had been averaging 20 flushes a week, dropped to *nil* in two weeks, and this improvement was maintained for another two weeks without further treatment. Thereafter the flushes began to return. A dose of 2 g. brought about a marked improvement in 9 patients, and this effect lasted on an average three weeks without further administration. After this time the number of flushes increased again.

The next problem was that of a maintenance dose. This varied according to the severity of the symptoms, and it was eventually found that 0.2 g. per week was satisfactory. In this series it was administered in doses of 0.4 g. fortnightly. It was also found that if more than three weeks was allowed to elapse between the administrations it was advisable to give another initial dose. Increase of the maintenance dose was not satisfactory. Some of the side-effects of other synthetic oestrogens were observed. Four patients vomited after receiving 2 g. This started about 8 hours after taking the tablets, and continued for 36 hours. One of these patients had nausea but no vomiting after a small dose. Three others did not actually vomit but were nauseated by large doses. This began about 24 hours after taking the tablets and continued for some three days. Three patients had uterine bleeding or a brown discharge lasting for several days. In two this occurred two weeks after the last administration, and in one immediately after taking a large dose. Two other patients had severe uterine colic following a dose of 2 g., and one of these developed a white vaginal discharge which was found to be due to the excessive secretion of mucus from the cervical glands. Five patients experienced headache for 24 hours after a large dose: they had not previously suffered from headache. In those cases in which headache was a prominent feature of the menopausal syndrome it was relieved by D.B.E. Four patients complained of lassitude during the course of the treatment. Although this symptom does not appear to be generally recognized as an effect of synthetic oestrogens I have found that it frequently occurs in patients receiving stilboestrol. Most of these effects occurred only when large doses were given.

Results

Of the 11 cases 5 were completely relieved of their symptoms; 3 were greatly improved, and the average reduction in the weekly number of flushes in these patients was from 80 to 6. The remaining 3 patients failed to respond at all even after doses of 3 g.

The 3 who were improved but not completely relieved were put on to stilboestrol 1 mg. t.d.s. This brought about complete relief in all cases. Two of the three failures were similarly treated and were also completely relieved within three weeks of starting stilboestrol therapy. The third patient in this group suffered from disseminated sclerosis and failed to attend again. One of the patients had a severe leucoplakic vulvitis which did not improve on the doses given and has subsequently undergone vulvectomy.

Summary

D.B.E. ($\alpha\alpha$-di-(*p*-ethoxyphenyl)-β-phenyl bromoethylene) is a synthetic oestrogen with a prolonged action.

This substance was used to relieve menopausal symptoms in 11 patients who had undergone surgical or radiological castration: 5 were completely relieved, 3 greatly relieved, and 3 showed no response.

The dosage required for the relief of these symptoms is an initial dose of 2 g. followed by a maintenance dose of 0.2 g. weekly. Mild cases may require only half this dosage.

The side-effects of other synthetic oestrogens have been noticed with D.B.E.

It appears from this small series that D.B.E. is probably not as effective as stilboestrol in the relief of menopausal symptoms.

It is probable that its sole advantage is that it needs to be administered infrequently and not daily as with other synthetic oestrogens.

I should like to thank Dr. A. N. Macbeth for her help and advice, and Organon Laboratories Ltd. for the supplies of D.B.E. used in this investigation.

A. H. Williams (*Delaware State med. J.*, 1945, **17**, 179) records a case of myelitis following chicken-pox in a boy aged 4. Recovery took place without specific therapy.

CONCENTRATING MALARIA PARASITES IN THIN FILMS

BY

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The diagnosis of malarial infection has often to be made on samples provided by practitioners, and the pathologist frequently finds fault with the smears provided—usually because they are too thick, are unevenly spread, and are allowed to dry too slowly.

The thick-film technique is widely employed to give concentrated films, but the parasites are not intracellular and many pathologists do not like them. Wilcox (1942), in her monograph, describes the thick-smear technique very clearly, but obviously it is one that only the trained laboratory worker can employ; she states that the thin film is ideal for demonstrating the morphology of the individual parasites. Figures are given for the degree of concentration obtained by many authors, using the thick-smear method; these vary from 10 to 50 times. Todd and Sandford (1943) quote the method of Bass and Johns, as described it is very laborious, but it does provide concentrated intracellular parasites.

There will be many cases of malarial relapse in the next few years, and it is hoped that the following technique may be a help in proving if such cases are suffering from a genuine relapse; the proof may be of great importance in the gaining of a pension for the patient. The technique was evolved to secure the advantage of concentration as well as that of seeing intracellular parasites; it allows a practitioner to obtain the blood samples, using the technique he employs for obtaining blood for a Wassermann reaction, and saves making blood smears.

