drop, with an immersion lens. Under the microscope it will be seen that the bacilli gradually form groups of three or four, which, by the addition of other bacilli, constantly increase in size until the majority are in "clumps" with impaired or lost motility. If the reaction is marked within thirty minutes the case is one of enteric fever, but without greater experience it is impossible to say that the absence of the reaction negatives such a diagnosis. In any negative result more than one examination should always be made, for it occasionally, although rarely, occurs, probably from experimental errors, such as varying quality of bouillon, &c., that the reaction is seen on one day and not on another. And it has happened in one case, in which the typhoid fever bacilli were cultivated from the blood, that the reaction was better marked in greater dilution. Complicated as the reaction may read it is really quite simple of performance and takes very little time.

The serum of man is very variable both as regards the power and the kind of agglutinines present under ordinary conditions. Excluding the cases of enteric fever, 32 specimens of serum were examined, of which 9 were from normal individuals (3 of whom, however, had had enteric fever) and 23 from cases of various diseases. Typhoid fever bacillus was acted on in 28 cases out of 37, in 13 markedly; 5 cases had had enteric fever from five to thirty-seven years previously and 8 were suffering from it. Cholera bacillus was acted on in 16 cases out of 29, in 9 markedly. Only 1 patient had previously had cholera. Coli bacillus was acted on in all 3 cases examined. In 2 of these 3 typhoid fever bacillus was also acted on. In the following table these results are better seen:

Disease.	Previous typhoid.	Action. Typhoid.	Cholera.	Coli.
Chronic rheumatism ...	*	†	†	—
Phthisis (acute)	*	—	*	—
Cirrhosis, icterus	*	†	‡	‡
Phthisis	*	—	*	—
Meningitis	? 4 years ago.	†	†	—
Typhoid (27th day)	—	‡ ($\frac{1}{25}$)	‡	‡
Typhoid (17th day)	—	‡	—	—
Phthisis	*	*	†	‡
Bronchitis	*	†	‡	—
Typhoid (11th day)	—	‡ ($\frac{1}{100}$)	‡	—
Icterus	*	‡	‡	—
Normal	*	*	*	—
Normal (placental blood) ...	5 years ago.	†	*	—
Normal ,, ,, ...	*	†	†	—
Normal ,, ,, ...	*	*	*	—
Hemiplegia	30 years ago.	‡ ($\frac{1}{4}$)	‡	—
Normal	37 years ago.	‡ ($\frac{1}{4}$)	*	—
Icterus	*	‡	‡	—
Tetany	*	†	†	—
Carcinoma	*	†	*	—
Gastric ulcer...	*	‡	—	—
Septicæmia	*	†	†	—
Chronic renal	*	‡ ($\frac{1}{4}$)	*	—
Carcinoma icterus	*	‡ ($\frac{1}{4}$)	*	—
Syringomyelia	18 years ago.	‡ ($\frac{1}{4}$)	*	—
Normal (maternal blood) ...	*	*	*	—
Cirrhosis icterus	—	‡ ($\frac{1}{4}$)	*	—
Normal (placental blood) ...	10 years ago.	‡	*	—
Normal (maternal blood) ...	*	‡ ($\frac{1}{2}$)	‡ ($\frac{1}{2}$)	—
Normal (placental blood ...	*	*	†	—
Normal (maternal blood) ...	*	‡ ($\frac{1}{2}$)	—	—
Normal (placental blood) ...	*	*	—	—
Normal (maternal blood) ...	*	‡ ($\frac{1}{2}$)	—	—
Normal (placental blood) ...	*	—	—	—
Typhoid (10th day)	—	‡ ($\frac{1}{64}$)	—	—
Typhoid (13th day)	—	† ($\frac{1}{64}$)	—	—
Typhoid (21st day)	—	‡ ($\frac{1}{64}$)	—	—
Typhoid (26th day)	—	‡ ($\frac{1}{64}$)	—	—
Typhoid (33rd day)	—	‡ ($\frac{1}{128}$)	—	—
Chronic rheumatism	*	*	—	—

EXPLANATION OF SIGNS.—* = no action. † = fair or distinct action. ‡ = marked action. The fractions indicate the greatest dilution in which the action was still distinct. Actually the dilution is double, through an equal quantity of emulsion being added.

