carpal tunnel. Further swelling slowly developed, together with acute tenderness both in the palm and just above the transverse carpal ligament on the front of the wrist. There was almost complete loss of median-nerve sensation in the thumb and index and middle fingers. Motor function of the short thenar muscles could not be tested because of the extreme swelling and tenderness. On January 7 it was decided to explore the front of the wrist.

Operation.—This was performed by Mr. A. Gourevitch under general anaesthesia, in a bloodless field. An incision was made along the ulnar border of the wrist, and Parona's space was opened. The tissues were all oedematous and a small quantity of blood-stained exudate was evacuated. A second incision was made, curving round the base of the thenar eminence and up to the distal wrist-crease. The palmar fascia and transverse carpal ligament were exposed. The latter was divided completely, exposing the median nerve. No macroscopic evidence of compression was noted, but some further blood-stained fluid was evacuated from here and from the mid-palmar space, which was explored by an incision through the palmar fascia. No frank pus was found. A small rubber drain was placed in each wound and the incisions were closed with silk sutures.

Organisms were not cultured from the swab taken at operation. Nevertheless, antibiotic treatment was continued in view of the persistent inflammatory changes in the hand. These slowly subsided over the next 48 hours, and there was patchy return of sensation except at the tips of the affected digits. Movements were encouraged from this stage as there was gross stiffness of the hand. Improvement was steady but slow. She was allowed home three weeks after operation, at which time sensory recovery was full except for the terminal pulp areas. Physiotherapy was continued for a further two months, during which period hand and finger movements returned almost to normal.

She was seen again recently, five years after her illness. Power of grip was very slightly weaker than on the left. Movements were normal. There was persistent minimal blunting of light touch sensation on the tips of the thumb and index finger, but this caused her hardly any disability apart from, she stated, making her slightly clumsy when doing very fine needlework.

Discussion

In their two cases of the same condition, Bailey and Bolton Carter (1955) suggested that interference with median-nerve function resulted from compression by inflammatory exudate in the radial and ulnar bursae deep to the transverse carpal ligament. They preferred this hypothesis of compression ischaemia to the alternative explanation that the changes were produced by the direct spread of infection to the nerve.

The present series would appear to support their view. Particularly in Case 1 did the appearance at operation suggest compression. In this case and also in Case 2 there was tight distension of the flexor tendon sheaths in the carpal tunnel. The somewhat later onset of nervous signs in Case 3, after the infection was coming under control, also suggests a pressure effect rather than an infective neuritis.

On the basis of the experience of these three patients, and in view of the two similar cases previously described, it is urged that a close watch be kept for signs of interference with median-nerve function in all severe acute hand infections, and particularly in those in which the tendon sheath is involved. Such cases should be treated by division of the transverse carpal ligament as soon as any signs of damage to the median nerve are noted. This division must be complete, and at the same time the ulnar and radial bursae should be opened to drain any infective exudate therein.

Summary

Three cases of acute infection of the hand complicated by median-nerve paralysis are described.

In two patients the tendon sheaths deep to the transverse carpal ligament were shown to be involved in an acute streptococcal infection.

The nerve lesion was probably due to pressure in the carpal tunnel as a result of the acute inflammatory swelling. All three cases were treated by division of the transverse carpal ligament.

I thank Mr. A. B. Watson for permitting me to treat Cases 1 and 2, and Mr. A. Gourevitch for allowing me to publish the details of Case 3; also for their help and encouragement in the preparation of this paper.

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AUTOMATIC CLOTTING-TIMER FOR CONTROL OF ANTICOAGULANT THERAPY

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In the control of anticoagulant therapy there are two basic requisites: first, the laboratory control; and, secondly, the equally important experience needed to prescribe anticoagulant drugs so as to allow for the inevitable changes in the maintenance dose which may occur owing to changes in health, diet, administration of other drugs, etc. Much can be done to maintain adequate anticoagulant control by recognizing these "periods of danger" (Toohey, 1959) and making any necessary changes in the dose as early as possible, and by taking more frequent blood tests during these "periods of danger." Here the great advantage of the physician who actually prescribes the anticoagulant drug seeing the patient at the time the blood test is taken, as opposed to a "postal service," is clearly evident. With regard to the actual anticoagulant drug, there are now available several good oral anticoagulants for the control of both short- and long-term anticoagulant therapy (Toohey, 1959).

Unfortunately, even to-day, after many years of experience with anticoagulant therapy, there is no universal agreement on the best laboratory method for the control of this treatment. Controversy still exists about the relative merits of the two most widely used laboratory techniques—Quick's one-stage technique and Owren's "P and P" method. Quick's one-stage technique has the great advantage of speed and simplicity. Owren's method is more sensitive and also allows more accurate comparison of results between different laboratories. Owren's method, however, has great disadvantages for widespread use: first, the

*Dr. Toohey died on March 21, 1960, after this paper had been prepared.

reagents are not available commercially, and they require some skill and experience in their preparation; and, secondly, when large numbers of patients are being treated the time needed to carry out the tests can be appreciable. Owren (1959) has produced a modification of the "P and P" method—the thrombotest—which can be used with capillary or venous blood and also with citrated plasma. It is unlikely that the use of capillary blood will become widespread, as with capillary blood the test has naturally to be done at the time the blood is taken. This will often be inconvenient for most hospital organizations. The great advantage of the thrombotest will lie in the availability of a commercial reagent which is stable and gives reproducible results.

