SUCCESSFUL TREATMENT OF ERYTHEMA MIGRANS AFZELIUS

BY EINAR HOLLSTRÖM
STOCKHOLM, SWEDEN

An efficacious method of treating erythema chronicum migrans has not been known formerly, nor was it considered strictly necessary to treat that condition as causing but mild discomfort. Since, however, erythema migrans has been shown in a proportion of instances to involve the central and peripheral nervous system (Hellerström, 1930; Bode, 1933; Bing, 1945; Gelbjerg-Hansen, 1945; Sälde, 1946; Dalsgaard-Nielsen and Kierkegaard, 1947; Leczinsky, 1949),[1] at the present moment the question of successful treatment is of current interest even from the practical point of view. On the other hand, the aetiology of the condition being obscure, apart from the established fact that in the major proportion of instances the eruption follows upon a tick bite, it has hitherto not been possible to attack the causal factor.

Using the spirochaetal stain envolved by him, Lennhoff has succeeded in demonstrating organisms resembling spirochaetes in biopsy specimens taken from the erythematous lesions. With a view to the possibility of the spirochaetes demonstrated being the causal factor, according to Lennhoff's directions groups of erythema migrans cases have been treated with spirochaeticides at the St. Göran's Hospital, Karolinska Sjukhuset, and Stockholm South Hospital. The series comprises 16 patients with typical erythema chronicum migrans.

Case Reports

CASE 1. — Man aged 44, record Nr. 13671/46 (St. Göran's Hospital). Duration 3 months. No statement as to tick bites. 21/11 1946. *Iodobismitol 2 ml.* 28/11. The eruption has practically disappeared. *Iodobism. 2 ml.*

CASE 2. — Boy aged 5, record Nr. 1773/47 (St. Göran's Hospital). Since the middle of July, 1946, an eruption spreading concentrically in the sacral region. On 19/10 an erythematous area the size of a palm and circular in shape was noted by the attending physician, who suspected a tick bite and predicted further spread of the lesion. After extending over half the dorsum and down on to the thighs, according to the mother's statement the circle turned pale but was replaced by a less discrete erythema, which remained unchanged for more than a month. 22/1 1947. *Bismuth subsalicylate 1 ml.* 29/1. The erythema has nearly subsided. 6/2. Just a trace left of the erythema.

CASE 3. — Man aged 39, record Nr. 6381/41 (St. Göran's Hosp.). Had suffered a tick bite in September or October, 1946. In December an extending erythema was observed at the site of the bite. 10/5 1947. Typical erythema migrans involving the left half of the chest. A biopsy was made by Dr. Lennhoff, who using his HgS stain succeeded in demonstrating occasional elements resembling spirochaetes in the sections. *Bismuth subsalicylate 1 ml.* Patient's weight, 110 kg. 16/5. *Bism. subsal. 1 ml.* 21/5. Peripheral spread of the erythema. *Bism. subsal. 1 ml.* 27/5. Central subsidence but upward extension, viz. to upper margin of left nipple. *Bism. subsal. 2 ml.* 7/6. Upper

[1] For references see Hellerström, S., Acta Derm.-Ven., Transactions Oslo Meeting.