The greater strength of the serum of enteric fever patients is thus very evident. Several specimens from each patient were examined, and although the power gradually diminished it was always still considerable when the patient was discharged. The cases in which jaundice is present yield a serum which, undiluted, has an action often as rapid and complete as an enteric serum; but the falling off in strength is quite out of proportion to the dilution, so that it is impossible to tell what degree of dilution a serum will stand from the initial intensity of its action. Moreover, jaundice is almost unknown in enteric fever.

Although no opportunity presented itself for examining a case of acute miliary tuberculosis, the case of fairly extensive phthisis with high fever gave no reaction, and the case of meningitis only a slight reaction, so that these two diseases for which enteric fever is liable to be mistaken do not, *per se*, seem likely to cause confusion in the serum test. It is interesting to note the different action of the maternal blood (obtained after separation of the placenta) and of the placental blood, especially in view of the general absence of hereditary immunity to infectious diseases. By the examination of a larger number of ordinary cases as well as of cases of enterica, at this season gradually becoming more numerous, I hope soon to present further evidence in support of the above test; in the meanwhile I commend it to the favour of others who may have the opportunity of applying it, especially in early cases.

Whilst this work was in progress a short communication by Widal applying a similar method macroscopically has been published in the *Semaine Médicale*. It requires, however, a larger quantity of blood and a longer time, and apparently, from the rather meagre description, a final resort to the microscope; and in one case, at any rate, I was unable to detect the reaction.

Vienna.

ON THE

ASSOCIATION OF SEROUS HÆMORRHAGES WITH CONDITIONS OF DEFECTIVE BLOOD-COAGULABILITY.

BY A. E. WRIGHT, M.D. DUB.,
PROFESSOR OF PATHOLOGY, ARMY MEDICAL SCHOOL, NETLEY.

IN previous papers I have pointed out that, on the one hand, excessive hæmorrhages from trifling wounds, and, on the other hand "spontaneous hæmorrhages," are in almost all cases attributable to a defect in blood-coagulability. The epistaxis and hæmorrhage from the bowel in typhoid fever, the epistaxis of growing children, and the excessive hæmorrhages of hæmophilic patients are typical instances of hæmorrhages which are due to this cause. Conditions of deficient blood-coagulability do not, however, manifest themselves only in a tendency to "actual hæmorrhages." They manifest themselves also in a tendency to increased transudation of plasma through the capillary wall—i.e., in a tendency to "serous hæmorrhages." I propose here to review the more important varieties of such "serous hæmorrhage" and to draw attention to the association of each of these forms of serous hæmorrhage with conditions of diminished blood-coagulability.

Serous hæmorrhage in the skin.—I have elsewhere[1] shown that urticaria or serous hæmorrhage into the skin is often associated with, and is probably dependent upon, a condition of defective blood-coagulability. In particular I have pointed out that this holds true (*a*) of the urticarias which supervene upon the injection of diphtheria antitoxin; (*b*) of the urticarias which supervene upon eating acid fruit; and (*c*) in all probability also of the urticarias which supervene after eating crabs or shellfish.[2] Two other urticarias—i.e., the urticarias which supervene occasionally after eating rhubarb and the urticaria which supervenes, more exceptionally, after the administration of soap enemas—

[1] THE LANCET, Jan. 18th, 1896; British Journal of Dermatology, No. 89, vol. viii.

