

# TREATMENT IN PEDIATRIC PRACTICE

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## TREATMENT OF WHOOPING COUGH\*

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Whooping cough is undoubtedly the most formidable of common acute specific fevers of infancy and childhood. The attack may occur at very early age. The liability of the infant to convulsions, and the long debilitating illness make it a serious disease. Secondary invaders frequently cause broncho-pneumonia. In view of the high mortality of young infants and children from pertussis, attention was directed towards effective methods of specific prophylaxis. Much of the difficulty, however, arose from the immunological instability of the responsible organism, *H. Pertussis* under conditions of cultivation.

### SPECIFIC PROPHYLAXIS

*Active Immunisation*:—Upto 1931 whooping cough vaccination was under an ever deepening cloud and most of the workers condemned it being worthless. Soon afterwards LESLIE and GARDNER found that the vaccine was made from the rough phase of the *H. Pertussis* culture and was therefore probably useless as an antigen. They produced *prima facie* evidence to show that the fresh phase alone could be expected to produce useful antibodies, because fresh *H. Pertussis* culture is antigenically different from *H. Pertussis* adapted to the laboratory life. In addition to the recognition of the necessity for smooth phase culture, SAUR (1934) has shown that large doses are probably more effective than small. SAUR lays further stress not only on fresh cultures and maximal dosage but also on the growth of the bacillus on human blood.

Active immunisation has now become an accepted procedure in U. S. A. Most of the American workers on the subject emphatically endorse the view, based on fairly good evidence,

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that whooping cough is a disease which can be prevented by prophylactic vaccination. Of course maximal dosage of freshly isolated virulent strains (Phase I of LESLIE and GARDNER) of the whole bacterial cells grown on human blood is to be used. Besides, SAUR, with the co-operation of local health authorities in Evanston, ILL., has established beyond question that whooping cough can be completely iradicated. On the other hand, MACFARLAN, TOPLEY and FISHER, using a plain vaccine in a long series of carefully controlled trials in Oxford, found no significant difference in incidence or severity between the inoculated and the controlled groups.

It is possible that the genus epidemicus may vary from period to period or in different localities and also under varying conditions of health and hygiene. WALLACE SAKO, however, thinks that the discrepancies might be due to the usage of non-potent lots of vaccines. Or *Bacillus para-pertussis* infection may be so indistinguishable from pertussis that diagnosis may easily be mistaken. Failures may also be in part due to use of vaccines differently prepared, injected in different doses and at different intervals, assessed in different criteria of immunity.

#### OPTIMUM AGE OF VACCINATION

Until recently it was thought that the young infant could not be effectively immunised against pertussis because of the immaturity of the immune mechanism. SAUR recommends immunisation after 7th month on the basis of his finding that only a small group of infants developed complement fixing antibodies following immunisation with *H. Pertussis* vaccine given at or below the age of 3 months, whereas most of the infants inoculated at an older age showed complement fixing bodies. However, SAUR did present evidence to indicate that immunisation of infant under 3 months was of value, since the attack rate in the immunised group was lower than in the non-immunised group and the disease in those infants was attenuated and none killed. Nevertheless, 7th month has generally been accepted as the optimum age for immunisation. Recently various groups of investigators, have shown that young infants can be effectively immunised in early infancy, during which the highest mortality occurs.

WALLACE SAKO *et al* showed that 75% of young infants under 3 months exhibited antibody response as measured by

agglutination. The disease if it occurs was milder and the mortality was lower.

#### CHOICE OF VACCINE AND DOSAGE

Comparative studies of fluid and alum precipitate vaccine (containing half as many total bacillus) injected, during the first month of life and later, invariably showed the A. P. antigen to confer a higher per cent of immunity response than with fluid H. Pertussis vaccine. Poor results were obtained with fluid H. Pertussis vaccine in early life at the Evanston Health Department Clinic and at St. Vincent Infant and Maternity Hospital. Its superiority is due, at least partly, to slower elimination whereby the immunisation mechanism has a longer opportunity to elaborate specific antibodies.

