flexing the toes in your shoes and frequently rising on tip toes.

3. Plan your day so that you can lie down for two to three half hour periods and elevate your leg to a 45 degree angle. The back of a small straight backed chair is useful for this purpose.

4. When ever you sit down, elevate your leg on a foot-stool, chair or chesterfield.

5. At night raise the foot of the bed on blocks about twelve inches high.

6. Apply a bland cold cream to the affected skin at nights about every second day.

7. Avoid irritation to the involved leg, especially in respect to sunburn and hot water bottles.

8. Be extremely careful to prevent bumping or scratching the affected leg.

SUMMARY

1. Retrograde venograms were successfully accomplished in 18 of this series of 28 cases of legs damaged by a previous deep phlebitis which showed the post-phlebitic complications of ulceration and eczema. All degrees of venous involvement were found ranging from valvular damage only to almost complete obliteration of the vein by organized thrombus.

2. No correlation was found between the degree of venous involvement as shown by the venogram and the extent of the postphlebitic complications, consequently the rôle of the damaged vein in producing these complications is believed to be slight. As a result of this finding, the surgical treatment of ligation of the femoral vein at present in vogue in these cases does not seem logical.

3. The etiology of the post-phlebitic leg and its complications is discussed and the belief expressed that interference of the lymphatic return is the greatest single factor and venous retardation a secondary one. The entrance of pyogenic organisms via superficial trauma in such a leg is the immediate cause of the complications.

4. An attempt has been made to group such cases into four types for the purpose of treatment. These are associated secondary incompetent varicose veins, those with evidence of sympathetic over-activity in the leg, those with marked soft tissue sclerosis about the ulcer and finally the group where the above factors are not present. Emphasis is laid on the point that these forms of therapy are only aids in healing of the complications, giving also some measure of protection against recurrence, but that the greatest single factor in keeping the leg free of troubles is the adoption of the "new way of life" for the remainder of the patient's existence.

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RÉSUMÉ

L'auteur expose le fruit de ses expériences dans le traitement des membres inférieurs ayant déjà été atteints de thrombo-phlébites profondes et de phlébo-thromboses. L'article est basé sur l'étude de 28 cas présentant les complications post-phlébitiques usuelles: les ulcérations et l'eczéma.

La phlébographie rétrograde fut choisie comme mode d'examen. La technique consiste à injecter 20cc. de Diodrast dans la veine fémorale profonde. On ne put établir un rapport entre le degré d'atteinte veineuse constaté sur les films et l'importance des complications post-phlébitique; ce qui semble prouver que le fémorale profonde n'a que peu à faire dans l'élaboration des complications. L'expérience de l'auteur semble confirmer l'hypothèse de Homans ayant trait à l'étiologie des complications. Il semble bien que ce soit le système lymphatique qui joue le plus grand rôle. Les traumatismes contituent la porte d'entrée des agents microbiens précipitant les complications. Dans le but d'assurer un traitement fondé, l'auteur divise ses cas en quatre groupes. Le premier comprend ceux qui sont associés à des veines variqueuses à valvules insuffisantes, le deuxième, ceux qui font preuve d'une suractivité lymphatique, le troisième ceux qui présentent de la sclérose des tissus mous et des ulcères et finalement le quatrième où on ne retrouve pas les facteurs précédents. L'auteur insiste sur le fait que les traitements actuels ne sont que des adjuvants de la guérison des complications et que le principal facteur pour garder une jambe saine et prévenir les rechutes est encore le régime de vie qu'il propose et les soins apportés par le patient.

YVES PRÉVOST

PENICILLIN IN THE TREATMENT OF PRE-NATAL SYPHILIS*

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SINCE the first publication in the autumn of 1944 on the use of penicillin in the treatment of pre-natal syphilis[1] numerous reports of its use have appeared. There has been a constant change in the total dose recommended by various writers and in the treatment schedule. Each writer in turn, when summarizing his results, has pointed out that the number of cases showing a serological relapse could probably have been materially reduced by increased dosage. All writers are agreed on the superi-

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ority of this method of treatment over the previously used arsenical and bismuth therapy but few emphasize the principal reason for this superiority, *viz.*, that penicillin effectively controls both the syphilitic infection and the intercurrent pyogenic infections, which before the days of antibiotics were the principal cause of death.

From February, 1945 to January, 1949 in the wards and out-patient department of the Hospital for Sick Children 58 infants with pre-natal syphilis have been seen; 32 were treated with penicillin alone, 9 with penicillin combined with stovarsol and 13 with stovarsol alone; 4 were moribund on admission and died before any treatment could be instituted.

The schedule for penicillin therapy has not been constant during the four years. The first few cases treated were given 12,500 units sodium penicillin intramuscularly every 3 hours for 10 days. The first infant treated in this manner suffered from what was considered to be a moderately severe Herxheimer reaction characterized by extreme listlessness, fever and toxæmia. The fourth infant was a three-pound premature who appeared to improve until the fifth day when it developed a severe hæmolytic anæmia and died within 24 hours. Death was at that time attributed to a penicillin reaction, the dosage being unusually large—33,000 units a day per lb. body weight—but in retrospect the true cause was probably Rh incompatibility. Unfortunately no blood investigation was done. Thereafter, the dosage of penicillin was built up gradually, taking 4 days to reach the maximum of 100,000 units a day and this built-up dosage with some modifications has been adhered to up to the present time.

