central nervous system: the intervertebral ganglia; the sympathetic chains; the ganglia of both vagus nerves external to the skull; the Gasserian ganglia; the olfactory bulbs; the sacral, lumbar, upper and lower dorsal, and cervical regions of the spinal cord; from the medulla; the mesencephalon; the diencephalon, and from each of the major lobes of the cerebral cortex of both hemispheres of the brain, as well as from the cerebellum, including the roof nuclei. These tissues were fixed immediately in 70-per-cent. alcohol and the sections eventually stained with thionin.

It was observed that lesions resembling those ordinarily found in the intervertebral ganglia in cases of typical anterior poliomyelitis were also present in the intervertebral ganglia of most of these monkeys. Moreover, similar lesions were almost invariably present in the large-celled portion of one or both vagus ganglia and, rarely, in one or both Gasserian ganglia. The lesions varied from extremely mild, doubtful ones to florid pathologic changes. They consisted of focal interstitial ganglionitis, with focal destruction of neurons and neuronophagia. Some degree of perivascular "cuffing" was usually present. The exudative cells were predominantly mononuclear types. These lesions followed intraperitoneal inoculation of treated stool from patients with clinical anterior poliomyelitis or from contacts. If, in addition to the intraperitoneal route, stool was exhibited to monkeys intranasally, then lesions of the olfactory bulbs sometimes occurred. In the olfactory bulbs, the lesions consisted of perivascular "collaring" with foci of cell necrosis and exudative accumulations principally in the mitral-cell layer. Degeneration of mitral cells had occurred, and although neuronophagia was not always easy to identify in the manner that one does in anterior-horn cells, evidence of it appeared to be present. No changes were noted in sections that were studied from the remainder of the central nervous system of these animals.

In the seven instances in which this syndrome was observed, other monkeys were subsequently inoculated with larger doses of the original stool specimens. In five of the seven, a monkey eventually contracted classical anterior poliomyelitis. Sometimes as many as four attempts in as many monkeys, with repeated occurrence of the mild disease described, were necessary to achieve, in one monkey, the accepted endpoint, that is, fever, flaccid paralysis and anterior-horn cell necrosis with neuronophagia and perivascular "cuffing." In one case, stool inoculation, intranasally and intraperitoneally, was made in two different monkeys. Although neither developed typical poliomyelitis, both showed lesions in the vagus and spinal ganglia and in the olfactory bulbs. The patient from whom this specimen of feces was obtained had clinical poliomyelitis. In the seventh instance, no illness and no lesions were obtained after the inoculation was repeated.

It is common knowledge that a characteristic pathologic picture may be found in intervertebral ganglia and olfactory bulbs in experimental and human anterior poliomyelitis. That similar changes may be present in the ganglia of the vagus nerves is not usually recognized. It may be opportune at this point to call attention to a publication of Goodpasture in 1925,[3] in which, after studying tissue obtained at autopsy from a patient with "polio-encephalomyelitis," he makes the following statement: "A case of polioencephalomyelitis in a boy is described in which medullary lesions were found which appear to be directly related to the central distribution of the ninth and tenth cranial nerves. It is suggested that the virus of poliomyelitis in human infections may enter the brain through peripheral nerves."

Further work is in progress to determine whether or not the syndrome described is truly atypical anterior poliomyelitis, and what possible significance lesions of the vagal ganglia may have. However, these observations demonstrate the necessity of killing and examining all inoculated monkeys.

SUMMARY

A mild clinical syndrome in *Macacus rhesus,* accompanied by pathologic changes in the sensory portions of the vagus ganglia, intervertebral ganglia, and sometimes in the Gasserian ganglia is described. This syndrome occurred following intraperitoneal inoculation of fecal material obtained from contacts and from patients with infantile paralysis in an epidemic in a rural community. When intranasal as well as intraperitoneal inoculation was practiced, the olfactory bulbs were sometimes involved.

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RESYNTHESIS OF BIOTIN FROM A DEGRADATION PRODUCT[1]

IN a forthcoming paper[2] we are presenting data which indicate that biotin ($C_{10}H_{16}O_3N_2S$) is a cyclic urea derivative. The basis of this conclusion was the formation of a diaminocarboxylic acid ($C_9H_{18}O_2N_2S$) from biotin by the action of $Ba(OH)_2$ at 140°. The loss of one carbon atom and one oxygen atom, the

[3] E. W. Goodpasture, *Amer. Jour. Path.*, 1: 29–46, 1925.