In spite of the superiority, alum precipitate antigen has not come into general use because of occasional alum abscess. The greatest factor in abscess formation was found to be intracutaneous introduction of alum, which can be prevented by adopting the following technique:—

(1) Alternate gluteal areas should be used for injection, (2) A 25 gauge  $\frac{1}{2}$  to  $\frac{5}{8}$ " needle should be used, (3) Separate needles should be used for injection (4) Each dose should be terminated by 1 c.c. of air injected so that most of the alum particles are eliminated from needle tract, (5) Deep subcutaneous or I. M. injection should be made with the needle directed distally.

Following pertussis immunisation, the agglutinins reach a plateau in 2 to 3 months, and this level is maintained usually for at least 2 years. The effect of a stimulating dose of pertussis vaccine administered a year or after the basic immunisation is to raise the protective titre to higher levels within a week.

To obtain optimum protection following basic immunisation WALLACE SAKO advocates the following measures:—

(1) A 'booster' dose of 20 billion cells when exposure occurs or in presence of an epidemic. (2) Annual stimulating dose of 10 billions in saline cells or 5 billion alum precipitate cells until 6 years of age or 'booster' dose of the above strength every 2 years.

There is diversity of views as to what constitutes adequate

dosage. Thus MACLEAN (1940) used an aggregate of 16,000 million organisms (ordinary plain vaccine) divided into 4 equal doses. The total recommended dose, however, for effective immunisation is 80 to 120 billion bacterial cells saline suspension (10 to 40 billion per c.c.) which should be divided into 3 doses and administered at monthly intervals for better antigenic response.

Plain vaccine, however, should not be used before 6 months of age. Weekly intervals which may be used in the presence of an epidemic or likelihood exposure with rapid production of immunity is not as durable as the monthly intervals.

Immunological studies show that 30 to 40 billion H. Pertussis alum precipitate cells are just as effective as 80 to 120 billion saline suspended cells. The A.P. vaccine (40 billion bacilli per c.c.) should be administered by 3 injections at monthly intervals, the dosage being, .2 c.c. first dose, .3 c.c. second dose and .5 c.c. third dose. Both BELL and KENDRICK, however, demonstrated the value of A.P. vaccine in two doses at the interval of one month representing a total of 20 billion organisms.

Soluble antigens and endotoxoids are of very little prophylactic value, unless the whole cells are used in combination. It is feasible to immunise simultaneously against diphtheria, tetanus and whooping cough. SAUR *et al* (1944) obtained best results with a mixed diphtheria and pertussis vaccine (A.P. vaccine) given in 3 doses at intervals of 3 to 4 weeks. Three monthly or bi-monthly dose of alum precipitate triple mixture of diphtheria toxoid, A. P. vaccine and tetanus toxoid administered after 6 months also confer immunity to diphtheria, pertussis, and tetanus.

#### PASSIVE IMMUNISATION

For the passive immunisation of contacts, both human and rabbit either anti-bacterial or antitoxic serum are available. BULLOWA and ALTERMAN found that rabbit antitoxic serum is capable of preventing whooping cough when administered in the incubation period prior to the onset of cough. BRADFORD SCHERP and BROOKS reported favourable protection of contacts by using rabbit anti-bacterial pertussis serum. The use of rabbit serum is, however, objectionable on the grounds of sensitisation.

The use of hyperimmune antibacterial serum, unconcentrated or lyophilized, has received considerable importance in recent years both in prophylaxis and treatment. The value of treatment, however, will be discussed later. LAPIN is of opinion that large number of contacts can be protected by hyper-immune-serum. SAUR recommends using of human pertussis immune serum to exposed non-immunised children, the dosage being 20 c.c. I. M. into the buttocks for casual exposure and two 20 c.c. for prolonged exposure (24 hrs.) given at 3 to 5 day interval. Since passive immunity is only temporary further exposure should be avoided and customary doses of phase 1 vaccine should be administered within a week. Injections being painful, most physicians have been loath to use this method.

The antibodies are part of gamma globulin. The immune bodies of 25 c.c. of human hyperimmune serum can be delivered in 2.5 c.c. of the globulin fraction which contains the antibodies, thus avoiding injection of a large volume of serum. LAPIN used this concentrated globulin fraction in 2 doses of 2.5 c.c. given at 2 day interval to contacts. He found that the majority was completely protected and those who developed whooping cough were very mild.