Technique

Any blood may be used, but, if the blood has clotted, many of the white cells and all the platelets are avoided, making the slide easier to examine. When clotted blood is employed it is shaken and the serum drawn off and centrifuged for 2 to 3 minutes in a small tube; the serum is discarded, except for a volume approximately equal to that of packed red cells. The residual serum and the red cells are mixed, and this blood is run into a capillary tube; the end of the capillary is sealed and the tube centrifuged hard (2,000 to 3,000 revolutions per minute) for 20 to 30 minutes.

The capillary is removed and a scratch made, with a glass-cutter or diamond, about 1/8 in (0,32 cm.) above the top of the packed red cells; the tube is held horizontally, and is broken at this mark. A second cut is made about 1/8 in. below the top of the red-cell layer; the tube is again held horizontally, and is now broken at this second mark. The tube is held horizontally after the first cut to prevent the plasma running down over the operator's fingers, and, after the second, to prevent any loss of the contents of the wanted specimen.

The next stage was evolved to allow easy handling and mixing of the contents of this small segment of the capillary tube. The butt end of a Pasteur pipette, where it starts to narrow down, is heated in a peak flame, and when soft the two extremities of the pipette are pressed towards each other, allowing the tube to bend into an S shape. The pipette is again heated in the peak flame, about 1 in. (2.5 cm.) from this bend; it is drawn out and sealed taking care to make the terminal portion thin. If the end is not thin it is difficult to break off the tip later, and some of the specimen will be lost. The short piece of capillary tube is dropped into this prepared pipette with serum uppermost; the tube is then placed in the centrifuge, which is switched on for from 2 to 5 seconds. The blood is now in the capillary end of the pipette; the thinned tip of the pipette is cut off, a teat is applied to the butt, and the blood is blown out on to a slide and a thin smear made. Alternatively, the blood is mixed on a wax slide. The edges of the film are examined for the parasites. The accompanying figure shows the completed pipette.

Results

The degree of concentration has been estimated by counting the number of parasites seen, under the 1/12 objective, in an equal number of fields, usually 100, in both the plain and the concentrated films. In the last 22 positive bloods the average degree of concentration has been ×15.8—made up of 426 parasites in the plain, as against 6,718 in the concentrated films. The concentration has varied from ×5 to ×56. Eleven of these lay between ×10 and ×24; others were ×5, ×6 (twice), and ×9. There were also specimens with ×56, ×50, ×35, and ×33 concentration. In a total of 52 positive bloods examined 5 were positive in the concentrated films only. These figures would seem to compare favourably with those obtained in the thick-smear method. Schüffner granules do not appear to stain well in the concentrated preparations made by me.

Since the technique was evolved only two cases of falciparum infection have been concentrated. The first was diagnosed as an M.T. infection on a thin smear provided on July 20, 1945; the hospital was informed by telephone and warned to apply intensive therapy, as a heavy infection with trophozoites was present. The patient had the following treatment:

July 20: 9 g. intramuscular quinine.
July 21: Mepacrine t.d.s.
July 22: Morning—mepacrine, 2 doses. Patient went into coma at midday. Afternoon—9 g. *intravenous* quinine.
July 23, 24, and 25: Mepacrine t.d.s.

On July 25 venous blood and thin smears were obtained and were sent by post to the laboratory; 7 gametocytes in 500 fields were seen in concentrated smears made on July 26; but several pathologists have failed to find parasites in the thin smears provided.

The other M.T. infection was a fatal case of gastro-intestinal and cerebral malaria (which it is hoped may be described in detail later). 1½-day-old blood, taken for a Widal test 18 hours before death, was used to provide the red cells; unconcentrated smears showed a very heavy infection with trophozoites (1 in every 3 of the red cells were infected). With such a heavy infection it is hard to demonstrate concentration, but the concentrated smears showed parasites in 2 out of every 3 red cells, and also demonstrated gametocytes and schizonts which were not seen in the plain smears.

Evidence of concentration of crescents based on two cases is not sufficient, and I would be grateful for both thin smears and venous blood samples from proved cases of M.T. infection, as I would like to use the method on more such cases.

Other Possible Uses for the Method

The method described has been used several times to concentrate the nucleated cells in marrow obtained by sternal puncture, to facilitate the search for Leishman-Donovan bodies. The marrow was placed in a tube containing dried heparin (the mononuclears tend to pick up the crystals of Wintrobe's oxalate mixture, so this could not be employed). Very good concentration of the nucleated cells was obtained, but no L.D. bodies were seen; in whole blood heparin often causes agglutination of the white cells; but, even after two hours and the centrifuging in capillaries, there was no tendency for the cells to clump in these sternal-marrow specimens. It may be that the technique could be used for the diagnosis, on stained smears, of other protozoal and spirochaetal infections, but I have not had the opportunity of trying it.

