artifact as seen on the oscillograph tube is reduced to an absolute minimum.

Finally, it might be pointed out that the circuit shown in Fig. 1 may find numerous other applications besides that of nerve or muscle stimulation. For example, by connecting an electro-magnetic marking key to the binding posts at (*M*), it is possible to record the moment of stimulation on a kymograph or similar apparatus. Furthermore, the unit may be calibrated and adjusted to mark any desired time intervals, from a frequency of once in fifteen minutes to the limiting frequency of the key. The entire apparatus, equipped for use as a stimulator and as a time recorder, may be enclosed in a small portable box suitable for research or for student use. If the device is to be used for nerve or muscle stimulation without oscillographic recording, the Thyratron filament may be heated by alternating current through a small transformer, rather than by a storage battery. The "B" batteries may likewise be replaced by an A.C. power pack, thus enclosing power supply and all in one box. Used as a master time recorder such a unit will turn out sufficient energy to operate a number of marking keys of the usual type.

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SPECIAL ARTICLES

EXPERIMENTS UPON THE CAUSE OF WHOOPING COUGH[1]

IT is an accepted observation that it is frequently impossible to differentiate the symptoms and signs of the catarrhal stage of whooping cough from those of the common cold.[2]

Although the Bordet-Gengou bacillus is widely regarded as the specific etiological agent of whooping cough, it is fair to say that carefully controlled proof of this belief is scant. With the exception of the report of Sauer and Hambrecht,[3] in which it is stated that a characteristic paroxysmal cough had been produced in eight out of twenty-eight monkeys inoculated with *B. pertussis,* the reports of the experimental reproduction of this disease in animals are open to serious criticism.

On the other hand, the epidemiological, immunological and pathological aspects of whooping cough have led many to believe that a filterable virus might play a rôle as the causal agent. Recently this view has been stressed by McCordock,[4] who reports the finding of intranuclear inclusions in the lungs of twelve out of thirty-five patients with whooping cough, who had succumbed to pneumonia, which not infrequently occurs in pertussis. He suggests "that the possible rôle of a filterable virus must be considered in this disease."

It is evident that final judgment in regard to the etiological agent in whooping cough has not been reached, and it was with this in mind that we commenced our investigations upon the problem of pertussis.

Chimpanzees have been used in all the transmission experiments because of their well-known susceptibility to human diseases. During experimental periods the animals were in strict isolation, and rigorous precautions against cross infection were exercised by the attendants and observers.

Three apes, inoculated by spraying their throats with either Berkefeld V, W, or Seitz filtrates of sputum from early human cases of whooping cough and by subcutaneous inoculations of citrated blood from the same patients, developed febrile upper respiratory catarrhs after incubation periods of from five to seven days. A transfer of this catarrhal infection to a second ape was made by spraying its throat with a Berkefeld W. filtrate of the rhinopharyngeal washings from an ape infected with human filtrate. Two apes inoculated with unfiltered pertussis sputum developed similar catarrhal affections after two or three day incubation periods. These catarrhs differed only in minor points, such as length of incubation period, and absence of leukocytosis from the typical picture of experimental common colds in the apes. No cough occurred during or following these affections with one exception, which will be noted later. Cultures of all filtrates remained sterile on appropriate media and Bordet bacilli were cultivated in each instance from the unfiltered sputa.

One of the two apes inoculated with unfiltered sputum developed a second catarrhal affection thirty days after being inoculated. Within a few days a typical paroxysmal cough appeared and was accompanied by a leukocytosis and a marked absolute increase in the lymphocytes. Cough plates on Bordet medium on several occasions showed numerous Bordet bacilli. The cough lasted for seven weeks. Another

[1] From the Departments of Pathology and Bacteriology, Medicine and Pediatrics and the Biological Laboratory of the John J. Abel Fund for Research on the Common Cold, The Johns Hopkins University Medical School, Baltimore, Maryland.

[2] "Osler's Principles and Practice of Medicine," McCrae. Tenth edition. D. Appleton and Company, New York.

[3] L. W. Sauer and L. Hambrecht, *Am. J. Dis. Child.,* xxxvii: 732, 1929.