[1] We wish to thank Mr. W. O. Frohring, of the SMA Corporation, for supplies of biotin concentrates used by us in the preparation of the crystalline biotin and for a research grant which has aided us in this work.

[2] K. Hofmann, D. B. Melville and V. du Vigneaud, *Jour. Biol. Chem.*, 141: 207, 1941.

formation of an acid containing two primary amino groups from the acidic biotin, the inactivation of biotin with nitrous acid without evolution of nitrogen are all in keeping with the interpretation which we placed on the action of $Ba(OH)_2$ on biotin. We should now like to report the resynthesis of biotin from this diaminocarboxylic acid.

If our interpretation of the degradation reaction were correct, it should be possible to convert the diaminocarboxylic acid back to biotin through reactions employed for the synthesis of urea derivatives. Accordingly 10 mg of the diaminocarboxylic acid were treated with phosgene under conditions ordinarily employed. Crystalline biotin was obtained from the reaction mixture in 98 per cent. yield. The compound melted at 228–230° (uncorrected), which agrees with that recorded by us for natural biotin.[3] The melting point of a mixture of the synthetic compound with biotin isolated from natural sources showed no depression. The specific rotation of the resynthesized biotin was $[\alpha]_D^{22} = +92°$ (0.2 per cent. solution in 0.1 N NaOH). By treatment of the synthetic compound with diazomethane, a methyl ester (m.p. 166–167°) was formed which showed no depression in melting point when mixed with a sample of biotin methyl ester. As tested by the yeast-growth method the synthetic biotin exhibited the same degree of activity as natural biotin.[4] Since the resynthesized biotin is identical in melting point, optical activity and biological potency with the natural product, it is obvious that little or no racemization could have taken place during the $Ba(OH)_2$ treatment of biotin. The synthesis of biotin from the diamino compound affords additional and conclusive proof for the cyclic urea structure in biotin. The possible relation of the urea structure of biotin to the affinity of biotin for avidin is being subjected to experimental test.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

AN INEXPENSIVE SQUARE-WAVE GENERATOR

BECAUSE the square wave contains an infinite series of harmonics of its fundamental frequency, and because its precise wave-form is readily recognizable on an oscilloscope it is an easily applied severe test for an amplifier. It shows at a glance the high and low frequency cut-offs, other frequency and phase discrimination, resonance, overshoot, etc.

The generator here described is light, compact,

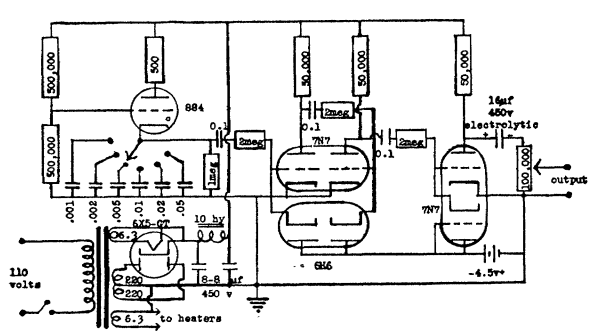

FIG. 1. Circuit of square-wave generator. (Values are not critical.) The 100,000 ohm output potentiometer should be tapered as for an audio gain control.

simple and portable. Its principle is to feed the output of an oscillator first into a limiter which clips off the peaks and gives waves with flat tops and bottoms, thence into an amplifier and second limiter, etc. The sides of the wave become steeper with each amplifier stage.

Frequency stability is provided by the thyratron oscillator. The fundamental is variable in six steps from 35 to 1,200 cycles. The grids of the amplifier tubes together with the diodes constitute effective limiting circuits. The output is variable from 40 volts to less than 100 microvolts by a single control. The rates of rise in the two sides of the square wave are not exactly equal, but the slow one is faster than 10 microseconds. Thus the generator will test an amplifier to over 50,000 cycles.

The power transformer should be a well-shielded one, and should be mounted a few inches away from the thyratron tube to prevent magnetic action on the latter.

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AN ADJUSTABLE RESISTOR FOR FLOWMETERS

ONE of the most common types of flowmeters for air is that consisting essentially of a resistor and a gage for measuring the pressure drop across it. The pressure gage may be a manometer with its two arms connected to the air line, one ahead of and the other following the resistor; or if one end of the resistor is open to the atmosphere, so may be the correspond-

[3] V. du Vigneaud, K. Hofmann, D. B. Melville and J. Rachele, *Jour. Biol. Chem.*, 140: 763, 1941.

[4] We wish to express our appreciation to Miss Eleanor Hague of this laboratory for carrying out the assays.