border of erythema now 2 cm. above left nipple. *Bism. subsal. 2 ml.* 14/6. *Bism. subsal. 2 ml.* 28/6. Upper border, now manifested by a slightly erythematous zone, 4 cm. above left nipple. The lower portion of the erythema has disappeared. *Bism. subsal. 2 ml.* 5/7. Upper border 5.6 cm. above the nipple. *Bism. subsal. 2 ml.* 2/8. 7 cm. above the nipple. *Bism. subsal. 2 ml.* + *neoarsphenamine 0.6 g.* 9/8. No appreciable erythema. *Bism. subsal. 2 ml.* + *neoarsphen. 0.6 g.* 2/8. 7 cm. above the left nipple a festoon-shaped erythema of 10 cm. in length. *Bism. subsal. 2 ml.* + *neoarsphen. 0.6 g.* 13/9. Condition unchanged. 4/10. Slight spread of erythema, most clearly apparent on the back. *Bism. subsal. 2 ml.* + *neoarsphen. 0.6 g.* 8/10. According to information received from the patient, no visible erythema. 11/10. Still no visible erythema. *Bism. subsal. 2 ml.* + *neoarsphen. 0.6 g.* 18/10. The erythema has recurred within a very small area. *Bism. subsal. 2 ml.* 15/11. The erythema has completely disappeared from the anterior aspect of the chest, whilst a slight trace still remains in the right half of the back. *Bism. subsal. 2 ml.* + *neoarsphen. 0.6 g.* 29/11. The erythema has entirely disappeared. *Bism. subsal. 2 ml. (16th injection)* + *neoarsphen. 0.6 g. (7th injection).*

CASE 4. — Man aged 67, record Nr. 9851/47 (St. Göran's Hosp.). No history of tick bite but exposure during the summer. 13/8 1947. Discrete erythema, treated with a mild ointment. 19/8. The erythema has extended, viz. 12 by 13 cm. *Bism. subsal. 2 ml.* 23/8. *Bism. subsal. 2 ml.* 29/8. *Bism. subsal. 2 ml.* 2/9. The erythema has disappeared.

CASE 5. — Man aged 27, record Nr. 12137/47. (St Göran's Hosp.) 1/10 1947. No statement as to insect bites. Typical erythema migrans. *Iodobism. 2 ml.* 4/10 *Iodobism. 2 ml.* 8/10. Erythema paler. *Iodobism. 2 ml.* 11/10. *Iodobism. 2 ml.* 15/10. *Iodobism. 2 ml.* 18/10. *Iodobism. 2 ml.* 23/10. *Iodobism. 2 ml.* 1/11. The erythema has disappeared. *Iodobism. 2 ml.* 8/10. Erythema paler. *Iodobism. 2 ml.* 11/10. *Iodobism. 2 ml.* 15/10. *Iodobism. 2 ml.* + *neoarsphen. 0.6 g.* 12/11. Erythema unchanged as to size but paler. *Iodobism. 2 ml.* + *neoarsphen. 0.6 g.* 15/11. Erythema scarcely visible. *Iodobism. 2 ml.* + *neoarsphen. 0.6 g.* 22/11. No visible erythema. *Iodobism. 2 ml. (12th inj.)* + *neoarsphen. 0.6 g. (4th inj.)* 29/11. There is just a slight trace of discoloration occupying a small portion of the site previously involved by the erythema.

CASE 6. — Man aged 62, record Nr. 9902/47 (St. Göran's Hosp.). No history of insect bite. 13/8 1947. Typical erythema migrans, treated with a mild ointment. 3/10. The erythema has spread. *Iodobism. 2 ml.* 7/10. *Iodobism. 2 ml.* 23/10. Erythema unchanged. No treatment. — Defaulter.

CASE 7. — Woman aged 48, treated in private practice. Had suffered a tick bite in the left popliteal fossa towards the end of July or early in August, 1947. 24/10 1947. Typical erythema chronicum migrans measuring roughly 3 dm. in diameter. *Iodobism. 1.5 ml.* 7 days later the erythema had paled very considerably. 6/12. Just a trace of discoloration. *Bism. subsal. 1.5 ml.* According to the patient's statement, a couple of days later the eruption had entirely disappeared, showing up once more about new year's day, however, when the patient observed an upper margin of about 5 cm. in length, which a week later was followed by a short lower border. 25/3 1948. Complete, closed circle, now with a diameter of approximately 5 dm. *Mapharside 0.06 g.* 26/3. The erythema has paled. 31/3. Now just discernible discoloration. *Maphars. 0.06 g.* Nausea. 6/4. *Bism. subsal. 1 ml.* 9/4. No skin lesions, but the patient states that in the morning, when she was having a hot bath, the erythema showed up with a somewhat elevated border. 14/4. Slight but clearly visible erythema. *Bism. subsal. 1.5 ml.* + *neoarsphen. 0.45 g.* Nausea. 23/4. Only upper border of erythema clearly visible. *Bism. subsal. 1.5 ml.* + *maphars. 0.06 g.* Vomiting and diarrhoea. 3/5. Poorly visible upper erythematous border. *Iodobism. 2 ml.* 12/5. Condition unchanged. *Iodobism. 2 ml.* 16/5. Toxoplasmosis test, negative. There is just a suggestion of an erythematous margin.