At present only 2 days are spent in the building up and in those cases suffering from a severe intercurrent infection on admission the full dose is given at once, since the danger resulting from an uncontrolled broncho-pneumonia far outweighs that of a possible Herxheimer reaction. Two infants in 1945 were given one injection daily for 10 days of 100,000 units in oil and beeswax; 23 hours after injection the penicillin blood level in one child was > 0.05 units and in the other < 0.025 units. The clinical and serological response in both was excellent. Crystalline penicillin G. was used during 1947 and 1948 and in October, 1948 procaine penicillin was started, the schedule being 300,000 units every 48 hours. Since then all patients have been treated in the out-patient department following two days' hospitalization during which spinal fluids have been examined, bone x-rays done and small doses of crystalline penicillin given on each hospital day. This method permits treatment of patients in the doctor's office, avoids the expense to the government of 10 to 14 days' hospitalization and also liberates a valuable bed for another infant.

Since February, 1945, when penicillin therapy was commenced at the Hospital for Sick Children much larger dosage has been given than that advised even in the most recent publications.

One case received 50,000 units per lb. total dosage; 7 cases received 50,000 to 100,000 units per lb. total dosage; 19 cases received 100,000 to 200,000 units per lb. total dosage; 7 cases received over 200,000 units per lb. total dosage. The largest dose given was 550,000 units per lb.; the average 138,000 units per lb. or 300,000 units per kilo.

Lenz[2] in 1944 gave 16,000 to 19,000 units per lb. Platou[3] in 1945 gave 7,000 to 15,000, but soon raised the amount to 28,000. Ingrahan[4] in 1946 started with 11,000 increased to 74,000 but concluded that the dose should be still markedly increased. Yampolsky[5] in 1946 started with 18,000 but increased to 32,000. Platou[6] in 1947 gave 18,000 but advised increasing to 45,000 per lb. Barber[7] in 1948 gave small dosage but repeated the courses two or three times.

The necessity for the build-up dosage has been a controversial one. It has been advocated by Stokes[1] Lenz and Ingraham[2] but frowned upon by Ingraham[4] in a later publication. In this series the build-up method has been employed and up to the present time there has been no cause for regret. On the contrary, one case quoted below suggests that the initial dose of 10,000 units given once on the first day was too large and may have been responsible for one fatal outcome.

The routine for stovarsol has been ½ tablet (0.25 gm.) a day for the first week, ½ tablet b.i.d. for the second week and ½ tablet t.i.d. until the blood Wassermann has been negative for one month.

Reactions.—Temperature elevations followed the initial dose of penicillin in one-third of the cases and did not seem to be dependent on the size of the dose. A definite Herxheimer reaction occurred in one case quoted above and a

possible one occurred in 1948 which resulted fatally. This was a 5 months' old infant in good physical condition who died suddenly after an initial dose of 10,000 units. Autopsy revealed no evidence of intercurrent infection and no obvious cause of death. A fatal reaction to penicillin seemed to be the only logical explanation. Reactions to stovarsol therapy consisted in an occasional skin eruption or a mild diarrhœa. No reaction was severe enough to warrant interruption of treatment.

Results.—There were 9 deaths in the series of 58 cases, a mortality rate of 15.5%. Eliminating the 4 infants who died a few hours after admission the death rate for the treated cases was 9%. Of the 41 cases treated with penicillin alone and with the penicillin-stovarsol combination 3 died, a mortality rate of only 7%. Of the 12 cases treated with stovarsol 2 or 16.6% died. Although the series is small, a comparison of these two mortality rates is very significant. Of the 9 fatal cases 7 died of broncho-pneumonia, 1 of hæmolytic anæmia (quoted above) and one as the result of a possible Herxheimer reaction.

Broncho-pneumonia occurred as a complication in 5 penicillin cases but only 1 died. This infant in spite of its pneumonia was given the built-up dosage and died on the 4th hospital day. I have no doubt that this death would have been prevented by giving full doses of the drug on the first day. After this experience the build-up routine was never employed when there was a complicating pyogenic infection. Broncho-pneumonia occurred as a complication in 2 stovarsol-treated cases and both died. These figures provide a further demonstration of the superiority of penicillin over arsenical therapy.

Serological response. — Of the 38 infants treated with penicillin, or the penicillin-stovarsol combination, who survived, all except 4 became serologically negative in a period varying from 6 weeks to 11 months following the completion of treatment. The average time of appearance of the negative Wassermann was 5 months. One case, that of a hydrocephalic with positive spinal fluid findings, had a serological relapse after becoming negative. This child was given a two months' course of arsenic and bismuth and the blood Wassermann returned to negative. Four infants treated in the last three months of 1948 have shown a satisfactory serological response, one from 1,360 Kahn units to 40 in 4 months, one from 320 to 40 in 3 months, one from 80 to 40 in 2 months and one from 250 to negative in 8 weeks. All surviving stovarsol-treated cases became negative in an average of 3½ months without any instance of serological reversal. The small number of cases (12) does not permit a fair comparison with the penicillin group.

