columns 2 and 3, on the other hand, accurately represent the number of cases and deaths in the inoculated and uninoculated, inasmuch as none of those inoculated in previous years contracted enteric fever.

A further point adverted to by Colonel Fawcett is the circumstance that the only case which occurred among the inoculated was that of a patient admitted to hospital on the thirty-third day after inoculation. It would seem that the disease was in this case contracted before anything in the nature of protection had been established by the inoculation.

CASE OF SECONDARY ANÆMIA BECOMING PERNICIOUS :

WITH DETAILED EXAMINATION OF THE BLOOD.

By WILFRID EDGEcombe, M.D.LOND., F.R.C.S.ENG., Harrogate.

THE following case of anæmia afforded me the opportunity of making repeated examinations of the blood, extending over a period of several months, from the time when the patient first came under observation until her death, the last examination being made three days before her death occurred. The results are embodied in the accompanying table:

Date.	Hæmoglobin.	Red Corpuscles.	Colour Index.	Nucleated Red Cells : Proportion to 1,500 White Corpuscles.		White Corpuscles.	Polymorpho-nucleated.	Lympho-cytes.	Large Uni-nucleated.	Eosino-phile.
				Normoblasts.	Megaloblasts.					
	Per cent.	Per c.mm.				Per c.mm.	Per cent.	Per cent.	Per cent.	Per cent.
November 25th, 1899.	23	475,000	2.40	34	30	1,400	51.3	44.7	3.3	0.6
December 31st, 1899.	63	2,435,000	1.30	2	0	3,750	44.9	45.4	5.6	4.0
March 3rd, 1900	85	3,250,000	1.30	0	0	5,200	57.5	35.5	4.0	3.0
April 2nd, 1900	82	2,800,000	1.40	0	1	4,000	68.7	27.4	2.1	1.7
May 7th, 1900	63	2,100,000	1.50	0	2	9,200	72.3	23.2	2.3	1.5
June 13th, 1900	30	1,530,000	0.98	5	21	6,000	53.4	40.6	3.8	2.0
June 24th, 1900	25	512,000	2.40	94	227	5,400	51.7	43.0	4.1	1.1
July 2nd, 1900	27	1,150,000	1.10	9	30	7,500	63.6	31.5	2.3	2.5
July 17th, 1900	20	610,000	1.60	12	26	6,500	68.5	24.3	4.7	2.4
August 2nd, 1900	15	892,000	0.84	8	62	5,000	62.8	31.4	3.5	2.2
August 28th, 1900	8	485,000	0.84	9	23	9,100	75.1	18.9	4.6	1.3

History.—The patient was an unmarried lady, aged 38, in comfortable circumstances, and a member of a family which presented several examples of an unstable nervous system. She, herself, was highly neurotic. Her statement, corroborated by others, was that she had suffered almost continuously from anæmia for the previous twelve years, having had periods of ill-health followed by intervals of more or less complete recovery. As far as could be gathered the symptoms did not differ from those of ordinary simple anæmia, and they readily improved under iron, which she took periodically. During the whole of this time she suffered from trouble in the nasal cavity, attended by repeated discharge of blood and matter in small quantities, which she swallowed, particularly when lying down and during sleep. More pronounced bleeding from the nose occasionally occurred, but profuse epistaxis never. She was, however, seldom free from the persistent slight loss of blood. During the last two years the symptoms of anæmia became more severe, and yielded less readily to iron, until, in the summer of 1899, she began to suffer from attacks of troublesome diarrhoea, which she attempted unsuccessfully to control with large doses of the pernitrate and other forms of iron. Her menstrual periods occurred at irregular and distant intervals, and the discharge was scanty. She did not appreciably lose weight.