CASE 8. — Man aged 27, record Nr. 13270/47 (St. Göran's Hosp.). Tick bite in July, 1947. 28/10 1947. Typical erythema migrans. *Iodobism. 2 ml.* 1/11. No appreciable change. *Iodobism. 2 ml.* 6/11. Erythema still unchanged. The patient declines further treatment.

CASE 9. — Woman aged 53, record Nr. 7343/48 (St. Göran's Hosp.). Had suffered a tick bite in the right breast in July, 1948. 31/8 1948. Typical erythema migrans slightly larger than a palm on the right breast. Itching and intermittent stinging pain. *Mild ointment, penicillin 450 000 units (in oil and wax).* 8/9. The itching and pain have abated. *Penic. 450 000.* 8/9. *Penic. 450 000.* 16/9. The subjective symptoms have subsided. A small patch still remains of the erythema.

CASE 10. — Man aged 36, record Nr. 6551/48 (Karol. Sjukh.). Since July, 1948, erythema around the left nipple following tick bite. 4/11 1948. Typical erythema-migrans circle over the right half of the chest. *Iodobism. 1 ml.* 9/11. *Iodobism. 2 ml.* 15/11. *Iodobism. 2 ml.* 19/11. Two days ago the erythema disappeared. *Iodobism. 2 ml.* 23/11. *Iodobism. 2 ml.* 27/11. Erythema as conspicuous as prior to the injections. *Iodobism. 2 ml.* 11/12. The erythema has entirely disappeared. 31/1 1949. Still no visible skin lesion, but the patient complains of slight intermittent stinging pain at the site previously involved.

CASE 11. — Woman aged 49, record Nr. 2657/48 (Karol. Sjukh.). Tick bite on the right thigh in September, 1948. A fortnight later migrating erythema around the site of the bite. Early in November erythema also on the right fore-arm and, since 14/11 1948, around the left nipple. 16/11 1948. Spinal puncture, Pandy, weakly positive; Nonne, weakly positive; Mastix, 1, 1, 0, 0, 0, 0; total proteins, 17.88; globulin, 7.09; albumin, 10.79; ratio globulin/albumin, 0.66; monos. 16; reds 3/mm^3. *Neoarsphen. 0.3 g.* 14/1 1949. The patient on request returned for examination. The three erythema circles have somewhat extended. The borders are rather diffuse on the leg and arm but well-defined on the left breast. *Neoarsphen. 0.6 g.* Vomiting. 18/1. *Maphars. 0.06 g. in lactose solution.* Vomiting. 21/1. No skin lesions visible on the leg and arm but still present, though with diffuse margins, on the left breast. *Penic. 300 000 units (in oil and wax).* 25/1. No visible erythema. *Penic. 300 000 units.*

CASE 12. — Woman aged 62, record Nr. 2683/48 (Karol. Sjukh.). Early in June, 1948, the patient suffered a tick bite beneath the left breast. In the middle of October a fairly discrete erythema developed on the right calf, and early in November a small erythematous area appeared on the left upper arm. No pain, no itching. Headache in October, persisting until after the 1st injection. 18/11 1948. Spinal puncture, Pandy, negative; Nonne, negative; Mastix, negative; total proteins, 26.01; globulin, 5.13; albumin, 20.88; ratio globulin/albumin, 0.25; monos. 2/1 ml. *Procain-penic. 300 000 units.* 22/11. Borders diffuse. The erythema has paled. *Procain-penic. 300 000 units.* 31/11. Just a slight trace of erythematous margins. 9/12. The erythema has entirely disappeared.