Clinical response.—Signs of the disease disappeared with equal rapidity with both forms of treatment, the eruption in 7 to 8 days, rhinitis in 2 to 4 weeks and osteochondritis in 3 to 5 months. In only the cerebrospinal cases, which constituted 25% of the group, did penicillin appear to be more effective than stovarsol. Two cases of syphilitic hydrocephalus seen in 1945 were given both intramuscular and intrathecal penicillin with complete clinical and serological cures in both, although one (quoted above) suffered a temporary serological relapse. Since 1945 the dose of penicillin has been doubled in every case showing positive spinal fluid findings and this has obviated the necessity for the use of the drug intrathecally and avoided any danger attendant upon this route of administration.

The increased permeability of the blood-spinal fluid barrier in infants as shown by Katz[8] emphasizes the importance of early recognition of cerebrospinal infection.

Treatment of the older child.—Effective treatment of the child over one year of age has always been a problem. Two or three years of unremitting treatment with arsenic and heavy metal resulted in cures in only 35 to 40%. Many Wassermann-fast cases were encountered and serological relapses were common. It was hoped that the use of penicillin would offer greater hope of serological cure.

In the last three years 28 older children have been so treated: 3 were given a total dosage of 1 to 2 million units; 1 was given a total dosage of 4 million units; 24 were given a total dosage of 5 to 10 million units.

Thirteen children returned to isolated rural districts following treatment and all efforts to obtain information as to their condition have failed. It has been possible to observe the progress in 15; 8 have been followed for periods over 1 year; 5 for 6 months to 1 year and 3 for less than 6 months; 11 showed a declining Kahn titre; 9 to the level of 4 units; 5 to the

level of 20 to 40 units; 1 was unchanged and only 1 became negative. This was a child of only 18 months and the serological reversal was not unexpected. It is an accepted axiom that the younger the child the more striking is the response to treatment. The average age of 7 children receiving 10 million units was 10 years. In 1 there was no reduction in the Kahn titre 10 months after treatment; in 3 there was a reduction to 4 units and in 3 to 40 units. It was noted that a greater length of time was required for any notable reduction of reagins than was the case with infants under 1 year.

Several children, after observation for 9 to 12 months, were started on arsenic-bismuth routine with a further reduction in the Kahn titre. The impression formed as a result of observation of this group was that penicillin treatment in massive doses in the older child, followed by arsenic and heavy metal therapy probably shortens the total period of treatment required to effect a satisfactory serological result.

The clinical response was very similar to that formerly obtained with arsenical treatment. Clutton's show very slow improvement; deafness is not appreciably affected; in cerebrospinal syphilis the activity of the disease, as evidenced by the cell-count and total protein, is arrested more rapidly than with arsenical therapy; the results in interstitial keratitis are uncertain. The first three children with this manifestation given 10 million units showed a rapid improvement. A fourth child admitted with hydroarthrosis of one knee-joint and no eye involvement developed, during his course of penicillin, fluid in the other knee-joint. This was not unexpected, since the condition is nearly always bilateral, but two weeks after completion of treatment he developed bilateral interstitial keratitis. I have the records of one other similar instance reported by a general practitioner and Yampolsky[5] reports an identical occurrence in his series. A possible explanation is that they are examples of a delayed Herxheimer reaction. The statement of Stokes[1] that the results of penicillin treatment of interstitial keratitis are equivocal but at times dramatic coincides with the impression formed in the author's series.

In conclusion one can predicate that penicillin therapy of the early stage of pre-natal syphilis is superior to any other form of treatment. Further experiments with dosage schedules and drug combinations are necessary before an authoritative statement can be made concerning the treatment of the older children.

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A METHOD OF TREATMENT OF URETHRAL STRICTURES

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URETHRAL stricture has been with us since time immemorial and the treatment of this condition is still one of the most vexing problems in urology. Since the advent of the sulfa drugs and the newer antibiotics such as penicillin and streptomycin the incidence of this condition has decreased tremendously. However, in any large general hospital there are still many patients attending the clinics with strictures dating back anywhere from five to thirty years.

These patients constitute a great problem in therapy, mainly due to the fact that they will not attend clinic regularly and it is virtually impossible during their infrequent visits to maintain their strictures at an adequate calibre. A certain number will not return for periods up to one or two years and here at the Montreal General we receive from 15 to 20 admissions per year to our urology service with filiform strictures and varying degrees of urinary retention. It is in this hospitalized group that we have our greatest opportunity to obtain maximum or at least reasonable dilatation and the hope of maintaining a more adequate calibre following discharge. However, even with maximum dilatation it is amazing how rapidly the lumen of the stricture closes down again. Even a week's interval between dilatation and return to clinic will often