[2] Since writing the above this inference has been confirmed by observations made by Dr. Wm. John Scott on a case of shell-fish urticaria, which was successfully treated by him with calcium chloride.

are also almost certainly referable to a condition of diminished blood-coagulability, depending upon an abstraction of lime salts from the blood. This abstraction of lime salts occurs in the first case under the influence of the oxalates of the rhubarb, and in the second case under the influence of the fatty acids of the soaps. To this list of urticarias, which are almost certainly referable to defects of blood-coagulability, we may probably also add the urticarias which occur not infrequently in hæmophilic patients. Several instances of these urticarias have come under my observation. In connexion with the general question of the etiology of urticaria it may be well to point out that serous hæmorrhage under the skin, like every other variety of serous hæmorrhage, may be due either (*a*) entirely to a condition of diminished blood-coagulability or more commonly (*b*) to a combination of causes—i.e., to a local injury superadded to a condition of diminished blood-coagulability. As an instance of an urticaria which is referable to this combination of causes I may instance the local urticaria which so frequently manifests itself at the site of injection after the administration of antitoxic serum. I have recently had instructive experience of such an urticaria in my own person, having suffered from a severe local urticaria after an inoculation of 1 c.c. of tetanus antitoxin. This urticaria, which had been very troublesome for three days, disappeared in two or three hours under the influence of one 30 grain (2 gramme) dose of calcium chloride. The disappearance of this urticaria was coincident with an increase of blood coagulability[3] from five minutes (to which it had declined under the influence of the antitoxin) to its normal of three minutes. It may, therefore, be reasonably inferred that this urticaria was not attributable only to the local injury which resulted from the injection, but also in part to the state of diminished blood coagulability.

Serous hæmorrhage into the subcutaneous and muscular tissues.—The best example of this variety of serous hæmorrhage is found in the serous hæmatomata which are so commonly seen in cases of hæmophilia. These serous hæmatomata may be distinguished from subcutaneous blood effusions by the fact that they leave a very trifling amount of discolouration behind. Other instances of œdemas which are referable to a condition of diminished blood-coagulability are the widespread œdemas which occur after the inoculation of viperine poison,[4] and in all probability also the œdema of the feet which occurs in patients whose blood-coagulability has been serously reduced by prolonged tropical fevers. Again, it would be well worth investigating whether chilblains are or are not dependent upon a diminished blood-coagulability. The following facts speak in favour of an association between the two phenomena: (1) in a case of aggravated chilblains which has recently come under my notice (a case in which the puffiness and blueness of the hands persists even in summer) I find that there is a notable defect of blood-coagulability (blood coagulation-time seven and a half minutes instead of from two to four, or at most five, minutes); (2) I have noted the occurrence of aggravated chilblains in one of the families of "bleeders" I have under observation; (3) I have frequently noted the association of chilblains with a tendency to epistaxis and to urticaria; and (4) chilblains are in many respects comparable to a deep-seated urticaria. For instance, the itching that accompanies chilblains, like the itching that accompanies urticaria, is most troublesome in the evening and is aggravated by every change of temperature.

Serous hæmorrhage into the tubules of the kidney.—The association of so-called "cyclic albuminuria" with a tendency to epistaxis has been noted by Marie,[5] and is suggestive of a connexion between low blood-coagulability and albuminuria. The connexion between the two phenomena is suggested also by the fact that albuminuria occurs independently of any verifiable kidney disease in persons whose blood-coagulability has been reduced by tropical fevers. I have not as yet met with any albuminuria in "bleeders." I have, however, not as yet sufficiently examined for it.

Serous hæmorrhage into joints and serous cavities.—That effusions into joints may be dependent upon a defect of blood-coagulability is evident from the fact that next to actual hæmorrhages joint effusions constitute the most characteristic clinical manifestation of hæmophilia. Effusions into other serous membranes do not appear to have been specially noted in cases of hæmophilia. Probably, however, attention has not been directed to this point. In a case I have under observation symptoms which are suggestive of a serous hæmorrhage into the brain—i.e., stupor followed by "fits"—have several times occurred simultaneously with effusions into joints. Again, quite independently of hæmophilia, the possible dependence of serous effusions upon a defect of blood-coagulability is often suggested by the fact that pericardial and pleural effusion are often in the post-mortem room found associated with signs of hæmorrhages from mucous membranes, and with defective clotting of blood in the larger bloodvessels. The joint pains which occasionally supervene upon injections of antitoxic serum are also suggestive of a dependence of serous hæmorrhages into joints upon defects of blood-coagulability. For these joint-effusions, like the urticaria which they so frequently accompany, may be reasonably referred to the defect of diminution of blood-coagulability which, as I have pointed out, is frequently induced by the injections of antitoxin. In view of these facts it would be well worth investigating whether cases of hydrocele and pleural- and joint-effusions for which no other sufficient cause can be detected are, or are not, dependent upon defects of coagulability. In this connexion it would also be interesting to examine the condition of blood-coagulability in beri-beri.

