massage. Métivier (1935), Duggan (1937), and Hopkins and Robyns-Jones (1937) recorded cases due to the instillation of atropine eye solutions. The last mentioned occurred with washing out the eye with 1% atropine solution after an iridectomy operation. Carter (1940) described the case of a man who swallowed 5 drachms (19.4 g.) of the liniment (equivalent to $1\frac{1}{2}$ gr. (90 mg.) of alkaloid) in mistake for a cough mixture. The onset of symptoms was delayed 10 hours, and complete recovery followed treatment by spinal drainage, morphine, and physostigmine.

Glaister comments on the variations in dosage found to cause symptoms: 2 gr. (0.13 g.) of atropine have proved fatal, while recovery has followed a dose of $5\frac{1}{2}$ gr. (0.35 g.). Although in our case the amount was ten times the pharmacopoeial dose of the liquid extract (1 min.), the dosages in previously recorded cases have generally been much higher. It appears, therefore, that symptoms of poisoning accompanied by a gross mental disturbance can result from only a moderately excessive dosage.

Summary

A case of accidental belladonna poisoning is described, presenting as an acute confusional state.

The onset of visual symptoms occurred within half an hour of taking 10 minims of the liquid extract, while the onset of general symptoms was delayed for three hours.

Recovery occurred within twelve hours without active treatment.

Subsequent testing for idiosyncrasy proved negative.

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SUPPRESSION OF SYPHILIS AND PRECOCIOUS TERTIARISM

BY

JAMES MARSHALL, M.D.

Director, Venereal Diseases Clinic, Royal Northern Hospital,
London

In cases of early syphilis treated with penicillin in standard doses (2,400,000 units or more) relapse or failure of treatment may be manifested in the following ways (Marshall, 1945): (a) Surface relapse. The relapse lesions may be "primary" or "secondary" in type and have occurred, in patients treated personally, between 59 and 200 days after treatment (average 83 days). (b) Serological relapse, which may occur with or without signs of surface relapse. (c) Sero-resistance. (d) Less common types of treatment failure include neuro-recurrence, ocular and osseous relapse, and persistence of *Treponema pallidum* in surface lesions in spite of treatment.

Precocious tertiarism has not, until now, occurred as a manifestation of relapse in any of the patients I have treated with penicillin alone. This phenomenon has usually been seen in the past in patients who had been inadequately treated for syphilis by a few injections of a trivalent arsenical unsupported by bismuth. It is presumed that the rapid destruction of the spirochaetes by arsenicals deprives the body of its one primordial and essential stimulus to fight

the infection on its own account—namely, the presence over a long period of the pathogenic agent (Stokes *et al.*, 1944).

There is good presumptive evidence that the administration of an inadequate dosage of penicillin in the following case of early syphilis has upset the normal response of the body tissues to infection with *T. pallidum*.

Case Report

A man aged 30 was first seen in June, 1947, and attended for examination because his wife had been found, at routine antenatal test, to have latent syphilis. (He had been married for one year, and, as a pre-marital serum test for syphilis is obligatory for women marrying serving American soldiers, it can be presumed that his wife was then healthy.) He had not previously shown any manifestations of any venereal disease and gave the following history.

In November, 1945, while on active service in Italy with the U.S. Army, he developed a very itchy rash on the sides of the neck, anterior borders of axillae, trunk, and genitals. The limbs, apart from the upper thighs, were unaffected. The rash did not begin on the genitals and he could not recall any genital ulceration before this time. His last exposure to infection was, he thinks, some six to nine months previously. A diagnosis of scabies was made and he was treated intensively with benzyl benzoate on several occasions over three weeks without relief. At the end of this time he was given 15 or 16 injections of penicillin over two or three days. Individual doses were of 40,000 units, presumably in aqueous solution. The effect was the disappearance of the rash and of the itching in a few days.

