tian Government, to stamp out the epidemic at Torr, and prevent its introduction into Egypt and Europe. As it has succeeded on the previous occasions I have mentioned, there is good reason to hope that it will succeed again now, though the circumstances are much more serious.

The station of Torr is practically a desert, water being supplied from wells. There are no running streams to pollute, and the pilgrims are lodged in tents. Each ship as it arrives is assigned a section apart for its pilgrims, the sections being at a considerable distance from each other, with guards placed to prevent intercommunication. Healthy and infected sections are kept well apart. The period of quarantine is fifteen days, dating from time of arrival if healthy, or dating from the last case of cholera in the section after arrival. During the quarantine the vessel bringing the pilgrims is cleaned and disinfected, and the personal effects of the pilgrims are disinfected by steam under pressure, for which the Quarantine Board possess disinfecting machines established at the station. If considered necessary, the camping ground of an infected section is changed. The number in a section varies from perhaps 300 to 900, according to the number brought by any one steamer. After having undergone the prescribed period of quarantine without a suspicious case the foreign pilgrims are re-embarked on the steamer which brought them, and pass the Suez Canal in strict quarantine and well guarded, to prevent communication with Egypt. In the case of Egyptian pilgrims, after having undergone the prescribed period of quarantine at Torr and being declared healthy, they undergo a further three days' observation at a fresh camping ground at Rass Mallays—a healthy spot at a considerable distance from Torr—and are thence brought to Suez, generally in clean vessels sent by the Egyptian Government, allowed to land in free *pratique*. Vessels leaving Jedda with pilgrims receive their papers for Torr and go straight to the quarantine station on the peninsula. The station is guarded by military sent by the Egyptian Government, and I believe there are about a thousand soldiers at present there on duty. All likely places where where sambocks or other small craft might land pilgrims "in contravention" are strictly watched and every precaution taken by camel patrols and coastguard cruisers to prevent return pilgrims from landing in Egypt except by the stations established by the quarantine board. Personal effects too worthless and dirty for disinfection are ordered to be burnt, the Egyptian Government at its own expense having sent a supply of clothing to draw upon to replace them. Communication is kept up with Suez by small steamers lent by the Egyptian Government, which take provisions if required and mails, there unfortunately being no telegraph wire between Suez and Torr. Specimens of the water from the wells were examined some time ago at the Khedivial laboratory in Cairo and pronounced to be good. No complaints have reached the Board as yet as to quantity or quality of the water or food. Two great dangers in the present instance are the chance of the water giving out, which it has not done on previous occasions, and the station becoming overcrowded by prolonged quarantine should many sections continue long infected preventing their being sent off while fresh batches continue to arrive. The work of disinfection has been much and unfavourably criticised, and any one who has had personal experience of crowds of pilgrims the state of filth and dirt of their persons and clothes, the bundles of filthy impedimenta which they carry with them, can easily understand that the disinfection cannot be perfect, but if perfection cannot be achieved (and in what is it achieved?) it is no reason why something should not be done.

ORIGIN OF THE EPIDEMIC.

The usual vexed question will no doubt soon arise as to how the disease was this time imported into Mecca. According to information received in Egypt the first cases of cholera were observed amongst the Yemen pilgrims immediately on their arrival in Mecca. It is known that cholera must have been prevailing in the Yemen as lately as the end of last year.

A Turkish transport with troops from Yemen left Hodeida on the 19th of last September, and made for the Turkish quarantine station at Camaran, in the Red Sea. During their stay at Camaran there occurred 47 cases of cholera, 46

cases of chronic dysentery, 38 cases of intestinal catarrh, and 10 cases of pernicious fever. Probably some of the cases of chronic dysentery and intestinal catarrh were choleraic.

During the present season one vessel—the *Knight of St. John*—arrived at Camaran on May 5th from Bombay with over a thousand pilgrims of different nationalities, amongst whom were a few cases of cholera. These pilgrims underwent their quarantine at Camaran, and no further cases, as far as I know, have been reported amongst them.

Discussions on this subject in the past have usually been very unsatisfactory and the conclusions very indefinite. The serious fact remains that cholera epidemics amongst the pilgrims annually collected at Mecca are of very frequent occurrence, and are a standing menace to Egypt and Europe. Four times within the last twelve years the disease might have been introduced by the pilgrims into Egypt or Europe, or both, and the experience of Spain and France has shown how easily it may become endemic. The endeavours of the Quarantine Board have fortunately been successful in stamping out the disease before the pilgrims reached Egypt. The doings of the Board have been very severely criticised in England, often rightly, but oftener undeservedly, and without *connaissance de cause*. Its actions will in the future be very much modified by the decisions of the Conference of Venice, a Conference due entirely to the action of some of the members of the Board, who took the initiative and drew up a programme for their Governments with a view to settle on a more rational basis, and smooth over the ever-irritating question of Suez Canal quarantine.

