◆ ABSTRACTS ◆

TREATMENT WITH PRONTOSIL OF PUERPERAL INFECTIONS DUE TO HAEMOLYTIC STREPTOCOCCI

by

Leonard Colebrook, M.B., B.S. London, Meave Kenny, M.R.C.S. (Eng.) M.C.O.G., and the members of the Honourary Staff of Queen Charlotte's Hospital; Lancet, Vol. 231, No. 23, Dec. 5, 1936.

Two groups of cases are here discussed, making a total of sixty-four cases, treated with prontosil and prontosil soluble. Of these sixty-four cases only three died. The cases treated were not selected specially, and all infections, ranging from very mild, to peritonitis of several days duration before treatment, are reported.

Of twenty-six consecutive cases treated, six had positive blood cultures for Haemolytic Streptococci, but in spite of this recovery was prompt. Eleven were not severe and would have recovered under routine treatment, but there is substantial reason to believe their recovery would have been much slower and quite probably retarded by complications such as the development of an inflammatory mass in the pelvis. All but one of this group of twenty-six were notifiable as cases of puerperal fever and all but this one case were shown to be infected with haemolytic streptococci, of Lancefield's Class A. None of these patients died, and the rapid recovery of severely ill cases combined with the shorter stay in hospital than patients on other forms of treatment leads to the belief that prontosil compounds actually benefit the patient.

DOSAGE:

Prontosil (Red) by mouth

Gravely ill—12 tablets per day, total 4 gm.
Moderately severe—6 tablets per day.
Mild—6 tablets per day.

Prontosil soluble, intramuscular:

Gravely ill—20 c.cm. every eight hours.
Moderately ill—20 c.cm. every eight hours.
Mild—10-20 c.cm. twice per day.

Dosage is diminished as the temperature falls and the drug is stopped completely 1-2 days after it reaches normal. Experimental work is being done to determine whether this is the most beneficial administration.

TOXIC EFFECTS:

A mild urinary tract infection occurs but this clears up with cessation of treatment and apparently leaves no after effects and causes little discomfort during treatment. Commentary on the whole series of 64 cases treated to date at Queen Charlotte's Hospital:

(a) There has been an appreciable fall in the death rate of septicaemia caused by the Haemolytic Streptococcus.

(b) The incidence of peritonitis was the same but the death rate lower.

(c) Of the 64 prontosil treated cases none developed a pelvic inflammatory mass after treatment had been instituted, but of twenty mild cases just before prontosil treatment was instituted two developed masses. The average stay in hospital of the sixty-one prontosil cases (3 of the 64 died) was 18 days. That of 61 consecutive non-fatal cases not receiving prontosil was 31.3 days.

(d) None of the prontosil cases have returned to hospital for treatment of complications or flare-ups, and follow-up visits show no relapses.

(e) Analysis of those cases that had positive blood cultures for haemolytic streptococci:

12 of the 64 cases had positive blood cultures.

9 of these 12 recovered of which three exhibited signs of generalized peritonitis on admission.

3 patients died, and of these:

1 had a generalized peritonitis dating from several days before admission.

1 had extensive thrombophlebitis.

1 had no autopsy, but a similar condition was suspected.

DISCUSSION OF CLINICAL RESULTS:

A careful review of the prontosil treated cases seems to justify the view that the infections were of usual severity, there being no evidence of a sudden change in virulence of the organisms or of resistance in the patients. In 1935 this hospital had a death rate of 24% that has become 4.7% in 1936 with prontosil.

PROBLEMS OF THE FUTURE:

(1) Dosage can probably be greatly reduced.

(2) Uncertainty exists in the relative merits of oral and intramuscular administration.

(3) Uncertainty exists as to how the merits of this group of compounds is limited to the haemolytic group of streptococci.

(4) They may be of great value as prophylactics in cases in contact with hae-

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molytic streptococci, particularly in home obstetrics where sore throats, infected fingers, or filth abound.

(5) The relative merits of prontosil soluble and paraaminobenzenesulphoamide have not been thoroughly determined.

(6) Animal experimentation is very encouraging.

(7) The question of toxicity has not been thoroughly examined, but the compound does not cause any appreciable reaction.

J. A. WEBSTER, B.Sc. '38.

THE TREATMENT OF URAEMIA

D. Murray Lyon, M.D., D.Sc., F.R.C.P.E.
The Practitioner, No. 822, Vol. 137, December, 1936.

Uraemia has been defined as a toxic state which may appear in any kind of serious disease of the kidney. Because it still remains much of a mystery, its treatment to a large extent is traditional.