It was a routine procedure in his unit for all men to have a serum test for syphilis every six months. He had had tests with negative results in July, 1945 (before the rash), and again a month or two after penicillin treatment.

From November, 1945, he remained in apparently good health, without any skin lesions, until about five weeks before he first attended my clinic. He then developed a rash on his forehead. A few days afterwards a similar rash appeared on his chin, followed a little later by lesions on the penis. Two weeks after the first signs there appeared a spreading lesion of a different type on his left thigh. In the earliest days he had had a sore throat. He had had a serum test for syphilis at a U.S. Army dispensary about a week before he attended, and this was reported as positive.

On examination there were surface lesions of the face, penis, left thigh, and buccal mucosa. The facial lesions consisted of a band of dusky erythema, an inch (2.5 cm.) wide, extending all along the hair margin of the forehead, scaling at the edges and closely studded with pinhead pustules; there was a similar circular patch, one inch in diameter, on the centre of the chin. The mouth showed superficial ulceration of the mucous membrane of the left tonsil and of both commissures of the cheeks. On the shaft of the penis were numerous small purplish oval or circular papules, some eroded, of the type commonly associated with relapsing early syphilis.

On the anterior surface of the middle of the left thigh was a lesion of a different type. This was a roughly circular brown scaling patch, about two inches (5 cm.) in diameter, with a serpiginous edge. The edge showed signs of active spread and had scattered reddish-brown or bluish nodules with superficial scaling. The whole lesion was, clinically, a typical superficial nodular cutaneous gumma. There was moderate enlargement of the lymph glands of the posterior triangle of the neck, of the epitrochlear glands, and of the inguinal glands on both sides.

Dark-ground examination of serum from a penile lesion showed no *T. pallidum*, but in view of the positive serum test, confirmed locally, treatment was not delayed. It was not possible to arrange for lumbar puncture before beginning treatment.

The treatment given on the first day consisted of 0.09 g. "neohalarsine" and 0.2 g. bismuth oxychloride. Three days later the pustular lesions of the face had disappeared, leaving areas of erythema dotted with brownish pigmented spots. The penile lesions had disappeared and the lesion of the thigh was

apparently unaltered. Penicillin treatment was purposely delayed so that non-specific effects could be excluded. Ten days after beginning treatment, penicillin in oil-wax suspension having been superimposed on the arsenic-bismuth therapy, only scattered pigmentation remained on the face and the gummatous lesion was obviously healing rapidly.

Conclusions

It seems probable that in November, 1945, this man had secondary syphilis, possibly masked by scabies, and that the small amount of penicillin (about 600,000 units) given at that time was sufficient temporarily to suppress the disease. The relapse lesions, appearing 18 months later, were of a secundo-tertiary type.

This case suggests that penicillin in inadequate dosage over a short period can, like the arsphenamines, produce the phenomenon of precocious tertiarism. It illustrates the importance of making an accurate diagnosis in any dermatological condition before using penicillin by injection.

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NICOTINAMIDE AND BLOOD SUGAR

BY

J. N. CUMINGS, M.D.

Clinical Pathologist, National Hospital, Queen Square, London

The effect of nicotinamide (N.A.A.) on blood-sugar levels in normal controls and in diabetic patients has been discussed by Neuwahl (1943), Gordon (1946), and Wade (1947). In view of the different results obtained it would appear worth while to record the following observations, which were made at a time when investigations regarding co-enzyme were taking place.

Three fasting normal subjects were given 0.5 g. of N.A.A. by mouth, and all experienced slight effects such as flushing of the face. Blood-sugar estimations were made by Folin and Wu's method, and co-enzyme was estimated by that of Hoagland *et al.* (1942). The results obtained were all identical in type, and the following table shows one curve that was obtained.