Serous hæmorrhage into the intestinal canal —In my experience hæmophilic patients very seldom suffer from constipation. Their bowels are usually free and there is often a history of frequently recurring diarrhœa. These diarrhœas seem to be coincident with periods of abnormally diminished blood-coagulability. For instance, in one of the "bleeder" boys I have under observation blood coagulation time stood at over twenty-five minutes at a time when he was suffering from a persistent attack of diarrhœa. This boy's blood had in previous observations been found to clot in periods varying between seven and ten minutes. It seems a probable inference from these facts that diarrhœa may be caused by serous hæmorrhage, depending upon a defect of blood-coagulability. The association of a defect of blood-coagulability with diarrhœa may also be inferred from Osler's observations on the frequent association of diarrhœa and vomiting with cases of morbus maculosus Werlhofii[6]—i.e , with a disease which is plainly associated with a serious defect of blood-coagulability. The same association of serous hæmorrhage into the bowel with serous hæmorrhage into the skin and deeper tissues may be noted in the case of the urticaria which results from eating crab or shell fish. Again, the occurrence of diarrhœa after croupous pneumonia at a time when peptone (albumose) is being excreted in the urine is also probably referable to a serous hæmorrhage into the bowel induced by a defect of blood-coagulability. This inference is based upon the fact that diarrhœa due to serous hæmorrhage is invariably seen in dogs whose blood-coagulability has been diminished by an injection of peptone (albumose).

In addition to the facts just adverted to, a series of pharmacological facts seem to point to the existence of a relation between the state of blood-coagulability and the condition of the stools. In the first place non-irritant hydragogue cathartics appear, if I may judge from a very few experiments made with magnesium sulphate and bitartrate of potash, to owe some part of their efficacy to their power of diminishing blood-coagulability. Again, the marked constipating power of lime salts (e.g., chalk and calcium chloride) may quite probably be due to a diminution of serous hæmorrhage into the intestine dependent upon an augmentation of blood-coagulability. In like manner the notoriously constipating effect of a milk diet may be in part due to the large percentage of calcium salts contained in cow's milk. This last inference is to some extent confirmed by the fact that obstinate infantile constipation will often (I speak, however, from a very small experience) disappear when the child is put upon a diet of citrated milk[7]

[3] These observations of coagulation-time were made at the standard temperature of 18·5° C. (half blood heat) with coagulation-tubes of the standard size, 0·25 millimetre internal diameter, obtained from Mr. A. E. Dean, jun., 73, Hatton-garden, E.C.

[4] Dr. C. J. Martin (Proceedings of the Royal Society of New South Wales, July, 1895; Journal of Physiology, vol. xv.) has shown that when viperine poison does not produce instantaneous vascular coagulation it produces an extreme diminution of blood-coagulability, which is quite comparable to the "negative phase" of coagulability obtained after an injection of Wooldridge's tissue fibrinogens.

[5] Semaine Médicale, January, 1896.

[6] Johns Hopkins Hospital Reports, vol. v.

[7] I have in a previous communication (THE LANCET, July 22nd, 1893) recommended this milk as very suitable for administration to infants and invalids (especially to typhoid fever patients) whose digestions are not strong enough to cope with the firm clots which are obtained from ordinary cow's milk.

(i.e., milk which has been deprived of its excess of lime salts by an addition of 1-400th of citrate of sodium). It will be obvious that the lines of thought which are opened up by the above series of facts are too numerous, and, in some instances, too far-reaching to be followed up within the compass of a paper like the present. The following up of these lines of thought will, however, present no difficulty to anyone who takes as his starting-point the generalisation that a defect of blood coagulability tends to manifest itself, not only in "actual hæmorrhages," but also (according to the particular idiosyncrasy of the patient) in some one or more of the forms of "serous hæmorrhage" which have been adverted to. As testimony to the truth of this generalisation we have the case of hæmophilia, where every one of these forms of serous hæmorrhage (with the as yet doubtful exception of albuminuria) comes under observation.