I would like to express my thanks to Sir Philip Manson-Bahr for his encouragement and advice, to Dr. C. M. Wenyon for his helpful criticisms, and to the Regional Adviser in Pathology, Prof. Bernard Shaw.

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J. K. Mohanty (*Ind. med. Gaz.*, 1945, **80**, 187) treated 62 cases of whooping-cough by injection of maternal whole blood. It was efficacious in about 61% and was followed by some improvement in another 9.7%.

Medical Memoranda

Immunity to Sandfly Fever

In a previous article (Cullinan and Whittaker, *Journal*, 1943, **2**, 543) an outbreak of sandfly fever in two adjoining hospitals in the Middle East, occurring in the summer of 1942, was described. In that outbreak most of the N.C.O.s and men of the staffs of the two hospitals and, later, large numbers of patients admitted for other diseases to Hospital A were attacked (Hospital B was not at first functioning). In the summer of 1943 sandfly fever was rampant in the surrounding district, and close on 1,000 patients suffering from the disease were admitted to Hospital A from outside (Hospital B had now left). Inside the hospital, however, far fewer members of the staff and patients admitted for other diseases were affected. This lower morbidity within the unit may have been related to improvements in the camp site. Measures for "control" were the same in both years.

In 1942 both hospitals were newcomers to the district. Although Hospital A had been in the Middle East for a considerable time, it had come from an area where sandfly fever was unknown. Hospital B had recently arrived from the United Kingdom. In the 1942 outbreak it was recorded that 15% of the N.C.O.s and men had two and sometimes three attacks of sandfly fever at intervals ranging from 2 to 12 weeks during the period of the epidemic. Moreover, it was obvious that these later attacks were not relapses but were caused by reinfection. This suggested that one attack of sandfly fever conferred little or no early immunity, or that, if it did, it was remarkably short-lived.

In the 1943 outbreak, however, there was evidence that an attack of sandfly fever might confer a more distant immunity. During the time of this outbreak the average daily strength of N.C.O.s and men in Hospital A was 240. Between June 1 and Sept. 30, while 55 of the 142 who had not been with the unit in the previous summer caught sandfly fever, only 13 of the 98 who had been with the unit during both summers were affected. In other words, the disease was roughly three times less common among those who had been present in the 1942 epidemic than among those who had not.

The evidence suggests that while an attack of sandfly fever does not confer an early immunity, or that if it does it is short-lived, it may confer a more distant immunity.

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Frontal Lobe Abscess Treated with Penicillin

Spreading acute osteomyelitis of the frontal bone is a well-recognized complication of frontal sinus suppuration and carries a high mortality. When complicated by a frontal lobe abscess the prognosis is wellnigh hopeless. The following case illustrates, I think, not only the efficacy of penicillin in this condition but also the necessity for adequate surgery if treatment is to be successful.

CASE RECORD

A boy aged 16 was admitted to hospital on May 14, 1945, with a history of frontal and occipital headache, vomiting, and restlessness of a week's duration. There was no history of trauma. Temperature 101.6°, pulse 90 a minute. There was a red fluctuant swelling overlying both frontal sinuses, but no nasal discharge. A diagnosis of frontal sinus empyema was made, and this was confirmed by skiagrams. On the 16th both sinuses were drained externally and thick offensive pus evacuated. It contained *Staph. aureus* and diphtheroids which were 100% penicillin-sensitive. On May 31, in spite of good drainage and sulphathiazole in full doses, the boy became drowsy and irritable, and a spreading diffuse oedema of the frontal region extending backwards was now evident. On June 1 he became semiconscious and his temperature fell to 96° F. and pulse to 48. The right pupil became widely dilated and fixed, while the left pupil remained contracted. On June 2, under local analgesia, supplemented by chloroform on an open mask, a large semicircular flap was turned down over the frontal region. There was widespread necrosis of bone with some loose sequestra. All necrosed bone was removed, and a sinus was found in the anterior aspect of the right frontal lobe through which pus flowed out under tension. This sinus was utilized later for the insertion of a small rubber drainage-tube which was sutured to the dura. Several ounces of pus were aspirated from the abscess cavity. On June 4 penicillin therapy was begun, 2 c.cm. (123,500 units) being injected intramuscularly every 3 hours for a period of 10 days and 6 c.cm. instilled into the abscess cavity twice daily for 5 days. Rapid improvement was soon manifest, and the drain was removed after 3 weeks. The frontal sinuses, however, continued to drain, and on July 9 they were again exposed by an upturned flap and multiple polypi