ON A METHOD OF DETERMINING THE CONDITION OF BLOOD COAGULABILITY FOR CLINICAL AND EXPERIMENTAL PURPOSES, AND ON THE EFFECT OF THE ADMINISTRATION OF CALCIUM SALTS IN HÆMOPHILIA AND ACTUAL OR THREATENED HÆMORRHAGE.

[PRELIMINARY COMMUNICATION.]

By A. E. WRIGHT, M.D. DUBL.,
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It is evident that the foundations of a rational system of therapeutics in connection with the treatment of conditions of altered blood coagulability cannot even be laid until we are in possession of a method by which the necessary clinical data on blood coagulability can be collected. The method which I am about to describe allows of such determinations of blood coagulability being made in a drop of blood obtained from the finger. The clinical application of the method is, as far as I know, new; but the method itself is a very obvious one, and must have already suggested itself to other observers.

The necessary apparatus consists of half-a-dozen to a dozen capillary tubes of approximately equal calibre. The blood is aspirated into these, and the coagulation time is determined by blowing down one tube after another at regularly increasing intervals until the tubes are found to have become blocked by clot.

Such capillary pipettes can easily be made by a glass blower out of thermometer tubing, or they can be prepared out of ordinary glass tubing as follows: Soft glass tubing about $\frac{1}{4}$ inch external diameter is cut up into lengths of about 4 inches. Each of these pieces of tubing is heated in the middle in an ordinary blowpipe flame; and is drawn out into a capillary tube. The capillary tube thus obtained is broken across in the middle, giving us a couple of glass pipettes ready for measurement. Capillary tubes of any selected calibre may be employed, but it would obviously be convenient to constitute a standard size. Those I have employed ranged in diameter between 0.01 inch (circ. 0.25 mm) and 0.0125 inch. I employed a column of blood 2 inches (circ. 5 cm.) in length. A calibration, which was found quite sufficiently accurate for all practical purposes, was obtained as follows: Two pieces of brass wire, respectively 0.01 and 0.0125 inch in diameter, were selected by measurement under the low power of the microscope. The thicker wire was pushed down the mouthpiece of the pipette until it was nipped by the narrowing capillary tube. This point was marked with a red pencil, and the tube was broken across 2 inches below this point. The thinner wire was now passed down the pipette, and the calibration was considered sufficiently exact when this wire was found to pass out through the extremity of the tube.

These capillary pipettes can be cleared by passing a fine wire down, and then washing them out in distilled water. The tubes must then be thoroughly dried, either by passing them through a flame, or by removing the water with alcohol and the alcohol with ether.

These tubes are employed in the following manner in making an estimation of blood coagulability. Six or more capillary tubes are laid on the table before the observer, along with a watch provided with a seconds hand, and pencil and paper for noting the times of filling and testing the separate tubes. A drop of blood is now obtained from the finger in the usual way. This is aspirated into a capillary tube, and the time of filling the tube is accurately noted down. The finger is then wiped clean, and another drop of blood is pressed out for filling the next pipette. It will be found convenient to allow an interval of one quarter, to half, a minute to elapse between the filling of successive tubes. In dealing with normal blood two minutes may be allowed to elapse before testing the condition of coagulability in the first tube. The condition of the blood, as ascertained by blowing down the tube, is noted down opposite the entries of the time of filling and testing. If the tube is found blocked, coagulation has taken place, and the condition is noted down as "clotted." If, on the other hand, the contents of the tube can be blown out, the condition is to be noted as either "clotting" or "liquid." It is easy to differentiate between these latter conditions by blowing out the contents of the tubes on to a piece of blotting or filter paper. In coagulating blood a shred of fibrin can then readily be distinguished. If the contents of a tube, examined, say, at three minutes after filling, are found to be liquid, while the contents of the pipette next in series, examined after four minutes, are clotted, it is advisable not to delay further before testing the following tube. When the tubes have been filled at half-minute intervals we thus learn what the condition of the blood is at three and a-half minutes. An actual example may further elucidate the method.

Tube 1, tested 2 minutes after filling: contents liquid; Tube 2, tested after 3 minutes: liquid; Tube 3, tested at 4 minutes: liquid; Tube 4, tested at 5 minutes: clotting; Tube 5, tested at 4½ minutes: liquid; Tube 6, tested at 4½ minutes: liquid; Tube 7, tested at 5½ minutes: clotted; Tube 8, tested at 5½ minutes: clotted; Tube 9, tested at 5 minutes: clotted; Tube 10, tested at 4 minutes 50 seconds: clotted. It will be seen that coagulation time here lies between 4 minutes 50 seconds and 5 minutes.