The bearing of this generalisation upon the question of treatment is obvious. Methods of treatment which augment blood-coagulability will be methods of treatment that will be appropriate, not only to the prevention and treatment of "actual hæmorrhage," but also to the prevention and treatment of "serous hæmorrhage." The more important of these therapeutical measures appear to be the following: (*a*) the exhibition of calcium chloride (or other soluble lime salt) in suitable quantities; (*b*) the avoidance of such vegetable acids as citric, malic, tartaric, and oxalic acids, which form insoluble salts with lime; (*c*) the concentration of the blood either by diaphoretics or by such purgatives as do not owe their efficacy to a power of reducing blood-coagulability; (*d*) the restriction of the amount of fluid ingested; (*e*) the increase of the amount of carbonic acid in the blood, either by direct inhalation of the gas or by other methods; and (*f*) the avoidance of alcohol. The object of this paper will have been obtained if it should lead to a trial of such of these therapeutic measures as may not already be in use, both in the treatment of actual hæmorrhage and also in the treatment of the various forms of serous hæmorrhage which have been enumerated. Even where, as probably in a large majority of cases, these clinical symptoms are dependent upon something more than a mere defect of blood-coagulability, an augmentation of coagulability may be expected to alleviate the clinical symptoms by limiting the transudation through the capillary wall.

As an example of what can be done in controlling serous hæmorrhage I may subjoin the following protocols of experiments, which show that the serous hæmorrhage, which is associated with the hypodermic inoculation of typhoid bacilli can be controlled by the exhibition of calcium chloride.[8]

Horse—Typhoid Vaccination.

Aug. 6th.—Receives a hypodermic injection of 20 c.c. of virulent typhoid culture. (This is the seventh injection to which the horse has been subjected.)

Aug. 7th.—Yesterday's injection, like all previous injections, has given rise to an enormous local œdema. The horse now receives 1 ounce (30 grammes) of calcium chloride in a bran mash.

Aug. 8th.—The œdema, which has on all previous occasions lasted for some considerable number of days, has practically disappeared, leaving behind two small, sharply circumscribed abscesses at the site of the inoculations.

Aug. 20th.—Horse receives a hypodermic injection of 50 cc. of the same virulent typhoid culture. He at the same time receives one ounce (30 grammes) of calcium chloride in a bran mash.

Aug. 21st.—No noticeable œdema. Only a slight fulness can be detected when the hand is passed over the site of the inoculation.

Aug. 22nd.—No further local symptoms whatever.

Sept. 7th.—50 cc. of virulent typhoid culture hypodermically on right side of the neck. No calcium chloride.

Sept. 8th.—Painful tense swelling (size of inverted soup-plate) at site of inoculation. Œdema of dependent parts of the neck. Pain on moving fore-leg.

Sept. 9th.—Swelling at seat of injection still very tense and painful. Œdematous swelling at lower part of the neck practically unaltered.

Sept. 11th.—The swelling at the seat of injection which has been threatening to suppurate appears now to be slowly resolving itself. The œdema has, if anything, a little increased. It has now passed down from the neck on to the front of the chest.

M. D., an Officer of the Indian Medical Service—Typhoid Vaccination.

July 31st.—Inoculated hypodermically in flank with one-twentieth of a tube of dead typhoid bacilli.

Aug. 1st.—Extensive œdema extending from site of inoculation to pubis and for four or five inches upwards over the front of the abdomen.

Aug. 4th.—Swelling and redness gradually disappearing.

From Aug. 4th to Aug. 11th.—Several 1 to 2 gramme doses of calcium chloride.

Aug. 14th.—3 P.M.: three-twentieths of a tube of more virulent typhoid bacilli inoculated into flank. 6 P.M.: a small amount of swelling has developed at seat of inoculation. 20 grains (1·25 grammes) of calcium chloride. 11 P.M.: swelling not noticeably increased. Another 10 grains (0·6 gramme) of calcium chloride.

