SALVARSAN IN PERNICIOUS ANAEMIA.

BY

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As all evidence as to new treatment is of value, brief notes of the following case may be of interest. I believe it to be the first case treated on these lines south of the Tweed, and I publish it with the kind concurrence of my friends, Messrs. Dodd and Clarke, under whose care it was. I saw the patient first on May 23rd, 1912.

She had been very anaemic for more than a year and exceedingly ill in the previous summer, but had improved under large doses of arsenic, and been fairly well during the winter. Her blood picture in October, 1911, showed no signs of pernicious anaemia. On May 23rd she was very ill with daily fever up to about 101° F., almost unable to sit up or take nourishment, with very loud haemic murmurs all over the cardiac area; her colour was the characteristic lemon yellow. A film showed typical pernicious anaemia. On May 31st salvarsan 0.3 gram was injected intramuscularly. Within three days benefit was apparent, though local pain was severe for about a week. In four days the murmurs had almost disappeared, and the patient was much stronger. Blood examination on June 4th showed a distinct improvement.

On June 14th the improvement had continued, and the same dose was again injected in the buttock; this was followed by a sharp reaction; the temperature rose to 101° F. The patient looked exceedingly ill; the pallor and haemic murmurs returned, and she developed a large patch of dry pleurisy over the right back. This condition lasted a few days, when the fever slowly subsided and uninterrupted recovery set in. The blood examinations on July 2nd and 19th and August 7th (see table) showed a rapid change in the blood picture, and the change in the appearance of the patient was not less remarkable. She got quite a rosy look, and said she had not felt so well for years.

The blood reports speak more eloquently than any words, and I will only make two or three remarks further.

1. The rapid fall of temperature after the first injection suggests very strongly the destruction of some virus.

2. In another case I should certainly postpone the second injection as long as improvement was going on, for a week or two.

3. It is difficult to say to what the severe reaction after the second injection was due, possibly hypersensitization. I have come across pleurisy in another case after salvarsan.

4. It remains to be seen, I think, whether intravenous is equal to intramuscular injections where prolonged action is desirable, though the latter has undoubted advantages.

5. The results are so striking that though we know all cases do not react in the same way this treatment should always have a trial.

We have to thank Dr. Byrom Bramwell for sending us an advance copy of his paper, which I had the good fortune to hear at a meeting of the Association of Physicians in Glasgow in April, and also Dr. Galt for his kindness in taking much trouble about the blood examinations.

Date.	Red Cells.	Leucocytes.	Haemoglobin.	Colour Index.
			Per Cent.	Per Cent.
1. Oct. 3, 1911	1,425,000	5,550	30.0	1.0
2. May 24, 1912	800,000	9,050	18.0	1.0
3. June 4, 1912	976,000	9,150	36.0	1.7
4. July 2, 1912	2,372,000	6,900	63.0	1.19
5. July 19, 1912	3,792,000	8,300	90.0	1.0
6. Aug. 7, 1912	4,160,000	4,950	96.0	1.0
7. Oct. 8, 1912	4,704,000	6,300	110.0	1.05

Notes.

1. No anisocytosis or poikilocytosis and no nucleated reds; rather secondary anaemia due to toxic absorption.

2. Marked polychromatophilia and distinct though not extreme poikilocytosis and anisocytosis. Nucleated red cells common; 2 megaloblasts and 8 normoblasts counted with 200 leucocytes. The type is one of a true megaloblastic pernicious anaemia.

3. Marked polychromatophilia, slight poikilocytosis and anisocytosis; 4 megaloblasts and 1 normoblast in a very large number of fields.

4. Slight polychromatophilia. No anisocytosis or poikilocytosis. No nucleated reds after special search.

5, 6, and 7. Normal, except for the decreasing deficiency in red cells. The only point which is not absolutely satisfactory is that the colour index is still slightly above normal. This is possibly due partly to the fact that she went on taking largish doses of iron for some time.

Salvarsan 0.3 gram was injected on May 31st and June 14th.

THE SCIENCE COMMITTEE

OF THE

British Medical Association.

THE CYTOLOGY OF THE BLOOD IN PASSIVE IMMUNITY.

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(From the Pathological Departments of the Universities of Oxford and Birmingham.)

[ABSTRACT.]

