TABLE IV. Effect of Stress Upon Vit. E Content of the Adrenal Glands of Normal Rats.*

Group	Mean adrenal wt (mg)	Mean body wt (g)	Total tocopherol in the adrenals: Mean for group (mg/100 g of adrenals)	Total tocopherol in the adrenals: Mean of differences between litter pairs (mg/100 g of adrenals)
No stress	39.78	392	30.8	3.7 ± 4 (S.E.)†
Stress	38.64	380	34.6	

* One of each of 14 litter-mate pairs of male rats, raised on a complete stock breeding diet, was subjected to physiological stress (0.1 mg epinephrine by subcutaneous injection) 1 hr before sacrifice.

† This difference is not statistically significant ($p = 0.4$-0.3) by the Fisher "t" test.

hour, the animals were killed by a blow on the head and the adrenals removed and carefully dissected free of fat. They were weighed immediately to the nearest 0.01 mg on a Roller-Smith balance. Each pair of adrenals was then analyzed for content of total tocopherols. The extracts for analysis were prepared by homogenizing pairs of adrenals in all-glass apparatus (Potter-Elvehjem) in 6 ml of 1:1 ethanol-xylene, adding 3 ml of H_2O, agitating, and centrifuging. Aliquots of the xylene layer were then analyzed spectrophotometrically as in the micro method of Quaife *et al.*(12).

Results. Experimental data, including mean body weight of rats, mean adrenal weight, mean vit. E concentration in the adrenals (mg total tocopherols/100 g of adrenals) are summarized in Table IV. Also the mean of differences in adrenal tocopherol content for each pair (stressed vs. control) is given.

The apparent slight increase in tocopherol content of the adrenal glands, due to stress, was shown to be without statistical significance ($p = 0.4$-0.3).

Summary and conclusions. The nutritional status of rats with respect to vit. E had no effect on the adrenal cortical activity (as measured by change in adrenal ascorbic acid concentration) following acute physiological stress (epinephrine injection or exposure to cold). Neither the content of vit. E in the adrenal glands of normal adult rats nor the blood tocopherol content of tocopherol-supplemented or tocopherol-deficient rats was changed following physiological stress.

Thus, vit. E is apparently not a factor in the anterior pituitary-adrenal cortical response to acute physiological stress, although vit. E may be related to the manner in which the tissues utilize the adrenal cortical hormones released as a result of such stress.

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Chloromycetin Palmitate.* Its Use in Pediatrics. (19016)

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Chloromycetin is often difficult to administer to infants and children because of its bitter taste. Esters of Chloromycetin with higher fatty acids have been prepared in an attempt to produce a palatable form of the drug. One of these esters, Chloromycetin Palmitate, is now under clinical investigation. The ester is formed by replacing one of the hydroxyl groups of the propane diol side chain of Chloromycetin with Palmitic acid. Chloromycetin Palmitate has not previously been used in clinical medicine. Animal experi-

* The author is indebted to Parke-Davis and Co. which supplied the Chloromycetin Palmitate suspension and which gave permission to quote their studies of toxicity of the drug in animals.

TABLE I. Infections Treated with Chloromycetin Palmitate–Bacteriological Studies.

Case No.	Age	Diagnosis	Organism	Source	*In vitro* sensitivity to chloromycetin	Result of treatment
1	9 yr	Chronic pyuria	*E. coli**	Urine	Yes	Negative culture
2	2	Acute pharyngitis	Paracolobractrum	Throat	None	Symptoms subsided
3	2	Acute purulent otitis media	Streptococcus *Staphylococcus aureus*	Ear "	Yes "	Ear normal
4	9	Vaginal discharge, 2 wk	Pneumococcus	Vagina	Not done	Discharge subsided promptly
5	21 days	Impetigo neonatorum, 2 wk	*Staphylococcus aureus*†	Skin	Yes	Healed promptly
6	12	Diarrhea, 5 days	*Salmonella typhimurium**‡	Stool and Blood	" " "	Cultures of stool Blood neg
7	3 mo	Cystic fibrosis of pancreas	*Staphylococcus aureus*	Throat	"	Improved
8	2	Cystic fibrosis of pancreas	"	Duodenum and throat	"	"

* Not responsive to aureomycin. † Resistant to penicillin. ‡ Treated also with terramycin.

TABLE II. Common Infections of Children Treated with Chloromycetin Palmitate.

