

kinking and from being crushed by the bed cage. The large-celled ripple mattress does seem to be a real advance over other methods used in the prevention and treatment of bedsore.

## Jarisch–Herxheimer Reaction

The Jarisch–Herxheimer reaction occurs in over half the patients with early syphilis within a few hours of starting treatment with penicillin. It usually takes the form of fever, malaise, sweating, and headache, and it is often associated with an exacerbation of the symptoms and signs of the disease. The patient frequently describes the reaction as being similar to an attack of influenza. The reaction is harmless in primary and secondary syphilis, but the patient should be warned of its possibility before treatment is started, as it may be frightening and result in failure to continue with the treatment. In some patients with unrecognized early syphilis a Herxheimer reaction may follow penicillin administered for another reason, and may lead to the diagnosis of syphilis.

In a recent investigation of 251 untreated patients (109 with primary and 142 with secondary syphilis) T. Putkonen and his colleagues<sup>1</sup> in Helsinki in Finland found that a rise in axillary temperature to 37.6° C. or higher occurred in 95% of patients with seropositive primary syphilis but in only 55% of those with seronegative primary syphilis. Herxheimer reactions occurred as frequently in patients with early secondary syphilis as in those with seropositive primary syphilis, but their incidence decreased with increasing duration of the disease and only 32% of the patients with late secondary syphilis (all of whom had condylomata lata) developed fever.

Histological studies of biopsy specimens of skin lesions from patients with various stages of syphilis were carried out by W. H. Sheldon and A. Heyman.<sup>2</sup> Following treatment the capillaries and small blood vessels became congested and the vessel walls and surrounding connective tissue became oedematous and infiltrated with neutrophil polymorphonuclear leucocytes. As the reaction subsided large mononuclear cells appeared. These transitory acute inflammatory reactions were limited to the syphilitic lesions and appeared about four hours after treatment and disappeared within 18 to 24 hours. Similar changes were found in two patients with tertiary syphilis who had late nodular cutaneous syphilides.

The incidence of Herxheimer reactions in tertiary syphilis is difficult to estimate. Few individual doctors treat enough patients with this form of the disease to be able accurately to assess the frequency of the reaction. Reactions are certainly less common and frequently less severe than in early infectious syphilis. Nevertheless, M. J. Hoekenga and T. W. Farmer<sup>3</sup> observed febrile Herxheimer reactions in 34% of 349 patients with various types of neurosyphilis—in 74% of patients with general paralysis, 23% with tabes, 17–36% with other types of neurosyphilis. There was a close relationship between activity in the cerebrospinal fluid and febrile reactions, since the latter were found to occur in 93% of patients who had a raised cell count and concentration of protein and a strongly positive Wassermann reaction. Studying 229 patients with neurosyphilis, Putkonen and K. Rehtijärvi<sup>4</sup> came to similar conclusions, though they found a lower incidence of reactions.

The classical explanation of the Herxheimer reaction is that treatment results in the sudden death and destruction of large numbers of treponemes, with the liberation of protein products and toxins. Putkonen and his colleagues have shown that in the early stages of the disease the number of treponemes in the patients' tissues increases until it is sufficiently high for a reaction to treatment to be possible. The largest number of treponemes probably occurs during the seropositive primary and early secondary stages, and the Finnish workers found that febrile Herxheimer reactions were most frequent and most severe at these stages. Hence probably a minimal number of treponemes must be present in the patients' tissues for a reaction to occur. It is also known that a minimal amount of antitreponemal substance is required. The reaction is of the "all or none" type, and occurs with full force once an adequate amount of penicillin has been given. It cannot be prevented by giving small doses of penicillin at the start of treatment. Little or nothing is known about the sensitivity and reactivity of the patients' tissues in this phenomenon, but possibly these factors have an important role in determining which patients develop reactions to treatment.

In the past it has been traditional—especially in Europe—to try to prevent Herxheimer reactions in patients with tertiary syphilis by the use of preliminary intramuscular injections of bismuth. The efficacy of this measure has been disputed by some observers, and most workers agree that it will not suppress the reaction in cases of general paralysis. More recently the effects of corticosteroid drugs in attenuating and suppressing reactions at all stages of the disease have been studied, principally in France. Thus P. de Graciansky and C. Grupper<sup>5</sup> found that corticosteroids reduced the frequency and severity of reactions in early infectious syphilis and also in late syphilis, though they were not abolished altogether.

Recently the existence of the Herxheimer reaction has been questioned by some doctors. Discussion has been centred on whether dangerous or fatal reactions ever occur in patients with tertiary syphilis. Though there are reports of deaths attributed to Herxheimer reactions, reliable information on this point is not easily available. There is no universal agreement as to whether measures should be taken to try to prevent the reaction. Many argue that it is reasonable to take a calculated risk, which they feel is small or even negligible, and begin treatment with penicillin immediately the diagnosis is made. A minority of physicians believe that, though the risk is small, nothing is to be gained by speed of treatment in late syphilis and that reasonable precautions should be taken to prevent a possible reaction. Preliminary injections of bismuth at weekly intervals are advocated, especially in patients with cardiovascular syphilis when there is evidence of aortitis or cardiac failure. The position of corticosteroids in preventing Herxheimer reactions is still undetermined, and experience in their use is very limited. Further work on the nature of the Herxheimer reaction and methods of preventing its occurrence is needed, and the recent increase in the incidence of syphilis may perhaps provide opportunities for investigating this problem.

<sup>1</sup> Putkonen, T., Salo, O. P., and Mustakallio, K. K., *Brit. J. vener. Dis.*, 1966, 42, 181.

<sup>2</sup> Sheldon, W. H., and Heyman, A., *Amer. J. Syph.*, 1949, 33, 213.

<sup>3</sup> Hoekenga, M. T., and Farmer, T. W., *Arch. intern. Med.*, 1948, 82, 611.

<sup>4</sup> Putkonen, T., and Rehtijärvi, K., *Acta derm.-venereol. (Stockh.)*, 1951, 31, Suppl. 24, p. 120.

<sup>5</sup> Graciansky, P. de, and Grupper, C., *Brit. J. vener. Dis.*, 1961, 37, 247.