[4] H. A. McCordock, *Proc. Soc. Exp. Biol. and Med.,* xxix: 1288, June, 1932.

ape was allowed to drink a heavy suspension of freshly isolated Bordet bacilli. After an incubation period of twenty-four days, this ape developed typical whooping cough. The cough was accompanied by a marked leukocytosis and an absolute increase in the lymphocytes. Cough plates were positive for Bordet bacilli. The cough endured for six weeks. A third ape, which was inoculated with third generation cultures of Bordet bacilli isolated from the previous ape, developed typical whooping cough after an incubation period of seven days. Again, the cough was accompanied by a leukocytosis which at its height showed 63,000 white blood cells with an absolute increase in the lymphocytes to 44,730 cells. Cough plates were covered with Bordet bacilli. The cough persisted for six weeks. In all three apes, the complement-fixation reaction with pertussis antigen, which was negative during the incubation period, became strongly positive after the disease was well developed. Berkefeld W. filtrates of the rhinopharyngeal washings taken during the catarrhal stage in two of these three apes and inoculated into other apes did not produce catarrhal affections.

The interpretation of these observations is difficult. There can be no doubt but that the three apes inoculated with pure cultures of Bordet bacilli or whole sputum developed typical whooping cough, which in its clinical and bacteriological aspects was indistinguishable from the human disease. However, the results in those apes inoculated with filtrates from human cases are inconclusive and are open to two interpretations. One, that the catarrhal affections represented the action of a hitherto unrecognized filterable virus which acts as the primary infecting agent in whooping cough, or that the catarrhal affections were simply common colds and that we were dealing with whooping cough cases who were also carriers of the virus of the common cold. Further investigations are being made upon all aspects of the experimental disease.

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AN ENCEPHALOMYELITIS IN THE CHICKEN[1]

A NERVOUS disorder of chickens, in the form of a pronounced and rapid tremor of the head and neck with which, in some cases, there is also an associated ataxia, was first seen by us in May, 1930, when a group of nine diseased chickens was brought to the laboratory. In April, 1931, a second group of affected birds was received, a third in January, 1932, and a fourth in May, 1932. Throughout the spring of 1932 reports of the wide-spread occurrence of this disease have been frequent.

In an affected flock, the first symptom of the disease to be observed is the rapid tremor of the head and neck in certain birds. On manual examination, other muscles are found to be involved as well. The "trembling" becomes aggravated when the chickens are excited, tends to subside when the birds are left to themselves, and disappears in sleep. In some chickens the tremor is very fine, in others coarse; in some it is intermittent in character, in others it appears to be constant during their waking hours.

An ataxia was present in addition to the tremor in some of the birds when they were brought to the laboratory, and developed in others while they were under observation. An occasional bird, showing the tremor only, gradually recovered, and at the end of two to three months appeared to be normal; others continued to show the tremor over the same period; but those affected with an ataxia in addition to the tremor grew progressively worse, and sometimes within a week after onset of the ataxia were moribund.

The age of onset of the disease has been reported to be as early as two days after the chickens had been removed from the incubator. The youngest birds brought to us were five days old when we received them, the oldest, six to seven weeks.

A total of 102 affected birds have been studied. Detailed pathological examination of fifty of these has been made at the present time. Over thirty of the birds are still alive and are being used for further experiments.

Work with the disease has included experiments on production, transmission and cure. All efforts to produce the disease *de novo, i.e.,* by diet, high temperature, etc., have been unsuccessful. Transmission experiments, in which a suspension in salt solution of brain or of spinal cord of an affected bird was inoculated intracranially into very young normal chickens, have been successful in six cases. Typical disease with marked tremor and poor sense of balance was produced in four chickens; with marked tremor and pronounced ataxia in one chicken; and an atypical form with ataxia and no tremor was produced in one chicken.[2] The first two successful inoculations were made from suspensions of the cord from two chickens in the group brought to the laboratory in January, 1932. Inoculations with a brain suspension in each of these two cases were negative. The first

[1] Preliminary report.

[2] The lesions of the brain and spinal cord of this chicken were numerous and large. They were indistinguishable from lesions occurring in chickens with typical manifestations of the disease, *i.e.,* both tremor and ataxia.