The results, however, must be accepted with reserve, since it is difficult to be sure that effective exposure has occurred; that attack would have followed if no serum had been injected; in fact, all susceptible infants do not contract the disease following exposure. Nevertheless, it is worthwhile administering, passive immunity specially in the presence of an epidemic.

#### GENERAL PROPHYLAXIS

*Environment and Nutrition*:—The importance of environment and nutrition as a factor in the prophylaxis of infection, whether general or specific, has been stressed by many. The best environment will not, of course prevent the introduction of infection, but good environment and nutrition do exert a favourable influence upon the results of infection. What is true of other infective disease is also true of pertussis.

*Segregation*:—Isolation of patient who is even suspected to be a source of infection, is obviously an essential step to be instituted at the earliest possible moment. Much difficulty however has arisen from the fact that clinical diagnosis of

pertussis is difficult before the onset of paroxysmal stage. This is the stage of least infectivity, specially in the absence of an epidemic. Nevertheless isolation should be instituted in all children with a history of contact showing catarrhal symptoms and subjected to bacteriological examination for early diagnosis. A child who has whooping cough for a month may be regarded as no longer infectious.

Quarantine, however, is not necessary. Exposed susceptible children should be kept under observation for three weeks and isolated at the first appearance of catarrhal symptoms. The exposed children should not be deprived of the benefit of passive immunisation and vaccine prophylaxis.

#### TREATMENT

Whooping cough like most of the infective fevers, generally cure themselves, if judiciously left alone. Treatment is generally directed towards prevention of complications and amelioration of symptoms—factors which are responsible for the high mortality rate and sequelæ in pertussis. Although nothing specific has been found as yet in the treatment of whooping cough, the entire outlook of treatment has been changed during recent years with reduction in the mortality rate, facilitated by better nursing and a better understanding of feeding, by wider use of blood transfusions and by the advent of hyperimmune serum, sulpha drugs, penicillin, and streptomycin.

*General*:—The importance of fresh air, rest and nursing in the treatment of pertussis has in no way been overshadowed by the more recent therapeutic discoveries. KOHN and FISHER have definitely shown the efficacy and importance of experienced nursing and general care in the treatment of whooping cough, and this has been re-emphasised by many other eminent physicians. The following general measures have been outlined by KOHN and FISHER, the efficacy of which is well established:

1. Personnel should be schooled in the use of all mechanical life saving measures including insertion of an airway, use of suction and oxygen etc.
2. Since anoxæmia is present in varying degrees in all severely ill infants, every patient should be placed in an oxygen tent for a trial period. Poor general conditions, pneumonia, atelectasis and convulsions are indications for prolonged use of oxygen. Period of therapy varies from 24 hours to 6 weeks.
3. Young infants often choke

themselves as a result of thick tenacious mucous, which they are not able to cough up. Suction, therefore, is sometimes a life-saving measure of the desperately ill child. It should be applied when there is sign of obstruction of trachea or larynx. They used electrically driven apparatus. The infant was placed in a sitting position during severe paroxysms and pharyngeal suction was applied and repeated as often as necessary. If a child stopped breathing, it was immediately removed from the stretcher and the larynx and trachea were aspirated. Manual resuscitation by pressure and release method was applied in the mean time by another person. During the procedure oxygen with 5% carbon dioxide was administered through a funnel kept close to the mouth. When the child breathed regularly he was again transferred to the tent. 4. Because of danger of aspiration of food during or after a paroxysm, a special feeding technique was set up. Infants were fed often and small amounts. When there was evidence of accumulation of mucus in upper respiratory tract, aspiration was instituted before feeding. Exhausted patients were fed by medicinal dropper. Feeding is always given with the infant recumbent in nurse's arm. It was an invariable rule that a nurse never left an infant during feeding. Gavage was avoided because of the danger of stimulating paroxysms.

