

PENICILLIN TREATMENT OF ERYTHEMA CHRONICUM
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In 1946 the first attempts were made to treat erythema chronicum migrans (E.M.) with spirocheticides (Hollström, E., *Acta Derm.-Ven.*, 1951, 31, page 235). The impetus to this therapeutic trial had been given by Lennhoff's findings of spirochetes or spirochetoid organisms in skin presenting E.M. changes. As was found, rapid cure could be achieved with arsphenamine, bismuth, and penicillin. The erythema disappeared, but it recurred if the dosage had been insufficient. Of the drugs given penicillin was found to be the most effective and, the experience having meanwhile accrued, was later used throughout. Penicillin proved particularly beneficial in cases with supervenient — serous or purulent — meningitis.

The Material

From 1948 onwards to and including 1957, at the Department of Dermatology of Karolinska Sjukhuset 77 patients with E.M., 15 men (19.5 %) and 62 women (80.5 %), had been treated with penicillin. The age of the patients ranged from 2 to 70, and the distribution among the different age groups is given in fig. 1. In 27.3 % of the cases there was a history of tick bite and in 11.7 % of bites of insects of unknown species. In those instances where information as to the incubation period, i. e. the time between insect bite and appearance of the erythema, was available, this had varied between a fortnight and 4 months.

As will be seen from fig. 2, the incidence rates of E.M. during the years, 1948—1957, show a very considerable variation. The low rates in 1948—1951 would partly seem to be due to the fact that the skin clinic of Karolinska Sjukhuset was opened in 1948, and that during the first few years the number of patients treated in the outpatient service was much lower than later on. Particularly surprising, however, is the bottom rate in 1955, when no definitely established case of E.M. was recorded. A possible explanation is, that the summer of this year was exceptionally dry, to the great detriment of plants and insect. In the next year, on the other hand, there was a strikingly high culmination.

The Treatment

The penicillin dosage varied between minimum 300,000 units and maximum 7,300,000 units. Generally the dosage was between 600,000 and 2,400,000 units;

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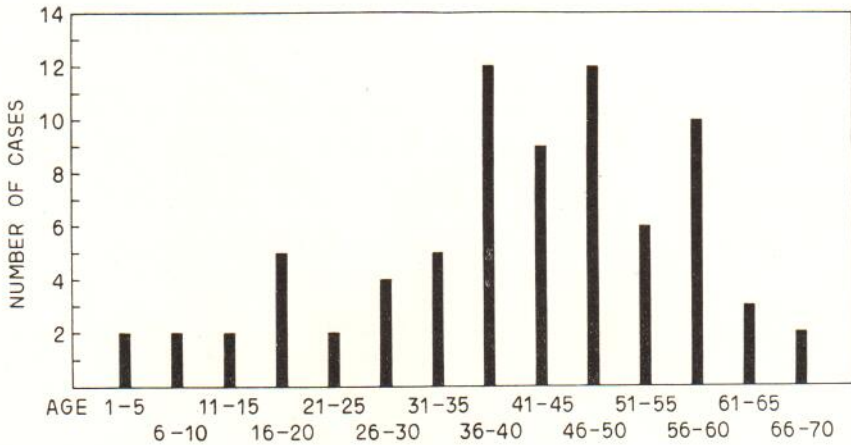


Fig. 1.