A SERIES of figures obtained by determining the numbers of cells present in the peripheral blood of man and rabbits before and after the injection of various samples of serum have been analysed. The serums used were, in the case of man, normal horse, diphtheria antitoxin, and antistreptococcic; and for rabbits, normal and agglutinating rabbit and goat, diphtheria antitoxin (horse) and antistreptococcic (horse). As far as possible the figures obtained during the control periods were subjected to the method of least square, the resultant figure giving a measure either of any error due to the various manipulations to which the blood samples were subjected for securing the counts of corpuscles or of any variation in their numbers arising from day to day and due to natural causes. These may be termed respectively the "Mean Deviation of the Experiment," when the differences between counts on blood samples collected practically simultaneously from the same animal are considered, or the "Mean Daily Variation," where the differences observable from day to day are analysed. The advantage accruing from the knowledge of these is that the mathematical chances in favour of any alterations observed in the blood counts being due to the experimental injection and not to a natural error or variation can be ascertained.

In some instances, when the rabbits had been subjected to daily haemorrhage, the method of least square could not be used in the examination of the numbers of corpuscles, and another procedure had to be adopted. This consisted in comparing the average number of cells during the control period with the average number present on the days subsequent to the injections of serums. In the case of rabbits a fresh animal was used for each injection of any sample of serum, which took place by the subcutaneous, intravenous, or intraperitoneal routes. For man one individual served for all the inoculations of serums which were performed hypodermically.

The results of a consideration of the numbers of blood corpuscles in the peripheral blood during the control and during the experimental period may be summarized as follows:

1. The method of least squares can be satisfactorily applied to the analysis of the deviations and variations in a series of enumerations of the blood corpuscles, and of estimations of haemoglobin in the blood of man and of rabbits.

2. The "mean deviation of the experiment" for a series of estimations of haemoglobin and blood corpuscles in rabbits is independent of the hour of day and of small haemorrhages.

3. The "mean deviation of the experiment" is, in rabbits, greater for leucocytes than for red cells, and for red corpuscles than for haemoglobin, being on the average in this series of experiments 7.73 per cent. for leucocytes, 3.81 per cent. for red cells, and 1.28 per cent. for haemoglobin.

4. The "mean deviation of the experiment" was larger in a series of animals examined immediately they reached the laboratory than in another series which had been allowed sufficient time to become accustomed to their new environment.

5. The "mean daily variation" for the haemoglobin, red cells, and leucocytes was smaller in rabbits which had been kept some days in the laboratory than in those examined immediately they had been procured from the market.

6. The "mean daily variation" for blood cells becomes smaller as the day advances in the case of rabbits, and can

be reduced to 5 per cent. or less for the leucocytes and to 2 per cent. or less for the red corpuscles.

7. The "mean daily variation" appears to be independent of the hour at which the rabbits are fed.

8. The "mean daily variation" in the experiments on man was found to be smaller for both the leucocytes and the red cells at 3 p.m. than at noon.

9. The number of leucocytes in the blood of the man examined was greater at 3 p.m. than at noon, whilst the reverse was the case with the red corpuscles and the haemoglobin.

10. Evidence is adduced that in rabbits the leucocytes are more numerous at 2 p.m. than at either 10 a.m. or in the evening, and that this is independent of the time of feeding.

11. The increase in the number of leucocytes in man was proportionately the same at noon and at 3 p.m., when an artificial leucocytosis was produced.

12. The introduction of horse serum subcutaneously into man produces no change in the amount of haemoglobin or in the number of red corpuscles, but causes a leucocytosis.

13. The injection of antitoxin in man produced no specific recognizable alteration in the cytology of the blood, the rate of rise and fall in the number of leucocytes being the same whether a normal or the antibody containing serum was injected.

14. The introduction of antimicrobial (antistreptococcic) serum was followed by an absence of any leucocytosis in the case of man. This may depend either on a specific inhibitory action of some substance (? the "immune" body) in the serum, or on a physiological failure of the body to respond with a leucocytosis to an injection of serum which follows on a series of previous ones, each of which had succeeded in producing such a change, similar to the failure in the formation of antibody noted by Axel Jørgensen when an antigen was injected daily for a certain length of time.

15. The varieties of cells taking part in the leucocytosis as a response to serum injections in the case of man are (1) the polymorphonuclear and the eosinophilous group, and (2) the transitional and large mononuclear group, no change being demonstrable in (3) the lymphocyte group or (4) the mast cell group.

16. Daily small haemorrhages in rabbits—that is, 5 per cent. of their blood volume or less—produce a progressive diminution of equal amount in the haemoglobin percentage, and in the numbers of red corpuscles and white cells per cubic millimetre. This diminution is less than corresponds with the quantity of blood removed, the blood elements being partially regenerated. Very little sign of regeneration of the blood elements can be seen when 2 c.cm. of the blood are daily removed for eight or nine days.

17. No change could be detected in the haemoglobin percentage or in the numbers of red corpuscles in rabbits as the result of injecting rabbit, goat, or horse serums, whether normal or containing antibodies, by whatever route they were introduced.