Aug. 15th.—No increase in the œdema.

Aug. 16th.—All swelling and tenderness have disappeared.

Sept. 5th.—One-quarter of a tube of dead typhoid bacilli hypodermically. 45 grains (3 grammes) of calcium chloride by the mouth.

Sept. 6th.—No œdema whatever. Considerable redness and tenderness of skin disappearing towards evening.

Sept. 7th.—No further local symptoms.

J. S., an Officer of the Indian Medical Service—Typhoid Vaccination.

Aug. 19th.—12 noon: receives a hypodermic inoculation of one-twentieth of a tube of dead typhoid bacilli (culture the same as that employed in the second inoculation of M. D. above). Blood coagulation-time—7 min. 6 P.M.: considerable fulness has developed round site of inoculation. Blood coagulation-time—9 min. Receives 45 grains (3 grammes) of calcium chloride in half a tumbler of water. 8 P.M.: blood coagulation-time—5 min. 10 sec.; no increase of œdema.

Aug. 20th.—No trace of œdema, no further local symptoms, except a little redness and tenderness at site of inoculation.

These facts would appear to have an importance altogether beyond that which attaches to this particular vaccination process. They have, for instance, an obvious application in connexion with the prevention and treatment of the serous hæmorrhages, which are associated with Haffkine's anti-cholera inoculations. (I need hardly point out that these anti-cholera inoculations have served as a pattern for the typhoid vaccinations detailed above.) They have a further application in connexion with the treatment of insect bites and of the œdematous arms which are sometimes seen after small-pox vaccinations. And, lastly, a more general therapeutical importance accrues to these facts when we consider that œdematous conditions not only lower the resistance of the organism to bacterial infection, but they also, if we may judge from what occurs in the case of bad chilblains and in the case of the traumatic œdemas of the bleeders, sometimes lead on directly to suppuration and mortification. Possibly the favourable results which are said to be obtained by the exhibition of calcium chloride in the treatment of boils, of croupous pneumonia, and of some cases of phthisis with considerable expectoration, may be due to the fact that any drug which controls serous hæmorrhage will, by virtue of that property, exert a favourable influence also upon suppurative processes.

Netley.

[8] I would here again warn against injecting calcium chloride solutions hypodermically. I find that the injection of perfectly aseptic 10 per cent. solutions of calcium chloride is in animals followed by widespread sloughing of the subcutaneous tissues.

PREGNANCY COMPLICATED BY AN OVARIAN TUMOUR; RUPTURE OF THE CYST NINETEEN DAYS AFTER DELIVERY; RECOVERY.

BY A. C. BUTLER-SMYTHE, F.R.C.S. EDIN.,

SENIOR SURGEON TO THE GROSVENOR HOSPITAL FOR WOMEN; SENIOR SURGEON TO OUT-PATIENTS, SAMARITAN FREE HOSPITAL FOR WOMEN.

A WOMAN aged thirty-five years was first seen by me in July, 1895. She had been married fourteen years, had nine children, and had entered the fourth month of her tenth pregnancy. Her youngest child was two years old. She came for advice on account of pains in her abdomen and legs, particularly in the right leg. The pains she attributed to rheumatism. On examining the abdomen a small ovarian tumour was discovered on the right side about the size of a cocoanut and freely movable. A consultation was held and it was decided that no attempt should be made to remove the tumour as it would not interfere with the pregnancy. The patient came under my observation each week up to Aug. 12th. In September she was examined by Dr. C. Gould May and Mr. R. T. Nariman, who noted "that she remained well and that the tumour had not much increased in size." I saw her again on Oct. 2nd, when to all outward appearances she had begun her sixth month of pregnancy. The tumour caused her no trouble and she professed to be very comfortable. On Dec. 30th she was admitted into the Grosvenor Hospital for Women, having had some suspicious pains that day. On examination I found the head presenting, but she was not then in labour. On the morning of Jan. 2nd, 1896, I was sent for, and on arriving found a male infant just born, but not separated. The placenta came away easily and there was no hæmorrhage worth speaking of. The tumour could now be felt in the right iliac fossa, and was not much larger