Time		Blood Sugar	Blood Co-enzyme
		0.105 g. %	4.3 mg./100 ml.
Fasting		0.093	4.0
1 hr. after 0.5 g. N.A.A.		0.098	4.3
1 1/2 hrs. "		0.103	4.0
2 " "		0.089	4.4

Two other normal subjects were each given 0.5 g. of nicotinamide and nicotinic acid, and neither showed any variations in blood co-enzyme up to six hours. Another normal subject showed no variation in blood co-enzyme content during the two hours of a blood-sugar curve following 50 g. of glucose by mouth. The blood sugar ranged from a fasting level of 0.099 g. % to a maximum height of 0.186 g. %.

Neuwahl showed two types of response to nicotinamide in normal subjects. One figure demonstrated a marked fall in blood sugar after 0.4 g. N.A.A. intramuscularly and also after 0.25 g. intravenously, whereas in another figure there was a considerable rise in blood sugar after 0.45 g. intravenously. He also showed that 0.06 g. N.A.A. and 2 units of insulin produced a greater fall in blood sugar than did 2 units of insulin alone. Burke and McIntyre (1939), however, had demonstrated earlier that the effect of insulin given to rabbits is not so great—i.e., the blood

sugar is depressed less—in those receiving nicotinamide acid.

Wade has recently shown that nicotinamide produced no alteration in the blood-sugar curves of diabetics following 50 g. glucose, even though his patients had received 1.8 g. of nicotinamide daily for 14 days prior to the second blood-sugar curve.

From these results it would appear that, in general, nicotinamide is without effect on the blood-sugar levels in normal subjects or in diabetic patients. The absence of any effect on the blood co-enzyme content is possibly a further proof of this fact.

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Medical Memoranda

Transient Hemiplegia following Injection of Sodium Morrhuate

The following case seems to be sufficiently unusual and disturbing to merit publication.

CASE REPORT

A married woman aged 32 complained of a small area of varicose vein situated between the knee and the ankle of her right leg. This was not causing any inconvenience, but the appearance was aesthetically objectionable. The injection of 0.25 ml. of sodium morrhuate 5% into the vein as initial treatment caused no general disturbance. One week later 0.75 ml. of the same solution was injected. On this occasion the patient complained of giddiness after approximately two minutes. She then fainted; but she recovered rapidly, and the incident was considered to be due to excitement common to any injection.

The following week 0.75 ml. of the solution was injected into the section of the vein which remained unsclerosed. Once more nothing occurred for two or three minutes, when the patient fainted again. On this occasion, however, she did not recover consciousness as before, but sank into a state of deep coma. This rapidly merged into a generalized tonic spasm plus slight clonus of the facial muscles. At this stage the patient was pulseless and cyanosed. The tonic spasm persisted for about five minutes and then gradually changed into a state of semicoma. Vomiting now became severe and persistent, but the pulse was more satisfactory. The more anxious moments of the incident appeared to be passing.

The state of semicoma, however, persisted, and further improvement was barely appreciable for about half an hour. At that time it was observed that a complete hemiplegia had developed, involving the right arm, the right leg, and the left side of the face. The patient was then removed to hospital, still in a state of semicoma.

Two hours later the paralysis of the arm and leg had passed off, a limited degree of paresis of the left face still remaining. The patient was able to speak, but articulation was indistinct. In a further four hours the hemiplegia had completely cleared, tendon and surface reflexes were normal, and all movements were complete. Her speech had recovered and the mental state was excellent. Twenty-four hours after admission to hospital she was discharged, recovery being complete.

COMMENT

Alarming incidents following the use of sodium morrhuate have been reported occasionally in the medical press, but it is doubtful if the dangers of unusual sensibility to this common preparation are fully appreciated. A case of transient hemiplegia following its use must be exceedingly rare. The satisfactory outcome could not have been foreseen during the severe phase of the coma, and the clinical findings at that stage suggest that recovery was fortunate rather than inevitable. It would appear that the pharmacognosics of sodium morrhuate should be reassessed before its continued use as a sclerosing agent in the treatment of varicose veins be recommended.

W. S. GARDNER, M.B., Ch.B., F.R.F.P.S.