Case No.	Age	Diagnosis	Result of treatment
9	9 mo	Acute bronchitis	PR‡
10	2 yr	" gastroenteritis	"
11	18 mo	" "	"
12	11 days	Impetigo neonatorum	"
13	4 yr	Multiple furunculosis	"
14	7	Acute follicular tonsillitis	"
15	5	Bronchopneumonia* RLL, RML, LLL	"
16	2	Acute cervical adenitis	"
17	4	Pertussis†	CRI§

* Penicillin and sulfonamide resistant. † Not responsive to Terramycin. ‡ PR = prompt recovery. § CRI = cough rapidly improved.

ments, however, indicate that it is less toxic than Crystalline Chloromycetin.

A suspension of Chloromycetin Palmitate for pediatric use, containing 125 mg of Chloromycetin per 4 cc (one teaspoonful) was used in the treatment of 17 patients with a variety of diseases. Ages varied from 11 days to 9 years. Dosage was 50 mg per kg of body weight in 24 hours, divided in 4 or 6 equal doses and continued until the patient was clinically cured, from 3 to 7 days.

Table I shows 8 patients in whom bacteriological studies and *in vitro* antibiotic sensitivity tests were carried out. All patients in this group responded promptly to treatment with Chloromycetin Palmitate.

Table II shows 9 patients who received Chloromycetin Palmitate for conditions which are commonly encountered in children. No bacteriological studies were carried out in this group. All patients responded promptly to therapy.

Parents of these 17 patients reported that the Chloromycetin Palmitate suspension was taken without difficulty and in most cases with pleasure. No instances of nausea, vomiting, diarrhea, drug fever or drug eruption was noted in this small series.

Summary. A new preparation of Chloromycetin, in the form of Chloromycetin Palmitate suspension, was administered to 17 patients ranging from 11 days to 9 years of age.

The preparation is palatable and taken readily by these patients. A variety of mild and serious common childhood illnesses responded promptly to this medication.

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Histology of the Brain and Blood in Chronic Experimental Sedation with Barbiturates and Presidon.* (19017)

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The appearance of histologic changes in the central nervous system following indiscriminate use of barbiturates is held as a major argument against the unrestricted and prolonged use of these drugs. However, the evidence for this idea is not strong, especially in human beings. Hassin's(1) report on acute intoxication in man and Neumann's(2) recent report of a case surviving severe intoxication for five months show only non-specific changes in the brain that could well be the result of anoxia due to respiratory depression by the drug. More conclusive evidence as to effects of barbiturates on the human brain is lacking. Seevers and Tatum(3) examined dogs maintained for as long as three years on daily barbital administration. The post mortem examination showed thickened meninges and walls of cerebral vessels with some degeneration of neurons of the brain. However, such damage was poorly localized, varying in degree and location with the individual animals. Krop and Gold(4) could find no changes in the brain of the dog following barbiturate intoxication with lethal dosage. The present study was undertaken to compare the effects of barbiturates with those of 3,3 diethyl-2,4 dioxotetrahydropyridine, Presidon, a non-barbiturate hypnotic, on the histology of the central nervous system of dogs chronically sedated over long periods of time.

Method. Twelve mongrel dogs, fed on a stock diet throughout the experiment, were divided into two groups of six. Three animals of each group were given a minimum hypnotic dose of Presidon twice daily, two animals received a similar dose of barbital, and one animal received phenobarbital. The animals in one group were sacrificed after six months, and those in the remaining group after one year. The animals were sacrificed during the sleep following their daily drug intake, the brains perfused with formalin (U.S.P. 1:10), and the viscera examined grossly and samples taken for microscopic examination. The spinal cords and brain stems were frozen by Marshall's technic and sectioned serially. The cerebral and cerebellar cortices were sampled and prepared for examination in a similar manner. Alternate sections were stained with thionin, Weil's and a few with Masson's stains. During the last seven months of the experiment complete blood counts were made biweekly on all the dogs, and a sample of sternal marrow was taken at autopsy in order to observe any possible development of blood dyscrasias especially agranulocytosis which has been reported clinically following the use of Presidon.

Results. A single dose of Presidon produced a light sleep of about two hours duration. The dogs could always be aroused from such sleep at any time and upon undisturbed awakening were immediately alert. In none of the animals receiving this drug were overt

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1. Hassin, George B., *Arch. Neurol. Psychiat.*, 1939, v42, 679.

2. Neumann, Meta A., *J. Neuropathol. and Clin. Neurol.*, 1951, v1, 145.

3. Seevers, M. H., and Tatum, A. L., *J. Pharm. and Exp. Therap.*, 1931, v42, 217.

4. Krop, Stephen and Gold, Harry, *J. Pharm. and Exp. Therap.*, 1946, v88, 260.