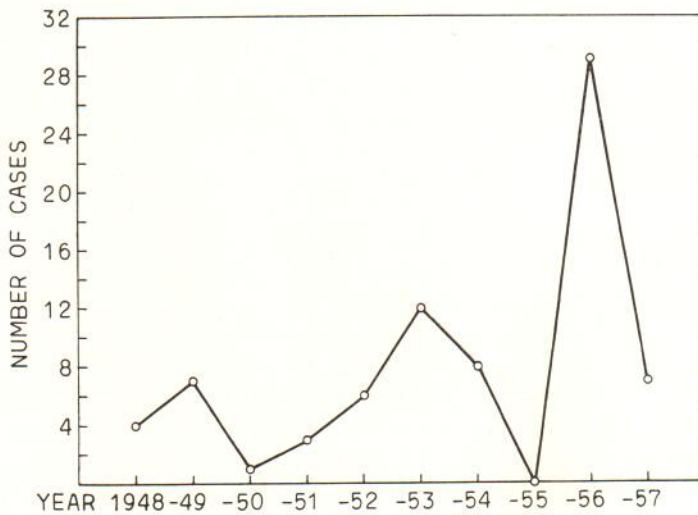


Fig. 2.

thus 18 patients were given 600,000 units, 14 patients 1,200,000 units, 8 patients 1,800,000 units, and another 8 patients 2,400,000 units, that is to say, 48 out of 65 (see below) were treated with one of the penicillin amounts stated. 600,000 units was administered as a single dose, whereas larger amounts were divided into injections given daily or every other day. In a few instances penicillin was given by injection as well as orally. Here, however, the totals are stated irrespective of the mode of administration.

Results and Discussion

It was possible to follow up 65 cases of E.M., viz. either by means of the notes entered in the records or of supplementary information. In 12 instances the data

were insufficient and no contact could be established with the patients, or these were unable to recall the course of illness.

In the assessment of the results the time required for cure was stated in weeks after termination of treatment, if daily examination of the patients was not feasible. In a proportion of the cases the erythema disappeared before the treatment was completed; none the less these instances were referred to the group, Cure within 1 week, after termination of treatment. Sometimes a weak brownish pigmentation remained when the erythema had subsided, but this was not included in the time required for cure.

Cure within 1 week	after treatment:	34 = 52.3 %	}	= 89.2 %
" "	2 weeks "	24 = 36.9 %		
" "	3 " "	5 = 7.7 %		
Recurrence		2 = 3.1 %		

Hence, in more than one-half of the series the erythema disappeared within 1 week and in 89.2 % within a fortnight. The two recurrences were observed in children. One of them, aged 5, was given 300,000 units penicillin, whereupon the erythema disappeared within 1 week. After 4 weeks the patient was still free of symptoms, but after another 2 weeks the erythema returned. 300,000 units penicillin was then administered once more and produced cure without further recurrence. The other child, aged 9, did not present any signs of E.M. 1 week after treatment with 600,000 units penicillin. Three weeks later there was a recurrence, which was treated with 1,200,000 units penicillin, definite freedom of symptoms resulting within 1 week. Since, accordingly, recurrences may occur after 600,000 units, totals larger than this dose are recommended, say 1,200,000 units or possibly even more, the latter, naturally, in cases with complications such as meningitis etc. (see the preceding paper).

Prior to the therapeutic trial with spirocheticides including penicillin there was no efficient treatment: the erythema spread over the entire body surface with central clearing. The whole integument having been affected, immunity was generally thought to exist. As E.M. is rapidly cured by penicillin, the formation of antibodies will probably be interrupted, analogously to what is the case in penicillin treatment of scarlet fever. It is thus to be expected that a patient suffering from E.M. and having been treated with penicillin may develop the disease afresh. Such a case is actually included in my material. The patient was a woman who in 1952 presented typical E.M. following insect bite. She was cured after treatment with 600,000 units penicillin. In 1957 she had the same disease again, although without a history of insect bite. Also at that time 600,000 units penicillin produced cure within 1 week.

Judging by the favourable results of penicillin treatment an infectious aetiology of E.M. would seem to be highly probable. In order to secure evidence in this respect I have tried to transfer the disease to healthy subjects, viz. by injecting minced tissue from three patients with E.M. into ten volunteers, but without positive result. In addition experiments were carried out in which blood of E.M. patients was injected, also these without result. Similar experiments have even been performed by other workers without success. Possibly a special disposition towards the disease is a necessary condition for its development.