Automatic Time-recording Apparatus

Even with a stable commercial reagent readily available, however, there remains one disadvantage with Owren's method as compared with Quick's technique—that is, the much longer time needed to carry out the tests. As mentioned earlier, when large numbers of patients are being treated (as is likely with the increasing use of long-term anticoagulant therapy) this time-factor is important. To overcome this disadvantage we have devised an automatic time-recording apparatus (see Fig.). This apparatus can be used for measuring the clotting-time of plasma such as the calcified plasma clotting-time, Quick's one-stage technique, Owren's original "P and P" method, and the more recently introduced thrombotest using plasma.

All these tests are carried out in the usual manner, except that glass tubes of special size to fit the apparatus are used. (It is also important to use sodium citrate† and not oxalate in collecting the blood sample.) As soon as the calcium is added, the time-recorder is started by moving switch A. The tube, the end being closed by the tip of the finger, is completely inverted once to mix the contents thoroughly, and the tube is then inserted into the aperture B. By turning the galvanometer sensitivity control 4, the galvanometer needle is adjusted midway between the two marks on the galvanometer scale. A few seconds are now allowed to elapse to permit of any slight drift that may occur. This drift is negligible in most cases if citrate is used as the anti-coagulant in collecting the blood sample; if, however, oxalate is used a considerable drift may occur for several seconds owing to precipitation of calcium oxalate.

Once the galvanometer needle is steady for a few seconds the time-recording switch A is moved in the opposite direction to that previously. This second movement brings into play an automatic cut-out. When clotting starts a turbidity develops in the plasma. This is one of the earliest changes to occur, and it develops immediately before an actual clot is visible to the naked eye. This turbidity causes the galvanometer needle to shift, and this in turn brings the automatic cut-out into action and stops the time-recording apparatus. The clotting-time can then at once be directly read from clock D in seconds. The apparatus has a temperature-regulating mechanism to allow tests to be carried out at 37° C.

Once the automatic timer is brought into action no further attention is needed. The operator may leave the laboratory, and when he returns the result of the test is clearly recorded. More important, the apparatus

†3.13% sodium citrate replaces the potassium oxalate.

Time-recording apparatus. A, time-recording switch. B, aperture for insertion of tube. C, galvanometer sensitivity control. D, clock.

has been devised to allow duplicate tests to be carried out simultaneously, so that once one test has been set up the second test can be started in the second part of the apparatus without waiting for the result of the first test. Subject only to the number of machines available, any number of clotting-tests can be carried out by one operator without the need to await completion of any single test.

Before the automatic cut-out is brought into action the galvanometer needle may be freely moved without stopping the time-recorder. Once, however, the automatic cut-out is brought into the circuit care must be taken not to move the galvanometer needle beyond the indicated marks on the galvanometer scale, otherwise the time-recorder will be stopped and thus give a false reading.

This apparatus not merely saves a good deal of time; it also results in standardization in reading the results of clotting-time, which is equally, if not more, important. Some operators find reading the end-point of clotting difficult until they have had considerable experience in the use of clotting techniques. This is evident from the obvious discrepancies between the results obtained in the reading of results by different operators, who are nevertheless using the same techniques and the same reagents. The apparatus described here eliminates any discrepancies in the reading of the end-point of clotting times and gives more accurate standardization of results. In over 500 tests done simultaneously with this apparatus and with the usual hand-water-bath technique, the apparatus gave more accurate and reproducible results.

Summary

An apparatus is described for automatically recording the end-point of clotting when blood-clotting tests are carried out using plasma. Quick's one-stage technique, Owren's "P and P" method and thrombotest, and recalcified plasma clotting-times can all be carried out

with this apparatus. Much time is saved when large numbers of tests have to be performed, especially if Owren's methods are being used. Just as important is the fact that much more reliable and reproducible results are obtained by using this automatic time-recording apparatus than with the hand-water-bath technique.

The apparatus was made for us by Evans Electroselenium Ltd., Colchester Road, Halstead, Essex. Cheap disposable glass tubes to fit the apparatus can be obtained from C. E. Payne & Sons Ltd., 131, Clapham High Street, London, S.W.4. Fine-pointed accurate 0.2-ml. pipettes, which are most convenient to use with the small glass tubes, can be obtained from Baird & Tatlock Ltd., Freshwater Road, Chadwell Heath, Essex. We thank Evans Medical Ltd. for a grant towards the development of this apparatus.