18. No change could be demonstrated in the numbers of leucocytes in rabbits as a result of the introduction of rabbit or goat serums, whether normal or containing agglutinin, by whatever route they were injected, whilst a leucopenia was found to follow the introduction of an antimicrobial (antistreptococcic) serum, but whether as a response to some special substance (? immune body) present in this type of serum, or in response to the horse serum itself, is not altogether clear, since a suggestion of a similar response, though not great enough to allow of definite proof, may be present after the introduction of diphtheria antitoxin contained in horse serum. If the leucopenia should prove eventually to be in response to some substance specific to the immune serum, it might help to explain the poor results so often obtained when antimicrobial serums are used as curative agents.

THE city and University of Montpellier have decided to erect a monument in memory of the famous doctor of the medical faculty, François Rabelais. The model of the monument, which is to be executed by the well known sculptor M. Jacques Villeneuve, was exhibited in the Salon of 1912. Subscriptions may be sent to Dr. Levère, General Treasurer of the Paris Committee, 77, Avenue de Villiers, Paris.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

AN IMPROVED METHOD OF TENDON SUTURING.

THE chief desiderata in the operation of tendon suturing are adequate strength and perfect smoothness of the site of union. The chief defect of the ordinary procedures is the violation of the latter detail involved by the presence of palpable knots and unsightly suture tags. The method to be described overcomes this defect and gives, I think, a bond as near perfection as possible.

The suturing material used is Japanese silk (Allen and Hanburys) for this happily combines great tensile strength with tenuity, a combination presenting obvious advantages in facilitating and giving smoothness of the bond.

Two long ligatures, A and B—one for each piece, proximal (A) and distal (B), of the tendon—are tied around the two portions (A₁ and B₁) of the tendon near the line of section, and knotted, not in the centre but near the side on its upper aspect. One end of the proximal ligature (A) is, or both ends thereof are, threaded on a curved needle. This needle is passed on the near side of the circular ligature (A) opposite its knot through the tendon (A₁) to its under surface; then below the line of section to the far side of the distal circular ligature (B); thereafter up through this portion (B₁) of the tendon to the upper aspect. It is now passed back again across and above the line of section to the starting point (A₁), and the penetrating process repeated as just described; and so on till the upper and lower surfaces of

the tendon are occupied and the line of section bridged by the lengthwise sutures.

The points at which the needle leaves and enters the two pieces of the tendon are always corresponding, but in traversing the tendon the needle is given an oblique direction so as to emerge to one side of the preceding longitudinal suture.

When this vertical longitudinal suturing has been carried from one side of the tendon

to the other the needle is made to emerge finally near the proximal knot. The two free ends of the proximal ligature (A) are thus brought together again; they are knotted, then threaded on the needle, which is made to penetrate the tendon in the immediate vicinity of the knot, and carried in a longitudinal direction for a little distance, and preferably in a wave-like manner, this so as to prevent the silk afterwards being drawn back towards its knot if that were possible when the tendon was put into action. After traversing the tendon these free ends are made to emerge therefrom at one side. In the latter manner the two ends of the distal ligature (B) are also similarly treated. These four ends, two emerging from either portion of the tendon, are now pulled upon and then severed by a knife flush with the surface of the tendon from which they are emerging.

If one thread has been used in the needle for the above procedure, this thread is made to emerge finally near the proximal knot. The two free ends of the proximal ligature (A) are thus brought together again; they are knotted, then threaded on the needle, which is made to penetrate the tendon in the immediate vicinity of the knot, and carried in a longitudinal direction for a little distance, and preferably in a wave-like manner, this so as to prevent the silk afterwards being drawn back towards its knot if that were possible when the tendon was put into action. After traversing the tendon these free ends are made to emerge therefrom at one side. In the latter manner the two ends of the distal ligature (B) are also similarly treated. These four ends, two emerging from either portion of the tendon, are now pulled upon and then severed by a knife flush with the surface of the tendon from which they are emerging.

If, however, the needle originally be threaded with both free ends of the proximal ligature (A) these finally are brought through the distal piece (B₁) of the tendon to appear in the region of the distal knot. The two ends of the proximal (A) and distal (B) ligatures are then knotted, the four ends threaded on a needle, and buried and cut in the same manner as before.

Whether the needle at first carries one or two threads will depend on the thickness of the silk; if a thick size be considered necessary the threads will naturally be more bulky and clumsy, but if a thin size will suit the double thread may be used if desired.

The above procedure may be somewhat modified by using one of the two threads of the one ligature (A) for the vertical suture and one of the two threads of the other ligature (B) for the horizontal suture, and then arranging