CONVULSIVE URAEMIA:

It usually occurs in acute nephritis or during an acute exacerbation in the course of a long standing case. It is also common in the hydraemic type of Bright's Disease when there is oliguria, salt and water retention, oedema and probably anasarca.

The principal features of this uraemia are: Convulsions and loss of consciousness; severe headache, which may precede or follow the fits; transient involvement of the special senses; local palsies or some muscular rigidity.

TREATMENT:

All cases of hydraemic nephritis should receive adequate treatment so that this complication could be avoided. Sodium rather than the chloride ion is believed to produce and maintain anasarca, and therefore sod. bicarbonate and sod. bromide should be used with care when oedema threatens.

When convulsions have developed, morphine is given at once and chloroform used till the opiate has come into action. Later chloral to clamp down the nervous system and prevent convulsion. Such measures are helpful, but do not strike at the root of the trouble. Attempts to reduce intracranial tension are made by giving a dose of croton oil, and by performing a lumbar puncture, allowing fluid to escape gradually. Venesection often relieves symptoms. Intravenous injection of 100 c.c. 15% NaCl or a 50% glucose solution or 200 cc. 10% mag. sulphate may cause prompt cessation of symptoms.

RETENTION URAEMIA:

Occurs commonly in advanced disease of the kidneys where they no longer can deal adequately with metabolic waste products. Phosphate retention tends to rise parallel with nitrogen bodies, while calcium falls. Excessive loss of base gives rise to acidosis. Dehydration and serious loss of chloride may result from persistent vomiting, diarrhoea and diuresis. Anaemia is often a complicating feature. The onset is usually insidious. Symptoms: Weakness, undue fatigue, depression and inability to concentrate, headache.

It is usual to describe three subdivisions of retention uraemia: 1. Cerebral or nervous; 2. Gastro-intestinal; 3. Respiratory.

TREATMENT:

All subjects of long standing nephritis are potential candidates for uraemia and should be kept under constant supervision. Suitable treatment of the nephritis may delay the advance of the disease. Later, when retention uraemia becomes fully developed, all the symptoms become more marked and new ones appear. Gastro-intestinal symptoms may be mild or severe. They are nausea, vomiting, anorexia, continued retching or persistent hiccough. Flatulence and vague abdominal pains may be present. The mouth is often the site of inflammatory trouble. Tongue is dry, coated, and the breath has an objectionable urinous odour. Respiratory system: Resistance to infection is low. Bronchitis and pneumonia are apt to develop. Pulmonary oedema, hydrothorax, "renal asthma", and air hunger may occur. Towards the end of life, Cheyne-Stokes breathing is not uncommon.

In the fully established cases little permanent benefit can be expected. Many individual symptoms can be relieved. The general measures designed to reduce work of the kidneys and favour elimination should be continued. **Headache:** drugs are of little value. Lumbar puncture or venesection may offer temporary relief. **Sleeplessness, restlessness and general irritability:** Warm bath before retiring, bromide with or without chloral, paraldehyde, etc. Morphine may be resorted to when other drugs fail. **Muscular twitching and spasm:** Calcium lactate or calcium gluconate intravenously, or parathormone hypodermically. **Itching:** Bran or alkaline baths, or surface bathed with 2% phenol solution or Calamine lotion. Ergotamine tartrate has been recommended. Anaemia, if present, should receive attention. **Gastro-intestinal symptoms:** Constipation avoided by a daily saline; drastic purgation is harmful. **Diarrhoea:** The usual remedies by mouth, and colonic lavage may be useful. **Persistent hiccough:** Nerve depressants, stomach washed out, mustard plaster or a turpentine stupe applied over epigastric area. **Vomiting:** A little sickness may be corrected by restricting the diet for a day to simple fluids, e.g., fruit juices with added glucose, citrated milk, or milk

and soda water. Gastric lavage is best. One pint of normal saline or glucose saline should be left in the stomach after each lavage. **Dehydration and hypochloraemia:** One pint 5% glucose in saline intravenously. For marked hypochloraemia 10% saline intravenously. When flatulence is troublesome, kaolin or powdered charcoal should be given by mouth. **Respiratory symptoms:** For pulmonary oedema—full doses of atropine; venesection sometimes offers relief. **Nocturnal dyspnoea:** full doses of bromide or administration of morphia with atropine. **Acidosis with air hunger:** Intravenous injection of 4% sod. bicarb., or sod. citrate by mouth. Heart failure should be watched for, and the patient brought under the influence of digitalis on first sign of it. For emergencies, intravenous injection of strophanthin (1/100 grain) is the most satisfactory treatment.