*Therapy*:—Hyperimmune serum; Recent studies claim considerable success in the treatment of whooping cough, by hyperimmune serum. In the series of KOHN *et al*, some children received lyophile human hyper-immune serum, some concentrated globulin fraction and some had refined hyper-immune rabbit serum which also contained a pertussis endotoxoid. Most of the children improved with human serum, although improvement was not so marked in children over one year. The improvement noted was a decrease in number of paroxysms and vomiting. In the group with rabbit serum, improvement was seen infrequently. Therapeutic response was equally good with concentrated human globulin and lyophile human serum. They recommended that one or the other should be given to infants severely ill with whooping cough. FELTON reviewed the use of lyophilised type of hyper-immune serum. She commented that there was dramatic reduction in the fatality rate. SCHEINBLUM and BULLOWA reported 23 ill children recovering after the use of lyophile serum, with 52% good and

26% moderate response. MACGUINNESS and associates also found good results.

There is no uniformity in the dosage used. KOHN *et al* used lyophilised serum dissolved in 10 c.c. of sterile distilled water, 2.5 c.c. of concentrated human globulin extract and 10 c.c. of refined rabbit serum. Three doses were given I.M. to each patient, the infants who were desperately ill receiving serum on 3 successive days and the remainder of the patients receiving every other day.

It is very difficult to evaluate the result of a single therapeutic measure for an illness such as whooping cough which has such a variable course. Although there was no dramatic change in the patients, most of the authorities agree that anti-pertussis serum definitely decreased the number and frequency of paroxysms.

*Drugs*: In spite of the various remedies that have been tried treatment of whooping cough by drugs remains unsatisfactory. Modern trend of thought regarding the use of cough mixtures containing expectorants and antispasmodics is that they are of limited value. It has been said that they are distinctly harmful if used in excess, because they probably stimulate the production of mucus and consequent choking. The following sedatives and antispasmodics are, however, generally used with some success as a palliative measure:

1. Belladonna:—This is probably most valuable of the older remedies, but it must be given in progressively increasing doses before a therapeutic effect is obtained. Initial dose of  $2\frac{1}{2}$  to 5 minims of tincture 3 or 4 hourly daily must be increased each day until 10 to 15 minims of tincture in each dose is being taken, depending upon the age of the child. The drug is well tolerated by the children.

2. Ephedrine:—It is frequently successful when belladonna fails. For an infant the dose is  $1/8$  gr. t.i.d.

3. Codein:—It is best given in the form of Syr. Codein Phos; 15 to 30 minims of syrup to an infant of 6 months is not too much.

4. Phenobarbitone:—If the paroxysms are very severe it may be tried in doses  $1/8$  gr. 2 to 3 times daily to an infant of 1 year, its effect being carefully observed



Streptomycin is effective against whooping cough *in vitro*. Recently it has been shown that aërosporin, an antibiotic produced by *Bacillus Aërosporus* protected mice against lethal doses of *H. Pertussis*. Experiments on human beings showed encouraging results. The clinical value of streptomycin and aërosporin, however, remains to be evaluated.

Voluminous literature of vaccine therapy in the treatment of pertussis leaves most of the observers with feeling that it offers no real hope. Other treatments are of very doubtful value but from which benefit has sometimes been claimed includes exposures to ultra-violet rays and application of X-rays to chest.

The treatment of the important complications from which young children suffer, demands consideration. The principal danger is infection. Lung infections should be treated either by sulphadiazine or penicillin. Some are of opinion that penicillin is more effective than sulpha drugs. Convulsions may not yield to mustard bath, whiffs of anæsthesia and sodium phenobarb, although these should be tried, the best way of terminating an attack is to perform lumbar puncture and withdraw a few c.c. of C.S. fluid. Dehydration is treated by parenteral fluid administration, either whole blood plasma or dextrose and isotonic sodium chloride.

In conclusion, it may be said that modern therapeutic weapons have definitely improved the prognosis of whooping cough. If mass active immunisation is practised in a community there will be very few patients to spread the infection to the younger age group and consequently the disease, like diphtheria, will be completely iradicated. Even when complete protection is not obtained from active immunisation, there is sufficient modification of the disease to justify the general recommendation of vaccination.

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