Summary. 1. Panthenol was found to be equally as effective as pantothenic acid in promoting antibody synthesis in pantothenic acid-deficient rats.

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Experimental Production of Post-Tonsillectomy Bulbar Poliomyelitis.* (18838)

HAROLD K. FABER, ROBERT C. MCNAUGHT, ROSALIE J. SILVERBERG, AND L. DONG.
From the Department of Pediatrics, Stanford University School of Medicine, San Francisco.

Poliomyelitis occurring within 30 days after tonsillectomy is predominantly bulbar(1). When compared with the incidence of the bulbar form in patients who have not had the operation within the same period of time, the difference is greater than can be explained on the basis of pure chance and indicates a causal relationship between operation and bulbar localization. This is particularly true of children, as shown by the two examples from the literature given in Table I.

In human bulbar poliomyelitis, including the post-tonsillectomy cases, the muscles of deglutition and phonation, supplied by the X cranial nerve and the nucleus ambiguus, are practically always involved, the facial muscles (N.VII) in about half, and those supplied by the V and XII nerves in lesser numbers(4). The nuclei of supply in all these are in the pons or medulla. Post-tonsillectomy bulbar poliomyelitis occurs almost exclusively during epidemics of the disease, and the onset of symptoms according to Aycock's(1) compilation nearly always occurs 6-24 days after operation, with the peak at 14-16 days. These figures agree closely with the incubation period of poliomyelitis in general, suggesting that virus may be introduced at the time of operation. Only rare cases have been reported in which the onset was less than 4 days after operation. Previous attempts(5-7) to reproduce experimentally the sequence of bulbar paralysis after tonsillectomy have nearly always failed, paralysis when produced usually having been spinal in type. In most of these studies, notably that of von Magnus and Melnick(7) exposure of the throat to the virus has been made *after* rather than before operation. Unpublished observations in our laboratory have shown that in order consistently to produce infection in divided nerve it is necessary to apply virus to the central cut end before it is sealed off by blood.

In the present study we have explored two hypotheses: (1) that virus already in the pharynx is directly introduced into the peritonsillar musculature, which is unavoidably traumatized during the human operation, and

TABLE I. Bulbar Poliomyelitis in Poliomyelitis Cases With and Without Recent Tonsillectomy.

	Poliomyelitis			
	Bulbar	Other forms	% bulbar	P*
A.(2) 0-10 years				
Tonsillectomy	24	12	66.7	
No tonsillectomy	771	6063	11.6	<.001
B.(3) 3-7 years				
Tonsillectomy	12	4	75	
No tonsillectomy	96	395	19.5	<.001

* From chi square of differences between bulbar and other forms. In both series P indicates that probability of differences occurring by chance are less than 1 in 1000.

* Aided by a grant from the National Foundation for Infantile Paralysis.

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TABLE II. Oropharyngeal Swabbing of Virus With and Without Tonsillectomy, Compared With Tonsillectomy After Intrathalamic Inoculation Without Swabbing.

	Oropharyngeal swabbing		Intrathalamic inoculation
	Tonsillectomy Series 1	No tonsillectomy Controls	and tonsillectomy Series 2
Animals exposed	7	7	6
Poliomyelitis	7	5	6
Onset (days)	7-10	8-10	5 (2)*
Bulbar paralysis	7	1	5†
Spinal paralysis	3	4‡	5
Cervical	3	4	5
Thoracic	0	?§	5
Lumbar	0	3	5

* 5 days after inoculation, 2 days after tonsillectomy.
† 1 animal found dead, not included in list of paralyses, had typical lesions.
‡ 1 animal, not included here, had typical lesions.
§ Not specifically noted.

hence into its supplying nerves; (2) that localized traumatic stresses to these muscles tend to localize paralysis in them presumably by making their supplying nerve centers in the medulla more vulnerable to the effects of poliomyelitic infection already present in the central nervous system.

In the test experiments, the tonsils were removed by enucleation with curved scissors; in Series 1, immediately after the application of virus to the pharynx; in Series 2, 3 days after inoculation of virus into the thalamus (no pharyngeal application of virus). In the control series, virus was gently swabbed on the surfaces of the mouth and pharynx but no tonsillectomy was performed. In all experiments a 17% suspension of the Wis '45 strain (Brunnhilde type) of poliomyelitis virus, PD_{50} 4.9, was used. All monkeys were cynomolgus (*M. irus*), previously prepared by division of the olfactory tracts to preclude entry of infection through the olfactory nerves. The results are shown in Table II.