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Medical Memoranda

Purpura After Administration of Piperazine

During recent years piperazine has replaced many other anthelmintics in the treatment of ascariasis and oxyuriasis. It is supposed to be non-toxic. Recently we observed a patient in whom a single 4.8-g. dose of piperazine citrate was followed by extensive purpura. We have not come across any other similar report in the medical literature so far. A brief account of the purpuric episode is given.

CASE REPORT

A girl aged 10 years was admitted to the E.N.T. wards of Hamidia Hospital, Bhopal, on January 15, 1959, complaining of epistaxis and bleeding from the gums for two days. At this stage she and her mother failed to co-operate in elicitation of a proper history. Anterior rhinoscopy showed a large number of punctate bleeding-points on the anterior part of the septum and inferior turbinate on both sides. Bleeding was moderate in amount. Examination of the buccal cavity revealed bleeding from the gums; posterior rhinoscopy did not show any more bleeding-points, and there was no bleeding from the pharynx and larynx. Skin of the whole of the body showed discrete purpuric spots. In the wards a gross haematuria was also found.

Investigations.—R.B.C., 3,400,000/c.mm.; haemoglobin, 62%; total W.B.C. count 6,400/c.mm. (polymorphs 54%, lymphocytes 40%, large monocytes 5%, eosinophils 1%); bleeding-time, 2 min. 30 sec.; coagulation time, 4 min. 54 sec.; prothrombin time (modified Quick's method using "thrombokinas" calcium tablets) 20 sec. (control 20 sec.); blood platelet count, 135,000; Hess's capillary test, positive. Urine: large number of red cells and albumin ++. Stools: N.A.D.

She was given vitamin C, 500 mg. intravenously and 100 mg. t.d.s.; vitamin K, 10 mg. t.d.s.; "stypobion," 1 tablet t.d.s., calcium lactate, 10 gr. (65 mg.) t.d.s. "Argyrol" nasal drops, gargles with Condy's fluid, and mist. bromide were also administered. Her condition remained stationary for four days, and on January 19 she was transferred to the medical wards. By this time the epistaxis had stopped. Purpuric spots were still present extensively over the trunk and extremities. She looked very weak, and pallor was marked. At this stage urgent blood grouping and matching were done, and a donor was found, though because of her subsequent recovery the blood transfusion was not administered. In the medical wards

she was given vitamin C, 500 mg. intravenously daily; vitamin K, 10 mg. intramuscularly six-hourly; and "coagulen-Ciba," 1 ampoule intramuscularly six-hourly. Haematuria and epistaxis had ceased by January 20, though purpuric spots over the trunk and extremities were still appearing.

On January 22 closer questioning revealed that the patient had had 4.8 g. piperazine citrate in a single dose eight days before the onset of symptoms, on the prescription of a local practitioner who suspected ascariasis on clinical grounds only. The patient did not pass any worms subsequently, but on January 13 she developed epistaxis. After the elicitation of this history all previous treatment was stopped and "synopen" tablet 1 t.d.s. was given on the presumption that the purpura might have been due to piperazine allergy. By next day all bleeding had stopped, the purpuric spots were fast disappearing, and Hess's capillary test was negative. By January 26 all purpuric spots had disappeared, and clinically nothing abnormal could be detected. Serial investigations revealed that the platelet count on January 21 was 135,000/c.mm., and on February 3 it was 350,000/c.mm. The bleeding-time and the clotting-time on February 3 were 1 min. 6 sec. and 4 min. 5 sec. respectively. Subsequently the patient made an uneventful recovery. All treatment was stopped on January 26. The patient was kept under observation in the ward for another 15 days, being discharged on February 11.

COMMENT

The anaphylactoid purpuras are diagnosed because of the absence of blood changes. Thus the bleeding-time in such cases is normal, and there is no diminution in platelet count. In our patient, though the platelets were reduced to 135,000/c.mm., they never fell below 40,000/c.mm.—a level below which bleeding is generally observed to begin (Whitby and Britton, 1957), though exceptional cases are known to exist in which bleeding had occurred at counts exceeding 40,000/c.mm., in all probability because of concomitant vascular damage. Though a clot-retraction test was unfortunately not done in this case, the bleeding-time was within normal limits throughout, and it seems unlikely, therefore, that thrombocytopenia was mainly responsible, if at all, for the symptoms. The purpura must have been due to vascular damage. The capillary endothelium and platelets are supposed to be antigenically similar, and it seems that the platelets were also reduced because of the same allergic phenomenon. Allergic thrombocytopenia is known to occur after administration of quinine, quinidine, "sedormid," thiouracil, methoin, and sulphonamides, and no doubt the same antigen can damage both platelets and capillaries.

So far, we are unaware of any published case of purpura after piperazine administration, and it is interesting to record that a supposedly innocent substance like piperazine, which is in extensive use, can precipitate a severe allergic purpura. In this patient the diagnosis of drug allergy was not in doubt, because of the onset of symptoms eight days after administration of the drug, and because of other negative laboratory findings already discussed. An experimental reproduction of purpura after readministration of the drug was not considered worth while because of the hazards.

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