In addition to employing our capillary tubes for determining the actually existing condition of blood coagulability, we may employ them to control our therapeutics by ascertaining whether an alteration of blood coagulability has been brought about by treatment. By this means we can evidently avoid inducing undesired or excessive alterations of coagulability.

We can further employ our capillary tubes to assist us in our selection of an appropriate method of treatment. We can, for instance, ascertain whether the addition of a lime salt to a particular blood will increase the coagulability of that blood. To determine this, it is only necessary to aspirate an appropriate¹ amount of a solution of a lime salt into the capillary pipette (it is a convenient plan to have the stem of the pipette divided into fifths and tenths), and to fill up to the usual mark with blood. Mixture of the contents can be effected by blowing out the contents of the tube on to any clean surface, and aspirating them again without delay into the tube. It will be shown further on that the more rapid coagulation² which is observed after appropriate additions of calcium chloride solution to the extravascular blood is obtained equally by the administration of lime salts by the mouth. On the other hand, too much reliance must not be placed upon forecasts based only upon the results of the additions which are thus made to the extravascular blood. For instance, an addition of either citrate of soda³ or leech extract⁴ will keep the

¹ About 1 volume or 1 per cent. calcium chloride to 4 volumes of blood.
² Acceleration of coagulation is also obtained by additions of distilled water in the extravascular blood. In making experiments on the effect of lime additions it is therefore well to employ solutions of calcium chloride in normal salt solution, and to employ normal salt solution, and not distilled water, in the control tubes.

³ Citrate of soda keeps the blood liquid by decalcifying it. An addition of 1 part of citrate of soda to 200 of blood (2½th volume of a 25 per cent. solution) is quite adequate for this purpose. I may perhaps be allowed to remark in this connection that this variety of decalcified blood appears to be even more suitable for purposes of transfusion than even the oxalated blood proposed by me in a previous communication (BRITISH MEDICAL JOURNAL, December 5th, 1891).

⁴ One leech head extracted with 5 c.c. of normal salt solution will keep about 25 c.c. of blood liquid. In other words, 1 volume of such an extract will keep 5 volumes of blood liquid.

blood in the capillary pipette liquid for an indefinite period; but the administration of these substances by the mouth appears to be quite ineffective.

The methods which have just been described have gradually elaborated themselves in connection with the examination of the blood in a case of hæmophilia which was referred to me for study, and if possible for treatment, by my friend Dr. H. Willoughby Gardner, of Shrewsbury. I am glad to have this opportunity of thanking him for his great kindness and help in this matter. I propose to put the results of the examination of the blood in this case of hæmophilia on record here, in as far as they bear upon the questions under consideration.

S. W., aged 11 years. No family history of hæmophilia. At 3 years of age was brought to a doctor for bruises; at 6 years of age and again at 10 years bled profusely—it is said for a week at a time—when on each occasion a tooth became loosened and fell out by natural processes. About 7 years of age patient bit his tongue, and bleeding continued until he was so weak that he was unable to stand without assistance. His pillow was saturated with blood during the night. On another occasion, when the hæmorrhage from a trifling cut on the finger was excessive, bleeding was only arrested by the application of the actual cautery. Patient has a history of perpetually recurring swellings of his joints and of large subcutaneous hæmorrhagic ecchymoses. He is often seriously crippled by the effusions in his joints.

Present Condition (May 24th, 1893).—He has a fair complexion with reddish hair; is fairly well nourished and tolerably robust for his age; presents a large livid ecchymosis on right upper arm and a considerable hæmatoma on the left buttock. His right knee-joint is considerably swollen and is full of fluid; the swelling is not painful, but it causes a certain amount of lameness. Synovial membranes of elbow-joint are considerably thickened.

When the patient came under observation at Netley, I proceeded to make a systematic examination of the blood, with the view of ascertaining whether any pathological alterations could be detected. The blood was examined daily at 3 p.m.—being an hour and a-half after midday dinner. It was obtained in the usual way, by pricking the tip of the finger. Daily observations were made with reference to the following points: (a) the number of red blood corpuscles; (b) the number of leucocytes; (c) the percentage of the various varieties of leucocytes; and (d) the condition of coagulability.