CASE 13.[1] — Man aged 22, record Nr. 1760/49 (Stockholms South Hosp.). Towards September the patient spends three months each year in camps, and during the period, October—December 1948, he has every sunday done voluntary work cutting timber. Previously healthy. Did not note tick bites. Headache since early in December, at the same time erythematous skin lesion in the upper portion of the left thigh. No itching, no fever. Slight giddiness. The skin lesion showed circular extension and central subsidence. On 3/1 1949 the patient saw a physician and was given tablets for the headache, no benefit. Since 6/1 nausea and vomiting after meals, was unable to retain any food. On 17/1 he was admitted to the Stockholm South Hospital, where

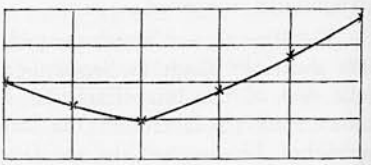
[1] In 1949 this case was presented by Dr. Leczinsky at the February meeting of the Swedish Dermatological Society.

Dr. Bäfverstedt made a diagnosis of erythema migrans with meningitis. Physical examination, urinalysis, and haematology, no abnormality. Pulmonary and cardiac skiagrams. N. A. D. Ekg., normal. Ocular fundi, N. A. D. Skin findings: In the upper portion of the right thigh a festoon-shaped, slightly elevated erythematous zone, measuring roughly one centimetre across and extending from the groin downward over the medial aspect of the thigh, its anterior aspect, and then turning on the lateral aspect towards the trochanteric region. In both groins firm, non-tender lymph nodes of bean size. Neurology, appreciable nuchal rigidity, Kernig's and Lasègue's signs at 45° positive in either leg, otherwise N. A. D. A biopsy, as was to be expected, showed a rather uncharacteristic histological picture. Biopsy material ground in a mortar, suspended in normal saline, and injected intradermally into a human subject, failed to evoke a response (period of observation, four months).

17/1. Spinal puncture:

W. r., negative
Meinicke's clarification test, negative
Müller's conglobation test, negative
1 ml. = 100 cells: monos. 1 140
polys. 60
reds 20/mm.³

Pandy ++
Nonne +(+)
Weichbrodt +

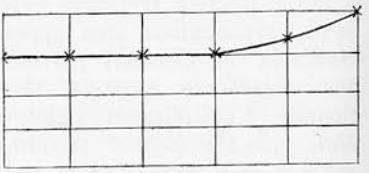


Estimation of protein fractions according to Izikowitz: Total proteins, 169.91; globulin, 42.83; albumin, 127.08; ratio, 0.34. Markedly pathological rates of total proteins, globulin, and albumin, but a normal ratio (meningitis type, yet not syphilitic, the ratio as a rule also showing considerable elevation in syphilis cases according to Flodén).

18/1, 12 o'clock. *Penic. 30 000 units at 3-hour intervals*; 6 p. m. *60 000 units at 3-hour intervals.* 19/1, 6 o'clock. *75 000 units at 3-hour intervals*; 9 o'clock, *100 000 units at 3-hour intervals.* 20/1. Striking subjective improvement. No headache, no nuchal rigidity. Lasègue's sign 60° in either leg. Just a slight trace of erythema.

