TABLE II

	No. rats	Adrenal ascorbic acid mg per 100 g fresh tissue
Controls	18	419 ± 8.2*
1 hr after admin. of 4 ml cortical extr.	6	423 ± 8.4
1 hr at 3 to 5°C	9	314 ± 18.0
1 hr at 3 to 5°C pretreated with 4 ml cortical extr.	9	415 ± 10.1
1 hr after admin. of adrenotropic hormone (10 μg/100 g body wt)	4	314 ± 12.1
1 hr after admin. of adrenotropic hormone (10 μg/100 g body wt) pretreated with 4 ml cortical extr.	6	310 ± 7.3

* Mean and standard error.

their experiments were chronic and did not concern the physiological response to acute stress reported here.

Summary. Administration of cortical extract prevents the decrease in adrenal ascorbic acid which accompanies exposure to cold but does not prevent the decrease which results from administration of exogenous adrenotropic hormone. Since reduction in adrenal ascorbic acid is initiated by pituitary adrenotropic hormone, cortical extract must act to inhibit elaboration of this tropic hormone by the pituitary. These results have been interpreted to mean that rate of release of adrenotropic hormone from the pituitary is regulated by the concentration of adrenal cortical hormones in the blood and tissues.

15127 P

Combined Anesthesia and Hyperimmune Serum Therapy in the Treatment of Experimental Western Equine Encephalomyelitis.

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Once the symptoms of a virus disease have become evident, the virus is well established in the host cell. For this reason, it is assumed that antibodies are unable to gain access to the virus, with the result that antiserum therapy is ineffective. The close association between the virus and the host cell likewise renders chemotherapy difficult, for an agent in concentration sufficient to destroy the virus would probably injure the host cell. The ideal therapeutic agent would bring about a reversible change in the metabolism of the host cell sufficient in degree and duration to cause destruction of the virus without injuring the cell. Such an agent should have the same tissue predilection as the virus. Studies on the treatment of neurotropic virus diseases have been discouraging. The results of experiments with hyperimmune serum therapy have been contradictory, probably because of variations in the virulence and incubation period of the virus strains employed and differences in the potency of antisera.[1,2,3] Reports with chemotherapeutic agents have likewise been discouraging.[4,5] Similarly, certain antibiotics have proved ineffective in

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TABLE I.
Anesthesia in the Treatment of Swiss Mice Infected with Equine Encephalomyelitis Virus (Western Type).

Group	No. of mice*	% of animals dying from encephalitis during successive days after injection of virus										Survivors %
		1	2	3	4	5	6	7	8	9	10	
I. Controls	25	0	16	28 (44)†	20 (64)	8 (72)	4 (76)	4‡ (80)	0	0	0	20
II. Hyperimmune rabbit serum§	25	0	4	12 (16)	32 (48)	0	0	0	0	0	0	52
III. Ether anesthesia‖	26	0	7.7	23.1 (30.8)	7.7 (38.5)	0	0	0	0	0	0	61.5
IV. Hyperimmune rabbit serum§ and ether‖	32	0	3.1	0	0	3.1 (6.2)	0	3.1‡ (9.3)	0	0	0	90.7

* Animals which died from trauma or anesthesia are not included in this table.

† Figure in parentheses indicates cumulative percent deaths.

‡ One animal from this group sacrificed when showing symptoms suggestive of encephalitis. Virus was recovered and identified as Western equine virus by serum neutralization test.

§ Three intraperitoneal doses (0.35 cc each) of undiluted hyperimmune rabbit serum given 18 hours, 30 hours, and 42 hours subsequent to the injection of the virus.