Gowers's hæmocytometer was employed for the enumeration of the red and white blood corpuscles. The diluting fluid employed was an 8 per cent. solution of magnesium sulphate, which had received a sufficient addition of gentian violet to stain the leucocytes darkly in the course of the few minutes required for the subsidence of the corpuscles. The percentage of the different varieties of leucocytes was determined in cover-glass specimens of blood. These were fixed by floating them for half a minute on a saturated solution of mercuric chloride (method of Muir and others). The preparations were then stained by the method recently described by Surgeon-Captain Bruce and myself.⁵ The leucocytes were enumerated under the following four headings: (a) leucocytes with coarse eosinophilous granules and subdivided nucleus (so-called "eosinophilous leucocytes"); (b) leucocytes with greatly subdivided darkly-staining nucleus and very minute eosinophilous granules (so-called "polynucleated or neutrophile leucocytes"); (c) large leucocytes with a single large not-subdivided faintly-staining nucleus (so-called "mononuclear leucocytes"); (d) small leucocytes containing a relatively large and very darkly-staining nucleus (so-called "lymphocytes"). The condition of coagulability was determined by the method of capillary tubes described above.

The results are entered in the tabular statements given below:—

Date.	Treatment.	Number of White Blood Corpuscles in 1 c.mm.	Varieties of White Blood Corpuscles.				Coagulation Time.
			E.	P.	M.	L.	
May 25th, 1893	None	8,400	2	58	11	29	10 minutes
May 26th, 1893	"	6,500	1	56	10	33	9 minutes
May 27th, 1893	"	6,800	2	48	9	41	9½ minutes
May 29th, 1893	"	5,800	1	57	10	31	9½ minutes

This tabular statement shows that the blood of this hæmophilia patient differed from the normal blood in three respects: (a) in containing a somewhat reduced number of white blood corpuscles; (b) in containing a diminished proportion of polynuclear leucocytes (54 per cent. of total leucocytes instead of about 75 per cent.); (c) in possessing an apparently altogether subnormal degree of coagulability (coagulation time 9 to 10 minutes, instead of as in normal blood from 2½ to 5, or rarely 6 minutes). The number of the red blood corpuscles ranged from 4 280,000 to 5 200,000.

⁵ BRITISH MEDICAL JOURNAL, April 3rd, 1892.

On consideration of these facts it will be seen that the indications for treatment were all in the direction of endeavouring to bring about an increased degree of coagulability in the blood. In view of the general paucity of leucocytes in the blood, it was evidently worth ascertaining whether an increased coagulability could be brought about by increasing the number of the leucocytes. With a view to effecting such an increase, I put the patient upon daily 1 gramme doses of nuclein. I had prepared the nuclein, by Horbaczewski's method, from thymus glands. The leucocyte enumerations which are tabulated below confirm, as far as a single case can, Horbaczewski's observations of the occurrence of leucocytosis after the administration of nuclein. The enumerations were in all cases made three hours after the exhibition of the nuclein. The degree of leucocytosis is to be gauged by reference to the figures for the four preceding and three succeeding days (vide *supra* and *infra*).

Date.	Treat-ment.	Number of White Blood Corpuscles in 1 c.mm.	Varieties of White Blood Corpuscles.	Coagulation Time.
May 30th, 1893	1 g. nuclein at 12 noon	8,600	E. 2 P. 57 M. 10 L. 31	14 minutes(?)
May 31st, 1893	"	10,200	2 58 6 34	12 minutes
June 1st, 1893	"	10,200	1 58 10 31	10½ minutes

It will be noticed that the coagulability of the blood was not increased as compared with the three previous days. I therefore determined to try the effect of the internal administration of lime salts. I was influenced in this (a) by the results of my experiments on the administration of calcium chloride to animals, some of which have been already reported in the BRITISH MEDICAL JOURNAL⁶; (b) by the following experiments, in which I observed that an increase of coagulability was obtained when calcium chloride was added to the extravascular blood of this particular patient. The experiments were as follows:—

May 31st, 1893. Capillary tubes of standard size filled with blood from tip of finger. Tube 1 tested 8½ minutes after filling contents liquid. Tube 2, after 9½ minutes, liquid. Tube 3, after 9½ minutes, liquid. Tube 4, after 10 minutes, clotting. Tube 5, after 11 minutes, clotting. Tube 6, after 10 minutes, clotting. Tube 7, after 12 minutes, clotting. Tube 8, with addition of ¼ volume 1 per cent. CaCl₂ solution found clotted when tested after 6 minutes. Tube 9, with addition of ¼ volume of 1 per cent. CaCl₂ solution tested after 6 minutes, contents clotted. Tube 10, with ¼ volume 1 per cent. CaCl₂ solution clotted after 5½ minutes.

