

78 per cent passed urine within the next few days. The pre-operative difficulty in urination might have been due to reflex spasms owing to the pain, the relief of which made it possible to regain control of bladder as in other cases. Twenty-two per cent of the total cases had definite involvement of the urethra by the malignancy, and in a few cases even catheterization was not possible and suprapubic cystostomy had to be done.

Difficulty in regaining control of bladder is generally mentioned as one of the complications in cordotomies, this being especially so in bilateral sections done at one stage operation and, therefore, it is often advised to do bilateral section in two stages at an interval of two to three weeks. All our unilateral sections regained control of bladder within 24 hours and most of the bilateral sections were done in one stage and they regained bladder control within three weeks, the longest being in 17 days. Fifty-three per cent of them passed urine within three days, 40 per cent within 10 days and only 7 per cent within 10 to 17 days. All these patients were encouraged in early mobilization allowing them to walk about, and all nursing methods were tried regularly and patiently every time before they were catheterized. Seitz-baths were also given at least twice a day to help regaining bladder control. If frequent catheterizations were needed tidal drainage was instituted and every third day nursing methods were tried again before re-institution of the tidal.

The level of analgesia depends on the depth of section. The more anterior the section the higher is the analgesic level that is obtained. Usually the level of the umbilicus is aimed at. The outlook and mental condition change dramatically with the relief of pain. Along with this the general condition of the patient also improves. Even though the life expectancy is short in these advanced carcinoma cases, to make it possible to have at least this last part of their life without the continuous agonizing pain, justifies every procedure. In the follow-up studies made for these patients it was found that the survival period was from 1 month to 1½ years. This simple procedure of spinothalamic tractotomy, which was done even in most cachectic patients with 3.5 gm. hæmoglobin, without practically any mortality, is to be considered in any condition of intractable pain and especially in carcinoma of pelvis.

#### Summary

Anatomical and physiological aspects of somatic and visceral pain of pelvis are discussed. A study was made of 57 cases of carcinoma of the pelvis who had spinothalamic tractotomy for intractable pain. Even though most of them had one stage bilateral spinothalamic tractotomy, bladder control was re-established within three weeks. Pre-operative urinary difficulty was also relieved if there was no direct involvement of

the urinary passage. The importance of spinothalamic tractotomy for the relief of progressively increasing agonizing and continuous pain is emphasized.

#### REFERENCES

- FOERSTER, O., and GAGEL, *Zeitschr. ges. Neurol. u. Psychiat.*, **136**, 335. O. (1931).  
 SPILLER, W. G. (1905) .. *Univ. Penn. Med. Bull.*, July and August.

#### BIBLIOGRAPHY

- BEST, C. H., and TAYLOR, *The Physiological Basis of Medical Practice*. Williams and Wilkins Co., Baltimore. N. B. (1945).  
 FRAZIER, C. H. (1920) .. *Arch. Neurol. and Psychiat.*, **4**, 137.  
 KAHN, E. A., and PEET, *J. Neurosurg.*, **5**, 276. M. M. (1948).  
 LEWIS, T. (1938) .. *Brit. Med. Jour.*, **i**, 321.  
 MORLEY, J. (1937) .. *Ibid.*, **ii**, 1270.  
 SPILLER, W. G., and J. *Amer. Med. Assoc.*, **58**, 1489. MARTIN, E. (1912).  
 WALKER, A. E. (1940) .. *Arch. Neurol. and Psychiat.*, **43**, 284.  
 WILSON, R. B., and J. *Amer. Med. Assoc.*, **134**, 857. MUSSEY, R. D. (1947).  
 WRIGHT, S. (1940) .. *Applied Physiology*. Oxford University Press, London.

### A PRELIMINARY REPORT ON THE TREATMENT OF LATHYRISM WITH PARENTERAL METHIONINE

By M. N. RUDRA

*Professor of Medical Chemistry*

L. M. CHOWDHURY

*Junior Research Fellow, Bihar Board of Medical Research, Department of Medical Chemistry*

and

S. P. SINHA

*Professor of Medicine, Darbhanga Medical College, Laheriasarai, Bihar*

THAT lathyrism can be caused by a diet exclusively or mostly of *Lathyrus sativus* is now generally admitted. Details are still obscure although various theories have been advanced from time to time. The senior author has been investigating the biochemistry of lathyrism for some time. His attention was attracted by a paper of Bodian and Mellors (1947) on the biochemistry of neurone regeneration. These authors found a decrease in creatine phosphate in the regenerating neurones. From this, the idea occurred to the senior author that the degeneration of the motor neurones in lathyrism may be due to a deficiency of creatine in the motor neurones. One of the contributory causes of creatine deficiency may be methionine deficiency or a disturbance in the transmethylation process. An analysis of different food grains showed that, although the richest in

protein content (29 per cent), the lathyrus peas were the poorest in methionine content (Rudra and Chowdhury, 1950). He (M. N. R.), therefore, suggested to his Research Fellow (L. M. C.) to try the effect of parenteral administration of methionine in lathyrism.