‖ Anesthesia for 3 four-hour periods beginning 18 hours, 23 hours, and 42 hours after inoculation of virus.

experimental neurotropic virus infections.[6,7]

The influence of anesthesia on the course of several diseases affecting the central nervous system has been reported. Anesthetics, alone and in combination with specific antitoxin, decrease mortality in experimental botulism[8] and alleviate muscular spasms in tetanus.[9,10] Preliminary observations have indicated that ether anesthesia is effective in the treatment of western equine encephalomyelitis in mice.[11] Of mice treated with deep ether anesthesia soon after the intracerebral injection of virus only 58% died as compared with 92.4% of control animals. When anesthesia was delayed until the animals first showed evidence of encephalitis, 60% died as compared with 92.4% of controls. Studies are now in progress to determine the mechanism whereby anesthesia alters the course of the infection. A completed report will be published later.

In view of these observations, it seemed desirable to investigate the effectiveness of combined ether anesthesia and hyperimmune serum in the treatment of experimental western equine encephalomyelitis. The virus strain was the same as that used in the preliminary study.[11] Three- to 4-week-old white Swiss mice were used in this experiment. Each mouse was inoculated intracerebrally under light ether anesthesia with 0.03 cc of a $10^{-8.5}$ dilution of virus. All inoculated mice were separated at random into 4 groups. Group I served as controls and received no further treatment; Group II received 3 intraperitoneal doses (0.35 cc each) of undiluted hyperimmune rabbit serum 18 hours, 30 hours, and 42 hours subsequent to the injection of the virus; Group III received 3 four-hour courses of deep ether anesthesia beginning 18 hours, 23 hours, and 42 hours following injection of virus; Group IV received both hyperimmune serum as described for Group II and deep ether anesthesia as described for Group III. Pooled hyperimmune rabbit serum of high potency was used.* Animals were observed frequently for a 10-day period. Two animals

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* The results of the titration of the hyperimmune serum will be reported subsequently.

(one from Group I and the other from Group IV) showed symptoms of encephalitis on the seventh day. These animals were sacrificed and suspensions of each brain were injected intracerebrally into normal mice. In both cases virus was present in high titer and was identified as western equine encephalomyelitis virus by serum neutralization tests.

As shown in Table I, 20% of the control animals (Group I) survived the observation period of 10 days while 52% of the serum-treated animals (Group II) survived. Sixty-one and five-tenths percent of ether-treated animals survived, as compared with 90.7% of animals receiving combined ether anesthesia and hyperimmune serum (Group IV). Statistical analysis indicated that the difference in effectiveness of hyperimmune serum therapy alone as compared with that of ether anesthesia alone was not significant. The effect of combined therapy, however, is markedly greater than the effect of either method alone. Whether the serum therapy and anesthesia act independently, or whether there is a synergistic effect between the two cannot be stated from the data obtained. The possibility that anesthesia may facilitate union of virus and antibody is under investigation.

Summary. Either intraperitoneal injection of hyperimmune rabbit serum or deep ether anesthesia administered beginning 18 hours following intracerebral inoculation of virus effects a significant change in survival rate among Swiss mice infected with western equine encephalomyelitis. A combination of the two methods is more effective than either method alone.

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Production of Extracellular Penicillin-Inactivating Substances Associated with Penicillin Resistance in *Staphylococcus aureus.*

JOSEPH S. GOTS. (Introduced by A. B. Gutman.)

When Abraham and Chain[1] discovered the penicillin-destroying enzyme, penicillinase, the question was raised whether a bacterium's susceptibility to penicillin varied inversely with its ability to produce the enzyme. The present data do not favor complete agreement.[1-5] Too many inconsistencies exist to permit the acceptance of enzyme formation as the sole factor in explaining variation in penicillin susceptibility. In some bacteria, however, penicillin resistance may be definitely ascribed to their ability to produce penicillinase. When Kirby[6] and others[7,8] found that an active intracellular penicillin inactivator was present in resistant staphylococci and not in sensitive strains, it became apparent that perhaps in cases of varied susceptibility among various strains of the same species, the variation might be due to difference in enzyme formation. This investigation was formulated with the hope that the use of technics which are dependent on the extracellular nature of the inactivating enzyme, might throw further light on the latter concept.

Methods and Materials. The staphylococci studied were isolated primarily from cases of

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