It will be noticed that we have here a reduction of coagulation time from 12 to 6 minutes as a consequence of an addition of calcium chloride to the extravascular blood. I have multiplied such observations on my own blood and upon other normal bloods of both man and animals, and find, as far as my experience goes, that such an acceleration of coagulation time is the invariable rule. Thus, for instance, my own blood clotted in 30 seconds with a lime addition at a time when its normal coagulation time was represented by 2½ minutes. Again, on another occasion, when the coagulation time of my blood was represented by 3 minutes, I found that my blood clotted in 45 seconds with the appropriate lime addition.

In view of the above facts I administered 1 gramme (*circ.* 15 grains) of calcium chloride three times a day to my hæmophilia patient. The results are tabulated below.

Date.	Treat-ment.	Number of White Blood Corpuscles in 1 c.m.	Varieties of White Blood Corpuscles.	Coagulation Time.
June 2nd, 1893	1 g. CaCl ₂ t. i. d.	7,200	E. 1 P. 47 M. 19 L. 33	5½ minutes
June 3rd, 1893	"	7,800	4 44 11 41	5½ minutes
June 5th, 1893	"	6,500	2 51 6 41	Over 1 hour

⁶ BRITISH MEDICAL JOURNAL, December 19th, 1891.

The administration of lime was thus immediately followed by a reduction of coagulation time to within normal limits. This normal degree of coagulability was also maintained on the next day. On the fourth day of the treatment, however, coagulability was found to be decreased to an extraordinary extent. At this stage my observations were unfortunately broken off by the departure of my patient.

In the absence of actual experiment, I have however the following reasons for surmising that the observed decrease of coagulability was due to the administration of calcium chloride having been carried too far (a) when too large an addition of calcium chloride is made to decalcified blood *in vitro* coagulability decreases,⁷ instead of being accelerated as it is with moderate additions; (b) on taking 2 grammes of calcium chloride three times a day I found that the coagulability of my blood rose during the first 24 hours, and then fell away to almost its original normal level (coagulation time 4 minutes) on the second day, and fell away further on the third day (coagulation time 6 minutes); (c) the greatest accelerations of coagulation time appear to be obtained with comparatively small doses of lime. Thus, in the case of my friend Dr. Leonard Rogers, coagulation time before administration of lime was 5½ minutes; it decreased in 24 hours after two 1-gramme doses of calcium chloride to 1½ minute. Again, in my own case,⁸ the effect of taking 2 grammes of calcium chloride in a single dose was a reduction of coagulation time from a normal of 4 minutes to 1½ minute 24 hours after the exhibition of the lime.

I believe that the facts which have been brought forward are sufficient to raise a strong presumption that calcium chloride will prove of utility in producing an increased coagulability of the blood such as is desiderated in the treatment of internal hæmorrhage, aneurysm, and hæmophilia. I have seen such arrest of hæmorrhage accompanied by an increase of blood coagulability in a case of perpetually recurring epistaxis and in a severe case of hæmoptysis, the opportunity of observing which last I owe to the kindness of Professor Cayley and Surgeon-Colonel E. Fairland. Similar successful results have been put on record in the BRITISH MEDICAL JOURNAL by Mr. Mayo Robson.

I may, in conclusion, refer to two sources of fallacy which might be supposed to vitiate the results arrived at in this paper. The observed increase of coagulability might evidently be attributed to some spontaneous variation of blood coagulability (such a variation might be conceived to be associated with the different stages of digestion); or, again, the alterations of blood coagulability might be attributed to differences in the gaseous composition of the blood in different experiments. As far as I have yet been able to study these questions, I see no reason to believe that these influences exercise a very large disturbing effect. In order, however, to minimise such sources of error in my experiments, I have in all cases made my estimations at the same hour on successive days, and I have invariably relaxed the ligature at frequent intervals whenever I have been drawing off blood from the finger.

A STUDY OF A CASE OF FOCAL EPILEPSY, AND OF THE RESULTS PRODUCED BY EXCISION OF A SMALL AREA OF THE MOTOR CORTEX.

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CASES in man which help to elucidate some of the difficult problems dealing with the functions of the cerebral cortex are so rare, that the following study of an instance in point may be interesting.

The patient had convulsive seizures of the right arm due to a sarcoma of the lower part of the left ascending parietal convolution. An oval area of cortex infiltrated with growth was excised. The piece taken away had the long axis antero-posterior, and extending from the fissure of Rolando in front to just across the lower extremity of the interparietal sulcus behind.

⁷ Wright, *Jour. of Pathology*, June, 1893, p. 444.

⁸ The condition of increased coagulability in this case was already apparent in 2½ hours. As in Dr. Rogers's case it passed off gradually on the third day.