Accordingly, the latter treated five lathyrism cases with methionine (i.v.) in the Darbhanga Medical College Hospital ward of one of us (S. P. S.). This preliminary report is being published as it is thought noteworthy that in two out of the five lathyrism cases treated with methionine the Babinski's sign was totally abolished and one of the improved patients regained 75 per cent normal gait.

#### Case 1

K. L., male, 20 years, student. Onset in October 1947, with difficulty in walking. Later the great toes used to get hurt during walking. First came under observation on 24th October, 1948, with the following signs: cranial nerves, sensation, co-ordination normal; crossing of legs during walking; KJ ++; AC ++; plantar ++; spasticity of lower limbs and abductor spasm +; cremasteric, abdominal and visceral reflexes normal; Kahn negative. Diet history, *L. sativus* 14 oz., rice 10 oz., vegetables 8 oz., milk, meat or eggs practically none.

He was treated with prostigmin, vitamin B complex and other drugs without any effect. He was admitted into the medical ward of the Darbhanga Medical College Hospital in October 1949 and 12 daily injections (i.v.) of concentrated liver extract (Heporal Forte of Continental Drug Company Limited, Bombay) were given without any improvement. He was given 1.2 gm. of methionine in 100 ml. (i.v.) daily from 19th October, 1949, for 4 days. The extensor plantar reflex became flexor on 20th October, 1949. At the end of the course there was great symptomatic improvement and the patient regained 75 per cent normal gait.

#### Case 2

P., male, 10 years. Onset in September 1949. Admitted into the Darbhanga Medical College Hospital on 17th October, 1949, with these signs: cranial nerves, sensation, co-ordination normal; scissors gait; KJ ++; AJ ++; AC ++; plantar ++; spasticity of lower limbs and abductor spasm +; cremasteric, abdominal and visceral reflexes normal; Kahn negative. Diet history, *L. sativus* 14 oz., rice 8 oz., vegetables 1 oz., milk, meat or eggs practically none.

He was given 0.5 gm. of methionine (i.v.) on 19th October to 22nd October, 1949, and 1 gm. from 28th October to 31st October, 1949. As the methionine stock was exhausted the treatment was interrupted. Physical signs remained unchanged but the patient improved in health and gait.

#### Case 3

R. C. M., male, 35 years, agricultural labourer. Onset during the rainy season of 1948, sudden; and confined to bed for 6 months. Admitted into the hospital on 3rd January, 1950, with the following signs: cranial nerves, sensation, co-ordination normal; walks with the help of two crutches; scissors gait; anæmia +; KJ ++; AJ ++; AC ++; plantar ++; spasticity of lower limbs and abductor spasm +; cremasteric, abdominal and visceral reflexes normal; Kahn negative. Diet history, *L. sativus* 10 oz., rice 16 oz., vegetables 4 oz., milk, meat or eggs practically none.

Given 1 gm. methionine (i.v.) on 1st and 2nd February, 1950. The treatment stopped for want of methionine but renewed on 21st, 22nd and 23rd February, 1950, when a fresh supply was available. No improvement in physical signs but the patient felt greatly improved and walking became easier.

#### Case 4

S. N. J., male, 40 years, agricultural labourer. Onset during the rainy season of 1947. Admitted into the hospital on 12th April, 1950, with these signs: cranial nerves, sensation and co-ordination normal; walks with the help of two crutches; scissors gait; KJ ++; AJ ++; AC ++; plantar ++; cremasteric, abdominal and visceral reflexes normal; Kahn negative. Diet history, *L. sativus* 10 oz., rice 16 oz., vegetables occasionally, milk, meat or eggs none.

He was given 1 gm. methionine (i.v.) from 16th April to 20th April, 1950, and 2 gm. (i.v.) from 22nd April to 28th April, 1950, followed by 6 daily injections of liver extract (Heporal Forte). At the end of the course the patient felt greatly improved and the Babinski's sign was abolished.

#### Case 5

S. T., male, 30 years, agricultural labourer. Onset during the rainy season of 1947. Admitted into the hospital on 12th April, 1950, with the following signs: cranial nerves, sensation, co-ordination normal; scissors gait; KJ ++; AJ ++; AC ++; plantar ++; cremasteric, abdominal and visceral reflexes normal; Kahn negative. Diet history, *L. sativus* 12 oz., rice 18 oz., vegetables occasionally, milk, meat or eggs none.

He was given 1 gm. methionine (i.v.) from 24th April to 27th April, 1950, and 2 gm. from 28th April to 1st May, 1950. There was symptomatic improvement but none in physical signs.