25/1. Spinal puncture:

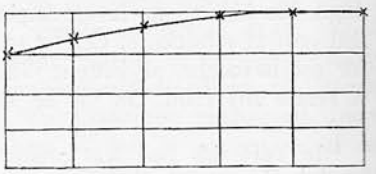
Fluid colourless, clear
Pandy (+)
Nonne, trace
Weichbrodt (+)
Cells: polys. 22
monos. 171
reds 14 (fresh)



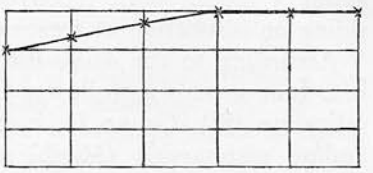
21/1. *Penic. 100 000 units 6 times daily until a total of 10 000 000 was reached on* 1/2. 28/1. Apyretic during the whole period. The erythema has disappeared. No nervous symptoms.

3/2. Spinal puncture:

Fluid clear
Pandy (+)
Nonne, trace
Weichbrodt (+)
Cells: polys. 10
monos. 42
reds 2/mm.³



$^{17}/_{2}$. Spinal puncture:
Pandy +
Nonne, trace
Weichbrodt (+)
Cells: polys. 6
monos. 17
reds 15.



CASE 14. — Woman aged 34, record Nr. 9280/48 (St. Göran's Hosp.). In the summer of 1948 itching all over the body. The attending physician, suspecting scabies, prescribed an antiscabious lotion and subsequently ammoniated mercury ointment. $^{22}/_{11}$ 1948. Oozing in the umbilical region. Typical erythema migrans on both breasts and right upper arm. (During the summer the patient had suffered a tick bite.) $^{22}/_{11}$. *Penic. 450 000 units (in oil and wax).* $^{23}/_{11}$. The itching has abated, the dermatitis in the umbilical region improved. *Penic. 450 000 units.* $^{29}/_{11}$. Still further improvement of the dermatitis in the umbilical region. The erythematous lesions have disappeared. $^{9}/_{12}$. Skin, perfectly normal.

CASE 15. — Woman aged 45, record Nr. 517/49 (Karol. Sjukh.). $^{31}/_{1}$ 1949. In 1948, viz. in the summer, the patient had suffered a tick bite in the right upper arm, where a typical erythema migrans is now observed. A week prior to this bite she had been bitten by a tick lower down in the same arm, but without local erythema ensuing. W. r., negative. Sedimentation rate, 30 mm./1 hour. Blood count, eosinophilia of 6 %, otherwise N. A. D. Material taken from the erythematous border was ground in a mortar and injected intradermally into two subjects without evoking erythema (period of observation, 4 months). $^{1}/_{2}$. Spinal puncture, no abnormality. $^{2}/_{2}$. *Procain-penic. 900 000 units.* $^{3}/_{2}$. *Procain-penic. 900 000 units.* $^{4}/_{2}$. Erythema paler. *Procain-penc. 900 000 units.* $^{5}/_{2}$. *Procain-penc. 600 000 units.* $^{7}/_{2}$. No infiltration is felt on palpation. The erythema is scarcely visible. $^{10}/_{2}$. The erythema is hard to discern. $^{15}/_{2}$. Condition unchanged. $^{23}/_{2}$. Only the lower border to be discerned on very careful inspection. The biopsy scar is enclosed in normal skin. $^{1}/_{3}$. Findings the same as on last examination. $^{5}/_{4}$. No changes visible.

CASE 16. — Woman aged 38, record Nr. 1520/49 (St. Göran's Hosp.). Has not noted a tick bite. Migrating erythema since December, 1948. $^{2}/_{2}$ 1949. Feels weak in one arm (decrease in muscular force). *Penic. 450 000 units.* $^{3}/_{2}$. Spinal puncture: Pandy +, Nonne —, cells: polys. 19, monos. 13, reds 271 per 1 mm.^{3}, Mastix, negative. *Penic. 450 000 units.* $^{4}/_{2}$. *Penic. 450 000 units.* $^{5}/_{2}$. *Penic. 450 000 units.* $^{7}/_{2}$. The erythema has disappeared. *Penic. 450 000 units.* Brachial muscular force, normal.