State on Examination.—When she consulted me late in November, 1899, she was obviously suffering from some grave form of anæmia. She was at once put to bed, and carefully examined. The lemon-yellow tint of pernicious anæmia was strikingly marked in the face, while the conjunctivæ, lips, and gums were perfectly bloodless. She suffered from breathlessness even while lying at rest in bed, and the slightest exertion gave rise to extreme dyspnoea and violent palpitation. The lungs were normal. The heart was dilated; a systolic *bruit* was heard at the apex, and loud hæmic murmurs over the pulmonary area and the external jugular vein in the neck. There was slight oedema of the feet. The tongue was clean and glazed; the teeth were discoloured, and there were a few painless stumps, around which, however, there was no sign of alveolar suppuration. The abdomen was distended and tender, especially over the liver, which was enlarged to 1½ inch below the costal margin, the vertical dullness in the nipple line measuring 3½ inches; the spleen could readily be felt level with the costal margin on the left side. There was obstinate diarrhoea, a poor appetite, and the stomach was very sensitive and readily upset by food or medicine. Examination of the eyes disclosed retinal hemorrhages, and on testing the sight it was found to be much impaired. The nasal cavity showed an atrophic condition of the mucous membrane, with a small ulcerated surface on the left side of the septum, covered with tenacious crusts, the removal of which caused capillary oozing of blood. In the right nasal cavity was a myxomatous polyp. The urine was high coloured from excess of a pigment, the nature of which was not

determined. It contained indican, but no albumen. Though the patient had never been out of England, the faces were examined repeatedly for ova of intestinal parasites, always with a negative result.

Blood.—The accompanying table shows the result of the examination of the blood at this and subsequent periods. For the enumeration of the corpuscles the Thoma-Zeiss hæmocytometer was used; for the estimation of hæmoglobin Oliver's hæmoglobinometer. The differential counting of the leucocytes and the enumeration of the nucleated red cells were made from films fixed with alcohol and ether, and stained with eosin and hæmatoxylin. Fresh blood under the microscope showed at this stage the red corpuscles to be somewhat irregular in shape and size, but poikilocytosis was not well marked. There was an absence of rouleaux formation; the corpuscles were well charged with hæmoglobin; the normal concave depression was generally absent, and many corpuscles showed a marked degree of vacuolation. In the stained films nucleated cells were found, normoblasts and megaloblasts being in about equal proportion.

Treatment and Course of Disease.—The patient was kept in bed on a light easily assimilable diet, and was freely stimulated. Further bleeding from the nose was prevented. Arsenic was given in minimum doses of the liquor, but under it she grew rapidly worse. She stated that she had tried to take arsenic previously, and that it had always upset her. Salol was then tried, but it caused vomiting, and had to be discontinued. Bone marrow similarly could not be tolerated. At this stage she was extremely ill, the dyspnoea urgent, palpitation violent, pulse very rapid (sometimes almost uncountable); there was irregular pyrexia, varying from 100° to 105° F. At times she was almost moribund. Oxygen was now administered, not through the usual glass funnel, which allows too rapid diffusion for much of the gas to be inhaled, but through a rubber tube passed into the mouth and held in position between the teeth. By this means, as the patient breathed always through the mouth, a large proportion of the gas was inhaled. The dyspnoea was rapidly relieved; indeed, the patient felt so much benefit from the oxygen that she inhaled

almost continuously night and day. No ill-result followed beyond transitory mental excitement. At the same time it occurred to me to try Hommel's hæmatogen, a preparation I had previously used and found to be readily borne. It was tolerated well, and rapidly pushed in large doses, with the result that immediate improvement set in and was maintained. By December 31st, that is, in less than a month, the corpuscles had risen from under half a million per c.mm. to nearly 2½ millions, and the hæmoglobin increased from 23 to 63 per cent. The oxygen was continued in progressively diminishing quantities until dyspnoea disappeared. How far the sudden improvement was to be attributed to the natural tendency to remission that exists in this disease, how far to the oxygen as supplying the necessary stimulus to recovery, and how far to the hæmatogen, must remain undetermined. It certainly appeared as if the last did good.

A noteworthy incident during this period was an attack of acute hysterical mania which lasted a few days, but did not interfere with progress.

When well enough she was sent to Dr. Bronner, of Bradford, who removed the polypus from the right nasal cavity, and treated the ulcerated surface on the left side.

During March and April, 1900, she expressed herself as feeling better than she had done for years. Her periods returned, and she went about as usual, had a phenomenal appetite, a good digestion, and generally enjoyed her life. The liver and spleen returned to their normal size, abdominal distension disappeared, and the bowels acted regularly. She continued to take the hæmatogen, as whenever she left it off she did not feel so well.