The present study shows that (i) penicillin has proved an excellent remedy for

erythema chronicum migrans, but that (ii) with insufficient dosage (in these instances 600,000 units or less) recurrence may occur, that (iii) an infectious aetiology is likely but that transfer experiments were unsuccessful, and that (iv) definite or permanent immunity does not always exist after penicillin treatment, but that the patients may develop the disease afresh.

SUMMARY

A ten-year material of erythema chronicum migrans was studied, which during the period, 1948—1957, had been treated with penicillin in the outpatient service of the Department of Dermatology of Karolinska Sjukhuset. In 89 % of 65 cases the erythema disappeared within a fortnight. A recurrence was noted in only 2 cases, i. e. 3 %, after penicillin doses of 600,000 and 300,000 units respectively. Penicillin has thus proved an admirable therapeutic agent, and 1,200,000 units or possibly a somewhat higher dosage is advised for even uncomplicated cases. One patient had the disease twice at an interval of five years, which is supposed to be due to the fact that penicillin treatment interrupts the immunisation. An infectious aetiology is considered likely, but all transfer experiments were unsuccessful.

RÉSUMÉ

L'auteur a étudié les dossiers des malades traités à la policlinique dermatologique du Karolinska Sjukhuset pour erythema chronicum migrans au cours des années 1948 à 1957 (traitement pénicillinique). Dans 89 % des 65 cas, l'érythème disparut en déans les 2 semaines. Une récédive se produisit chez 2 malades, c-à-d. dans 3 % des cas. Les doses utilisées chez ces deux malades avaient été de 600.000 et 300.000 unités. La pénicilline s'est donc révélée être la médication idéale et l'auteur recommande la dose de 1.200.000 u. ou même un peu plus pour les cas non compliqués. Dans un cas, l'affection se manifesta deux fois avec un intervalle de 5 ans ce qui peut être expliqué par le fait que le traitement pénicillinique interrompt le processus d'immunisation. Une origine infectieuse est très vraisemblable, mais toutes les tentatives d'inoculation ont échoué.

ZUSAMMENFASSUNG

Verf. hat ein 10-Jahrsmaterial von Erythema chronicum migrans untersucht, welches in den Jahren 1948—1957 in der Hautpoliklinik des Karolinska Sjukhuset mit Penicillin behandelt worden war. In 89 % von 65 Fällen verschwand das Exanthem binnen 2 Wochen. Ein Rezidiv trat bei 2 Kranken auf, d.s. in 3 %, und zwar nach Penicillindosen von 600 000 bzw. 300 000 Einh. Penicillin erwies sich somit als ein ausgezeichnetes Mittel, und Verf. empfiehlt 1 200 000 Einh. oder evtl. eine etwas höhere Dosis sogar bei unkomplizierten Fällen. In einem Fall trat die Krankheit zweimal im Abstand von 5 Jahren auf, was darauf zurückgeführt wird, dass die Penicillinbehandlung den Immunisierungsprozess unterbricht. Eine infektiöse Genese wird für wahrscheinlich gehalten, aber alle Übertragungsversuche waren erfolglos.

RESUMEN

Se estudió el material de diez años de eritema crónico "migrans", que durante el período de 1948—1957 había sido tratado con penicilina en el servicio ambulatorio del Departamento de Dermatología del Karolinska Sjukhuset. En 89 % de 65 casos el eritema desapareció en dos semanas. Recidiva sólo se observó en 2 casos, es decir 3 %, después de dosis de penicilina de 600.000 y 300.000 unidades respectivamente. Por tanto, la penicilina ha demostrado ser un admirable agente terapéutico, y posiblemente como dosificación un poco mayor es aconsejable la de 1.200.000 unidades incluso para los casos no complicados. Un enfermo tuvo la enfermedad dos veces en un intervalo de cinco años, lo que permite suponer que el tratamiento penicilínico interrumpe la inmunización. Se considera como probable una etiología infecciosa, pero todos los intentos de transmisión fracasaron.