D. J. TONNING, '38.

EXTRINSIC FACTOR IN PERNICIOUS ANAEMIA

W. B. Castle, M. D., and Thomas Hale Ham, M.D., J.A.M.A., Oct. 31, 1936.

Patients suffering from pernicious anaemia seem to be unable to derive from food some substance essential for normal function of bone marrow. The nutritional defect is apparently the result of a failure of a reaction between an extrinsic factor in food and an intrinsic factor of normal gastric secretion. This is based on experimental evidence:

(1) The daily administration of either (extrinsic factor) 200 gms. of beef muscle or (intrinsic factor) 150-300 c.c. or normal gastric juice separately is without significant effect on blood formation.

(2) If such amounts of each substance are administered daily in such a way as to permit contact either before or after administration to the patient, clinical improvement and evidence of increased blood formation are usually apparent within ten days and are progressive for the duration of such therapy.

This has apparently been confirmed by various workers but Greenspen has concluded that the food factor is not essential, and inferred that in the experiments where normal gastric juice and beef muscle were incubated together, the latter served only to absorb the pepsin which will destroy the intrinsic factor.

To confirm and criticise previous work, ten typical cases of Addisonian pernicious anaemia were selected. Each had achlorhydria, an initial red blood cell count of less than 2,000,000 per cubic millimetre, and each was placed on a special diet. The haematopoietic response was measured by the percentage of reticulocytes and the red blood cell count.

The observations were:

I. Normal human gastric juice does not contain an antipernicious anaemia principle effective on oral administration without contact with food (extrinsic) factor.

Certain positive results obtained from gastric juice alone may be due to: (a) Dietary restrictions included only liver and kidney and the extrinsic factor may well have been present in other foods eaten. (b) This being so, a period of only four hours after administration of gastric juice until food was taken was hardly sufficient to prevent effective contact between intrinsic factor and the food, as this has been shown to occur after a six hour interval.

II. Activity of dessicated hog's stomach mucosa is due to presence of both intrinsic and extrinsic factors. Boiling for at least five minutes and digestion with pepsin and hydrochloric acid for 48 hours at 37.5°C will each destroy the activity of hog's stomach mucosa. However, this inactivated mucosa along with gastric juice gives a positive response. Thus hog's stomach mucosa contains an extrinsic (thermostabile) substance as well as the intrinsic (thermolabile) factor.

III. Incubation of normal human gastric juice at 37.5°C for two hours inactivates only a portion of the intrinsic factor. It does destroy some of it, however, but whether or not this is due to peptic hydrolysis has not definitely been shown.

IV. Beef muscle and gastric juice administered without opportunity for contact are wholly ineffective. Gastric juice (which was not incubated for the above reason) was neutralized to prevent any possible peptic hydrolysis and administered without effect. Alternating daily with beef muscle by itself, the juice produced no effect. Only when so administered as to ensure effective contact was an appreciable increase in blood formation obtained.

V. Former experiments apparently demonstrating the absence of the extrinsic factor from certain substances are not necessarily valid. In these experiments the gastric juice was incubated for two hours at 37.5°C so that the intrinsic factor may have been destroyed to such an extent as to cause some of the negative results. Hence the number of substances believed to contain the extrinsic factor, such as beef muscle, eggs, autolyzed yeast, wheat germ, rice polishings and tomato extract, may be augumented by further work.

Finally we may note that certain types of macrocytic anaemia will respond to foods rich in the extrinsic factor. Here we may assume the deficiency of this factor in the diet to be the dominant defect.

Old Way...

CURING RICKETS in the CLEFT of an ASH TREE

FOR many centuries,—and apparently down to the present time, even in this country—ricketic children have been passed through a cleft ash tree to cure them of their rickets, and thenceforth a sympathetic relationship was supposed to exist between them and the tree.

Frazer* states that the ordinary mode of effecting the cure is to split a young ash sapling longitudinally for a few feet and pass the child, naked, either three times or three times three through the fissure at sunrise. In the West of England, it is said the passage must be "against the sun." As soon as the ceremony is performed, the tree is bound tightly up and the fissure plastered over with mud or clay. The belief is that just as the cleft in the tree will be healed, so the child's body will be healed, but that if the rift in the tree remains open, the deformity in the child will remain, too, and if the tree were to die, the death of the child would surely follow.

