantitative effect on the respiration and blood-pressure as subdural injections; and in monkeys a single injection of trikresol serum following several injections of normal serum exerts usually a greater effect on the blood-pressure than when trikresol serum is injected first.

Tests with serums containing 0.3 per cent. chloroform, 0.3 per cent. ether or no preservative at all, showed that they exerted qualitatively the same effects when injected intraspinally as trikresol serum, but quantitatively the disturbances of respiration and blood-pressure were definitely less. Chloroform serum caused in general a smaller effect on the respiration and blood-pressure than trikresol serum, but the best results were obtained with 0.3 per cent. ether serum and with serum without any preservative, although both still occasionally produced in the dog stoppages of the respiration lasting a minute or two, and a considerable lowering of the blood-pressure. In the monkey, however, normal serum or ether and chloroform serum produced practically only negligible effects on the respiration and blood-pressure.

THE IDEAL ANTISEPTIC

Without discussing the necessity for preservatives in therapeutic serums, it is clear that a volatile antiseptic would be the ideal one to use, for such a preservative could easily be removed by warming the serum container before injection.

The opsonic index of the same antimeningitis serum kept without antiseptics or preserved by 0.3 per cent.

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1. For literature references see The Sources of Danger in Antimeningitis Serum, editorial, THE JOURNAL A. M. A., May 23, 1914, p. 1661.

trikresol, 0.3 per cent. chloroform or by 0.3 per cent. ether showed practically the same value after one month, according to experiments carried out by Dr. Martha Wollstein.

The experiments show that dogs in which laminectomy has been performed are much more sensitive to 0.3 per cent. trikresol serum than are monkeys in which intraspinal injection is directly made. The monkey in this as in other respects is more nearly related to man; and in view of the rarity of the accidents mentioned above in man it may be inferred that monkeys react to intraspinal injections in a manner more truly representing the effects in him.

It should be emphasized that respiratory failure is the great danger after trikresol injection in the dog, and that it occurs only rarely in the monkey. In my experiments the drop of blood-pressure even if profound was never fatal in the dog or monkey unless the respiration was permitted to fail. This danger was reduced in two ways: by being prepared to give efficient artificial respiration when necessary, and by replacing the trikresol with a volatile antiseptic like chloroform or ether. It must be pointed out, however, that artificial respiration was apparently necessary in some cases even when serums without any preservatives were injected intraspinally.

APPEARANCE OF NON-COLLOIDAL NINHYDRIN-REACTING SUBSTANCES IN THE URINE

UNDER NORMAL AND PATHOLOGIC CONDITIONS AND DURING PREGNANCY *

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While we were studying the question of the possible substitution of aluminum hydroxid cream for the parchment diffusion thimbles in the Abderhalden serum diagnosis of pregnancy, there appeared Warfield's paper[1] on the presence of dialyzable ninhydrin-reacting substances in the urine of pregnant women. This led us to turn our attention to a study of the urine under normal and pathologic conditions and during pregnancy.

LITERATURE

Since the publication in 1906 of Pfaundler's[2] work on the determination of amino-acid nitrogen in the urine, there has remained little doubt as to the appearance of appreciable amounts of this class of compounds in normal urine. This work was confirmed a few months later by Krüger and Schmidt,[3] using a different method. These investigators found amino-acid nitrogen to the amount of from 0.325 to 0.45 gm. in from 5 to 6 per cent. of total nitrogen in normal urine.

Embden,[4] and Embden and Reese,[5] on the basis of results obtained by using their modification of the beta-naphthalin-sulphochlorid method, came to the conclusion that as high as 1 gm. of glycocoll may be eliminated daily under normal conditions.

In addition to the glycocoll compound there were found compounds of other amino-acids which Embden and Reese were, however, unable to identify. The weights of the amino-acid compounds isolated in five normal cases were as follows: 1.62, 2.74, 1.48, 1.73, 2.80 gm. daily. These amounts represent 4.32 to 5.10 per cent. of total nitrogen. This, according to the investigators, expresses the minimal amount. Since 1905 many investigations have been carried out on the amount of amino-acid nitrogen eliminated under normal conditions.

Frey[6] found from 0.2 to 0.5 gm. amino-acid nitrogen under normal conditions, Magnus Levy[7] from 2 to 6 per cent. of the total nitrogen, Henriquez[8] 2 per cent. of the total nitrogen on a mixed diet, Masuda,[9] in the case of low protein diet, from 1 to 3 per cent. of total nitrogen, and on high protein diet from 4 to 5 per cent. Joshida[7] found amino-acid nitrogen varying from 0.5 to 2 per cent., and Falk and Saxl[10] from 1.5 to 3 per cent., Siquorelli[11] found 2 per cent. of total nitrogen in normal cases on mixed diet. Galambos and Tausz[12] found from 0.236 to 1.05 gm. amino-acid nitrogen and 1.58 per cent. and 4.35 per cent. of total nitrogen.

It would appear from the evidence presented that amino-acids form an appreciable part of the normal nitrogenous elimination. If ninhydrin reacts with compounds containing the intact amino group in the α, β, etc., position to the intact carboxyl group, then all normal urine should react positively with the reagent, unless the urine contains interfering substances or the content of the amino-acids falls below the limits of delicacy of the reagent.

COLLECTION OF SAMPLES

The urine was obtained fresh and in nearly all cases about four hours after meal-time. The patients suffering from various pathologic conditions were on a liquid or light diet with the exception of the tabes and general paresis patients who were on a general diet. The pregnant women and the normal persons were on a general mixed diet.

METHOD

For the removal of the colloidal substances in the urine we used the aluminum cream according to the method of Marshall and Welker,[13] who showed that this substance can be used for the quantitative removal of colloids from their solutions. Ten c.c. of urine was mixed with an equal volume of aluminum hydroxid cream and the mixture was shaken and filtered. Ten c.c. of the filtrate was treated with 0.2 c.c. of a 1 per

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* Owing to lack of space, this article has been abbreviated in THE JOURNAL by omission of several tables. The complete article is contained in the author's reprints.

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