Fearing that improvement was but temporary, and that a relapse was certain to occur, I determined, as her digestion was now good, to try arsenic again in the hope of rendering her recovery more permanent. Beginning with minute doses, she took it for a week, during which she fell off markedly in appetite and general condition, so that it had to be discontinued, after which she improved again. Another attempt with salol met with a similar result. During May she was not so well, and in June the blood examination showed her to have lost ground to a considerable extent. She was therefore put to bed again, the hæmatogen was pushed, and the oxygen resumed occasionally. Nevertheless, she grew steadily worse, and all the former symptoms returned. The liver became enlarged to 2 inches below the costal margin, the liver dullness in the nipple line measuring 6 inches, and the spleen could readily be felt projecting beyond the ribs. On June 20th she was seen in consultation with Dr. Barrs of Leeds, who advised a diet consisting largely of meat, which she took readily, and a further attempt with arsenic, unknown to the patient. It was accordingly introduced surreptitiously into the hæma-

togen in half-minim doses of the liq. arsenici hydrochloricus, with the same result as in previous trials, a rapid aggravation of the symptoms. The subsequent progress of the case may be gathered from the blood state as shown in the table—namely, a steady decline in spite of all treatment. Transfusion of blood was offered, but declined by the patient and friends. She died on August 31st, and unfortunately no *post-mortem* examination was permitted.

REMARKS.

Reference to the table shows the importance of making repeated examinations of the blood, for during certain stages of the disease it would have been impossible to have diagnosed the condition from one examination, with the result that a too hopeful prognosis might have been given.

The following points of interest may be noted in the table:

1. The low percentage to which the hæmoglobin fell before death; 8 per cent. is the lowest reading I have recorded among many hundreds of examinations.

2. The high-colour index, which in itself would give rise to suspicion as to the nature of the disease. The colour index depends, of course, on the adjustment between the two instruments used for estimating hæmoglobin and corpuscles respectively. The scale of Oliver's hæmoglobinometer is based on the mean of a large number of counts made equally with the Gowers and Thoma-Zeiss cytometers, which differ slightly in their readings. The colour index, as here given, may be taken as very near the truth. It was maintained throughout (with one exception) at a level considerably above the normal (1.0), rising on two occasions to 2.4, until shortly before death, when it fell to 0.84.

3. The preponderance of megaloblasts over normoblasts among the nucleated red cells: This is regarded by many observers as characteristic of pernicious anæmia; for, though nucleated red corpuscles are found frequently in all grave anæmias, practically in no other condition do the megaloblasts so constantly outweigh numerically the normoblasts. Cabot,¹ in a recent valuable paper, the outcome of the study of 110 cases of pernicious anæmia, regards this as a distinctive feature of the disease, and a point of differential diagnosis from secondary anæmia. In the table of nucleated elements I have not classified separately the microblasts, nor the free nuclei, which were of fairly frequent occurrence; nor is mention made of myelocytes, which occurred not rarely. On two occasions coarsely granular basophile cells were met with. The relative diminution in the number of nucleated cells towards the end has been noted by other observers. Coles,² in one of two cases in which repeated counts were made, noted the same fact. It may, perhaps, be regarded as an indication of exhaustion of the regenerative power of the hæmogenetic tissues.

4. The leucocytes: Taking the average number of leucocytes present in health as from 8,000 to 9,000 per c.mm., it will be seen that the number present in this case was usually below normal. The lymphocytes were relatively somewhat in excess and the polymorphonucleated leucocytes somewhat under their normal proportion. Other observers (Hayem, Stengel, etc.) have noted the same facts, and Cabot³ contrasts the diminution in polymorphonuclear neutrophiles in pernicious anæmia with their frequent though not invariable increase in secondary anæmia. The large hyaline cells and the eosinophiles were present in normal numbers.

