him rightly, he means to leave open the possibility that during the succession of generations each succeeding generation may acquire an additional degree of immunity, and that this originally infinitesimal amount may accumulate to a finite appreciable amount, or even to total immunity, in the same way that Darwin, to account for the hereditary transmission of acquired characters, presupposes the accumulative effect of a long series of generations during which the influence which first led to the acquisition of the new character was constantly at work. In this form the theory of the hereditary transmission of immunity has indeed frequently been advanced in order to explain the immunity which certain human races—negroes and mulattos—enjoy with regard to certain tropical diseases. While originally liable to the deleterious influence of these infections in the same way and to the same extent as the white races, they are said to have become proof against them by living in regions in which every following generation is exposed to and attacked by the same poison, and in which every generation leaves to the next the “infinitesimal” amount of immunity inherited from the preceding *plus* the equal amount acquired by itself. With regard to this theory I have in the first place to remark that it is by no means identical with that first advanced by Dr. W. C. Wells as far back as 1813, and adopted by Darwin, which explains this racial immunity by natural selection, by the “survival of the fittest.” According to Wells, among the different varieties of men which populated the middle regions of Africa some were better able to resist the endemic maladies than others, they consequently survived and spread, while the others perished. It therefore is not an acquired character that was transmitted, but a natural immunity inherent in a dark-coloured race. This theory is unsatisfactory, because, while it may explain the extermination of the light-coloured races and the survival of the others, it does not account for the immunity of the latter. Not long ago the same hypothesis has been extended to the microcosm of the animal cell state, and has been made use of to explain acquired immunity in general (Grawitz). The “fittest” of the cells, those best able to resist the toxic influences of bacterial poisons, survive and multiply, while those of inferior powers of resistance succumb. But in this extension the theory is less satisfactory still, because there is no imaginable reason why of an aggregate of uniform cells, without any “racial” differences whatever, some should be endowed with defensive properties which the others want. Any theory which explains the immunity of certain races by some natural process of evolution will be more acceptable than this “first case of recognition of the principle of general selection,” which leaves the racial immunity altogether unexplained as a mysterious appendix of a pigmented skin surface. But this accumulation hypothesis, which implies the co-operation of inherited and acquired immunity, if at first sight plausible and captivating, is also not free from objections.

In the first place a more thorough study of tropical diseases in our colonies has somewhat shaken the unconditional belief in many a statement which by textbooks has been stamped with an almost axiomatic and catholic character. The immunity enjoyed by coloured races seems by no means so absolute as has been generally taught. In not a few cases on close inquiry—and a reliable previous history is, under the circumstances, not always an easy matter—the immunity of the adult natives seems to have been the result of an attack in early life. On the other hand, it is the newcomer, the inexperienced settler, who is most exposed to infection, while those who become accustomed to the climate and a suitable mode of living are much less in danger. But there is one circumstance in particular which more than any other detracts from the plausibility of this theory, that is, that no similar gradual immunisation has ever been observed in the white races with regard to any of the infectious diseases which they have suffered from.

With regard to vaccination it may be objected that a long enough time has not yet elapsed to produce such a result. The same objection, however, could hardly be raised in the case of syphilis, or indeed that of small-pox, unless one assumes that the struggle between the black races and certain tropical diseases dates back to prehistoric times. Until we have at least some clinical or experimental proof that infectious diseases lead by themselves to a gradually

increasing immunity in the offspring, the accumulation theory as an explanation of racial immunity, will remain an unsubstantial hypothesis.

NOTES AND REFERENCES.

¹ It goes without saying that I am not speaking here of the hereditary transmission of infectious diseases. Wherever this has been adduced to support the doctrine of the inheritance of acquired characters, it has been done in utter misconception of its meaning and scope. It has also to be remarked that bacillary infection of the germ plasma as the cause of congenital infectious disease, although perhaps a clinical postulate, has not yet been demonstrated pathologically. The experiments made by Baumgarten and Maffucci to prove germinal infection, by injecting tubercle bacilli into fowls' eggs, and thus producing chickens affected with tuberculosis, are based upon the same fallacy of which Sir John Falstaff was guilty when he objected to “pullet-sperm in his brewage.” The hen's egg (ovum) is not the female germ (ovum), but an intermediate stage between the latter and, as Cressida has it, the “chicken 1 the shell.” The argument which underlies those experiments reads like a kind of pathological quibble on the double entente of the term “ovum.” ² Hertwig, Oscar, *Die Zelle und die Gewebe*, Jena, 1898. ³ The remarkable experience which J. Schreiber (*Deut. med. Woch.*, 1891, No. 8) has had with tuberculin in newborn children of non-tuberculous extraction—he injected 40 healthy infants with large doses of tuberculin (up to 5 c.cm.) without any febrile or other effect—either seems to prove that the infantile tissues possess a degree of irritability to certain bacterial products which totally differs from that of the adult, or that the power of excretion is much higher. In the same way the tolerance which infants show to comparatively large doses of mercury may be explained. ⁴ *British Journal of Dermatology*, vol. ix, 1897, p. 436. ⁵ Indeed, the absolute proof of the possibility of the inheritance of acquired immunity should primarily be sought for on the paternal side. In this way all questions of mere evanescent immunity acquired from the mother *in utero*, or during suckling, and which is to be regarded as nothing more or less than an accidental poisoning of the fetus or child, would be entirely eliminated. No believer in the doctrine either of “acquired characters” or of “acquired immunity” would be likely to assert that the dominant factor was the ovum rather than the sperm. If we assume that the sperm equally well with the ovum can “pass on” an “acquired character” or an “acquired immunity” to the offspring, the convincing proof of the hypothesis were best sought for through the father, because, unlike the mother, his part in the production of life ceases with the act of coitus. ⁶ *Virchow's Archiv*, Bd. cxlii, 1888.

NOTE ON THE RESULTS OBTAINED BY ANTITYPHOID INOCULATIONS IN EGYPT AND CYPRUS DURING THE YEAR 1900.

By A. E. WRIGHT, M.D.,

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I AM indebted to the kindness of Colonel W. J. Fawcett, R.A.M.C., Principal Medical Officer in Egypt, for the following statistics dealing with the incidence of enteric fever and the mortality from the disease for the year 1900 in the inoculated and uninoculated among the British troops in Egypt and Cyprus.

	Average Annual Strength.	Number of Cases of Enteric.	Number of Deaths from Enteric.	Percentage of Cases Calculated on Average Annual Strength.	Percentage of Deaths Calculated on same Basis.
Uninoculated ...	2,669	68	10	2.50	0.40
Inoculated ...	720	1	1	0.14	0.14

These figures testify to a nineteenfold reduction in the number of attacks of enteric fever, and to a threefold reduction in the number of deaths from that disease among the inoculated.

In a note appended to the statistical table printed above, Colonel Fawcett observes that the measure of protection resulting from the inoculation is not fully disclosed by a comparison of the figures given in the table. Owing to the circumstance that soldiers inoculated in previous years are in the statistics included among the uninoculated, the number of the uninoculated was in reality smaller, and the number of the inoculated was in reality greater, than the figures set down for these groups in column 1 of the table above. The figures in

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 dulness 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 dulness 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-