It will be noted that in both series, bulbar poliomyelitis resulted, with the differences that in Series 1, the incubation period was 7-10 days after operation while in Series 2, the incubation period was 5 days after intrathalamic inoculation† and 2 days (or slightly less) after tonsillectomy; and that in Series 1 paralysis was limited to the bulbar and (in 3 animals) the cervical innervations while in Series 2, the entire cord, in addition to the bulbar centers, was paralytically involved.

The results with pretonsillectomy exposure of the pharynx to virus (Series 1) appear to correspond, in terms of incubation period and of distribution of paralysis, to the majority of human post-tonsillectomy cases(1) better than those of Series 2, in which tonsillectomy was performed after infection had become established in the CNS. The rapidity with which paralysis followed tonsillectomy in the latter, as well as its relative extent and severity, strongly suggests that the physical stress of the operation itself greatly enhances the speed, severity and, to some extent, the localization of the infectious process. A comparable human situation may be envisioned in those rare cases where bulbar or bulbospinal paralyses begin three days or less after tonsillectomy.

As regards the commoner type of human post-tonsillectomy poliomyelitis with its longer incubation period and paralyses primarily bulbar or bulbocervical, it is conceivable that the situation may be comparable with our experimental Series 1 in that the virus is being excreted on the pharyngeal surfaces but has not yet attacked the CNS. In other experiments(8) we have shown this excretory phenomenon to occur while infection is limited to certain peripheral ganglia,

† In 75 cynomolgus monkeys, used in other studies, the average incubation period after intrathalamic inoculation of Wis '45 virus was 8.7 days; primary bulbar and bulbospinal paralyses occurred in 17.3%, and primary spinal paralyses in 82.7%.

8. Faber, H. K., Silverberg, R. J., Luz, L. A., and Dong, L., *J. Exp. Med.*, 1950, v92, 571.

such as the gasserian and nodose. Assuming the same condition to hold in man during the early, presymptomatic period or in cases that might end without symptoms in the absence of operation, an opportunity would be open for direct introduction of virus into the peritonsillar tissues before the CNS is infected.

This possibility suggested a supplementary study of the preventive effects of local antisepsis in the throat. Six cynomolgus monkeys were subjected to the same procedure as in Series 1, excepting that 2% tincture of iodine was applied to the throat one-half minute after swabbing with virus and one minute before tonsillectomy. All these animals remained well.

Further exploration of this procedure is required before its meaning and implications can be properly evaluated. Although such pre-operative antisepsis appears to be harmless, no assurance of its preventive value against poliomyelitis in human beings can be offered.

Summary and conclusions. 1. Application of poliomyelitis virus to the pharynx of cynomolgus monkeys, followed by enucleation of the tonsils was regularly followed after 7-10 days by primary bulbar paralysis, accompanied less often by high spinal paralysis. This effect was probably due to introduction of virus into the innervations of the peritonsillar tissues, notably muscle. 2. Intrathalamic inoculation of virus followed 3 days later by tonsillectomy was regularly followed within 2 more days by bulbospinal paralysis in which all levels of the cord were involved. This effect probably indicates that trauma increases the vulnerability of nerve cells to infection already present in the central nervous system. 3. After oropharyngeal swabbing with virus and no tonsillectomy, spinal paralysis usually resulted, with bulbar manifestations in only one instance. 4. With pharyngeal application of virus followed by 2% tincture of iodine and then by tonsillectomy, all 6 animals remained well.

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In vitro Action of Cortisone on Vasoconstriction Due to Histamine.* (18839)

DURWOOD J. SMITH. (Introduced by William S. McCann.)

From Department of Medicine, University of Rochester School of Medicine and Dentistry and the Clinics of Strong Memorial and Rochester Municipal Hospitals, Rochester, N. Y.

Two questions prompted the present study. Does cortisone alter the response of isolated smooth muscle to histamine? If it does, what mechanism is involved? The experimental evidence suggesting the participation of the hormones of the adrenal cortex in the metabolism of histamine has recently been reviewed by Rose(1) and need be mentioned only briefly. Adrenalectomized animals have been found to have a markedly diminished resistance to histamine; an increased tissue content of the compound as well as a diminished capacity of the tissues *in vivo*(2) and *in vitro* (3,4) to destroy or inactivate histamine. While these changes are partially reversible by DOCA, adrenal cortical extract (which contains cortisone as well as many other compounds) will restore the metabolism of histamine by the adrenalectomized animal to an essentially normal state(1).

Experimental procedure. An angioplethysmokymographic technic(5,6) was used to

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