Causation.—Passing in review the definite history of long-continued repeated loss of blood in small quantities from the nose, giving rise to a state of anæmia lasting, with intermissions, for a long period of years, the case might be considered as one of pure secondary anæmia. If this be so then the condition in the later stages is clinically indistinguishable from the true pernicious form. Moreover, the prevention of further hæmorrhage failed to arrest the progress of the disease. The case must be regarded as originally a secondary anæmia, gradually merging into true pernicious anæmia, and must be classified with those described by Coupland⁴ as "symptomatic or secondary pernicious anæmia," differing only from the primary or idiopathic form in the fact that in the latter no obvious cause is to be found. Cabot, in the paper above referred to, states that he has no experience leading him to believe that there is any such condition as "secondary pernicious anæmia."

The case under consideration appears to me to clearly show the possibility of chronic secondary anæmia passing into the pernicious form, and tends to bear out the well-known

views of Stockman as to the pathology of the disease; that all cases of "idiopathic" pernicious anæmia are really forms of secondary anæmia, initially brought about by various causes, and subsequently perpetuated and rendered "pernicious" by repeated minute hæmorrhages into the tissues as a result of the anæmic state. In the idiopathic cases the hæmorrhages are internal and clinically invisible; in the obviously secondary cases the hæmorrhage is primarily external and visible, with the subsequent development, in the later stages, of the former condition.

The possibility, however, must not be lost sight of that the case may bear on Hunter's⁵ recently published hypothesis that the disease is due to blood destruction resulting from an infective process set up in the gastric or intestinal mucous membrane by the swallowing of repeated small doses of pus derived from some suppurating focus, usually alveolar supuration from carious teeth; for in addition to the blood continually swallowed there was a slight admixture of purulent discharge from the nose which passed down into the stomach, and may there have set up infection. The small size of the ulcerated surface and the slight amount of discharge render this supposition somewhat improbable.

REFERENCES.

¹ Cabot, Pernicious Anæmia; a Study of 110 Cases. *Amer. Journ. Med. Sci.*, August 6th, 1900. ² Coles, The Condition of the Blood in Two Cases of Pernicious Anæmia. *BRITISH MEDICAL JOURNAL*, vol. i, 1900. ³ *Loc. cit.* ⁴ See Allbutt's *System of Medicine*, vol. v, p. 522. ⁵ Hunter, Further Observations on Pernicious Anæmia, a Chronic Infective Disease. *Lancet*, vol. i, 1900.

THE TREATMENT OF TWO CASES OF NERVE LEPROSY IN WHICH RECOVERY TOOK PLACE.

By GEORGE THIN, M.D.

In the comparatively small number of cases of leprosy that recover—although in nerve leprosy the chances are considerably more favourable than in tubercular leprosy—it is often difficult to estimate how much the favourable result is due to general hygienic measures and how much to the action of medicinal remedies. I wish, therefore, to put on record the outlines of two cases of nerve leprosy in which the credit of the cure must, I believe, be chiefly attributed to the action of drugs.

A boy, aged 11 years, was brought to me suffering from fully-developed and severe nerve leprosy. He had been born in the West Indies, was brought to England when he was 4 years of age, and a few months afterwards it was noticed that there was something wrong with his skin. After the skin affection had lasted for several years it was recognised by Erasmus Wilson as leprosy. I found his legs and thighs discoloured and completely anæsthetic over a large extent of surface. The affected area of skin terminated behind on the gluteal region on both sides, and was marked by a strictly delineated, slightly raised, scaly border. A considerable part of the affected area on the thigh was of a faint bluish-violet colour. The fingers of both hands were "clawed" and some mutilation had taken place, but I have no notes of the exact condition of each finger. There was anæsthesia about the arms and wrists and also on the face, which was partially discoloured. The eyes were watery and bleared, and the eyebrows were defective. The boy had the physique of a lad of 7 or 8 instead of 11, the limbs being small and shrunken, and his appearance that of an atrophied and wasted creature.

The main line of treatment I prescribed was the use of chaulmoogra oil, which was applied externally and given internally. When I saw him again three months afterwards his general condition was improved, the erythema was less pronounced, and the doses of chaulmoogra oil had been increased until he was taking 21 drops daily without discomfort.

His third visit to me was eight months after I had first seen him, and my notes state that on the front of the right wrist there was a large bulla continuing down to the thumb. There were bullæ on the dorsum of the distal ends of the little and ring fingers, and he had a sensation of pain in these places. The right groin was erythematous and the seat of small papules. There were minute red papules on the abdomen, and