The authors are grateful to Professor R. A. Paterns, F.R.S., and Dr. C. R. Harington, F.R.S., for a generous gift of methionine from which part of the parenteral methionine used above was prepared.

One of us (L. M. C.) is indebted to the Bihar Board of Medical Research for a Junior Fellowship which enabled him to take part in the investigation.

## REFERENCES

- BODIAN, D., and MELLORS, J. *Biol. Chem.*, **167**, 655. R. C. (1947).  
 RUDRA, M. N., and CHOWDHURY, L. M. *Nature*, **166**, 568. (1950).

## CEPHARANTHINE IN EXPERIMENTAL TUBERCULOSIS

By M. SIRSI  
and  
N. N. DE

(Pharmacology Laboratories, Indian Institute of Science, Bangalore 3)

BECAUSE of its importance, pulmonary tuberculosis was among the first of the bacterial diseases to attract attention from the standpoint of chemotherapy. Unfortunately, though remarkable accomplishments have been achieved in the general field of infectious diseases, chemotherapy of tuberculosis has not had the same degree of success. The need for a specific anti-tubercular drug is as great as ever.

As a result of extensive experimental investigations and intensive research programme, it has been possible to synthesize various compounds having tuberculostatic properties (Rist *et al.*, 1940; Lehmann, 1946; Domagk, 1950) and to detect the presence of anti-tubercular activity in a variety of compounds of both synthetic and natural origin (Rake, 1949; Steenkens and Wolinsky, 1950; Editorial, 1950, 1951).

Great interest is now being evinced in the active principles of plant origin possessing anti-tubercular properties. Ayurvedic literature mentions quite a number of plants and plant products as being useful in tuberculosis (Kirtikar and Basu, 1933). Such plant products are being prescribed in the clinical treatment of tuberculosis but no experimental or clinical research has been undertaken to evaluate the usefulness of the drugs and to direct the treatment in a rational way.

A survey of some of the indigenous drugs and plant extracts for their ability to suppress and control the disease in experimental animals is being conducted in our laboratory. During the course of our investigation we were very much interested in the claims put forward by Hasegawa (1949) for cepharanthine, an alkaloid extracted from *Stephania cepharantha*. Hasegawa mentions that cepharanthine has healing effects both in tuberculosis of guinea-pigs and man.

Cepharanthine ( $C_{37}H_{53}O_6N_2$ ) is the biscochlorin type of alkaloid found in the roots of

*Stephania cepharantha* and in the stems of *Stephania sasakii*, both members of Menispermaceae family. The alkaloid is a yellow light powder with a melting point of 103°C. The drug has been used extensively in Japan during the war years and has been claimed to be therapeutically successful in tuberculosis. The alkaloid has also been used prophylactically in factories and schools in Japan.

The following detailed study was undertaken to evaluate the anti-tubercular property of cepharanthine. We present in this paper the *in vitro* and *in vivo* activity of cepharanthine, on a locally isolated virulent strain of *Myc. tuberculosis*, together with a comparison of its activity with para-amino-salicylic acid, a well-known tuberculostatic compound.

### I. Materials and methods

*Growth inhibitory effect in vitro.*—The *in vitro* activity of the compounds was tested against *Myc. tuberculosis* strain D13 in a modified Proskauer and Beck medium.

Strain D13 was isolated from the sputum of a case of pulmonary tuberculosis using the trisodium-phosphate technique (Sirsi, 1951). Patrick's medium (Gradwohl, 1948) has been found in our study to be a highly satisfactory medium for the primary isolation of tubercle bacilli.

The secondary sub-cultures required for the inocula were grown in the following glycerol asparagine medium:

Asparagine	..	5.0 gm.
KH <sub>2</sub> PO <sub>4</sub>	..	5.0 gm.
K <sub>2</sub> SO <sub>4</sub>	..	0.5 gm.
Glycerol	..	20 cc.
Distilled water	..	1,000 cc.

pH adjusted to 7.2 with 40 per cent NaOH and then mag. citrate 1.5 gm. added. Autoclaved at 15 lb. for 20 minutes.

A three weeks' growth was collected, weighed and emulsified using the same medium as diluent. A suspension was prepared so as to contain 1.0 mg. (wet weight) of bacilli per cc. and the inocula consisted of 0.1 cc. of the emulsion to each tube.

Concentrated solutions of the test compounds were first prepared and then so diluted that 0.5 cc. of the solution when added to 4.5 cc. of the Proskauer and Beck media gave the final required concentration.

The paraffin-sealed inoculated tubes were incubated at 37°C. and were examined on 14th, 21st and 28th day. Table I gives the results observed.

It will be noticed that at the end of 14 days complete inhibition of growth is maintained by cepharanthine at 5 µg./cc., while P.A.S. needs only 1.0 µg./cc. Partial inhibition by cepharanthine is observed and by P.A.S. at 2 µg./cc. and 0.5 µg./cc. respectively.