*Frazer, J. G.: The Golden Bough, vol. 1, New York, Macmillan & Co., 1923

It is ironical that the practice of attempting to cure rickets by holding the child in the cleft of an ash tree was associated with the rising of the sun, the light of which we now know is in itself one of Nature's specifics.

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Also, the conception of an intrinsic factor alone does not satisfactorily explain the immediate etiologic mechanism of those cases of macrocytic anaemia in which the intrinsic factor is demonstrably present in the gastric contents.

R. L. AIKENS, B.Sc., '39.

ASPHYXIA NEONATORUM

Nicholas J. Eastman, International Clinics, Series 46, Vol. II.

The term asphyxia is traced from its original meaning, absence of pulse, to its present use to denote suffocation and profound lack of oxygen in the circulating blood, arising from a number of conditions. In this review asphyxia neonatorum is limited to mean the failure of an infant at birth to breathe because of insufficient oxygen during labour; apnea will mean a similar condition, but due to combined or unknown causes.

Neonatal death and still birth have common causes: whether the organism dies before, during, or after birth depends on the nature, extent and the time of the accident or lesion. The knowledge of the exact causes of these two conditions is incomplete, but the major causes are doubtless haemorrhage, prematurity, and asphyxia. These three are closely interrelated. One of the effects of asphyxia is an engorgement of veins and capillary vessels all over the body. Where these structures are poorly supported, they often give way. In premature infants this is more likely to occur.

Cerebral haemorrhage ranks first as an immediate cause of stillbirth and neonatal death. Galloway's autopsy series showed 34% of foetal deaths (including prematures) with this lesion; it was present in 40.6% of full term infants. Hemsath and Canavan found 34 microscopic haemorrhages in the medullas of 53 children dying at birth and in the neonatal period. In 12 this supplied an anatomical cause of death. Some factors which may cause intracerebral haemorrhages are intense congestion in the delivered head caused by pressure on the undelivered body, and sudden compression and release of the head in breech deliveries. Anoxemia is produced by direct pressure of blood on the circulatory centres causing a slowing of umbilical circulation, or by general increase of intracranial pressure with slowing of cerebral circulation.

Prematurity is frequently accompanied by haemorrhages, but there may also be large areas of unexpandable pulmonary tissue, and the child dies from want of oxygen.

The third major cause, is the cutting off of oxygen supply to the foetus. This may be occasioned by compression of cord between presenting part and pelvic brim, or more frequently by contractions of the uterus abnormal in duration and intensity interfering with placental exchange of gases. The reviewer presents his series of blood gas studies of apnoeic infants without evidence of haemorrhage. The results showed low oxygen tension, rise in concentration of carbon dioxide and lactic acid, with a fall in pH.

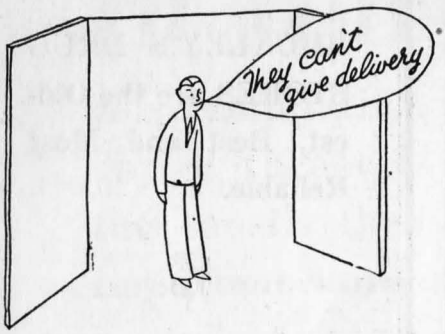
The phenomenon of asphyxia neonatorum can be closely reproduced by depriving animals of oxygen, the symptoms after the "oxygen crisis" being very similar to asphyxia pallida. A short period during the experiment, i.e. after respirations cease and before blood pressure falls, represents asphyxia livida.

The onset of respiration at birth at one time was thought to be due to physical stimulation. This, the older theory of Peyer, is not untenable. The explanations based on increased carbon dioxide tension and oxygen lack are unsatisfactory in the light of recent experiments. The author found that breathing commenced whether the carbon dioxide tension was high or low, and that oxygen tension had little effect on the onset of respiration. The experiments of Rosenfeld and Snyder point to the first breath as being a continuation of intrauterine respiratory movements.

The prevention of apnoea and asphyxia neonatorum consists in the preservation and protection of the delicate, already functioning, nervous respiratory mechanism of the foetus. In treatment of respiratory failure at birth administration of oxygen is the only suitable method in most cases. Mouth to mouth insufflation is tremendously practical in spite of its big drawbacks. Intratracheal and intrapharyngeal oxygen is recommended when available. The most suitable gas is oxygen alone, as any addition to the excess of carbon dioxide already in the infant's blood may be harmful. The reviewer states that slapping, swinging, and plunging have killed untold numbers of infants. The omission of these methods is a present tendency, and represents the most important fact to be recorded.

GEORGE PARSONS, '40.

Great men too often have greater faults than little men can find room for.—*W. S. Landor.*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