In eight cases, i. e. in one-half of the series, the out-patient records pertaining to instances of erythema migrans contain statements as to tick bites.

A patient presented three separate erythematous lesions, another one two, and the remaining one each.

The spinal fluid was examined of five patients (Cases 11, 12, 13, 15, 16), three of whom (11, 13, 16) presenting pathological changes in the form of increased cell content, viz. 16 monos., 1 140 monos. + 60 polys., and 13 monos. + 19 polys. respectively. Case 13, i. e. that with the high rise in cells, also had considerably elevated albumin and globulin rates in the C. S. F. In Case 11 there were neither nervous symptoms nor subjective discomfort, Case 13 presented frank meningitis, and in Case 16 the muscular force was impaired in one arm. One of the two patients without C. S. F. abnormality had for

about a month been inconvenienced by aetiologically obscure headache subsiding on institution of treatment.

According to the drugs used in treatment, the present series can be divided into four groups as follows: *Group I*, only iodobismitol (JBi) or bismuth subsalicylate (Bi); *Group II*, both bismuth (JBi, Bi) and neoarsphenamine (Neo) and/or mapharside (Maph); *Group III*, neoarsphenamine, mapharside, and penicillin; *Group IV*, only penicillin.

Case Nr.	*Totals*	*Divided up into injections Nr.*	*Results of Treatment*
Group I			
1	JBi 2 ml. + (2 ml.)[1]	1	7 days after institution of treatment the erythema had practically disappeared.
2	Bi 1 ml.	1	Disappearance of erythema after 13 days.
4	Bi 6 ml.	3	Disappearance of erythema 13 days after institution of treatment.
6	JBi 4 ml.	2	After 20 days condition unchanged. (Treatment abandoned).
8	JBi 4 ml.	2	After 9 days condition unchanged. (Treatment abandoned).
10	JBi 11 ml.	6	Temporary disappearance of erythema during treatment, definite 37 days after the 1st injection.
Group II			
3	Bi 29 ml. Neo 3.6 g. + (Bi 2 ml., Neo 0.6 g.)[1]	14 6	Temporary disappearance of erythema during treatment, definite after 6 1/2 months. (Patient's weight, 110 kg. Long interruption of treatment.)
5	JBi 24 ml. Neo 2.4 g.	12 4	Temporary disappearance of erythema during treatment; 2 months after the 1st injection still very slight discoloration.
7	JBi 5.5 ml. Bi 7 ml. Neo 0.6 g. Maph. 0.25 g.	3 5 1 4	Temporary disappearance of erythema during treatment; roughly 6 1/2 months after the 1st injection just a trace of erythematous border. (Long intervals between the first few injections.)
Group III			
11	Neo 0.9 g. Maph. 0.06 g. Penic. in oil and wax 300 000 units + (300 000 units)[1]	2 1 1	Disappearance of all the erythematous lesions about 9 weeks after institution of treatment. (Disappearance of two erythematous circles prior to institution of penic. Complete freedom from symptoms 4 days after the penic. injection.)
Group IV			
9	Penic. in oil and wax 1 350 000 units	2	Coin-sized erythematous residue 16 days after institution of treatment.
12	Procain-penic. 600 000 units	2	Disappearance of erythema 20 days after the 1st injection.
13	Penic. 10 000 000 units	105	Disappearance of erythema and nervous symptoms within 10 days after institution, and prior to termination, of treatment. Gradual improvement of the C. S. F. changes.

[1] Injection given on last day of observation or after disappearance of erythema.

Case Nr.	*Totals*	*Divided up into injections Nr.*	*Results of Treatment*
14	Penic. in oil and wax 900 000 units	2	Disappearance of erythematous lesions 7 days after institution of treatment.
15	Procain-penic. 3 300 000 units	4	Disappearance of erythema within 2 months after the 1st injection.
16	Penic. 1 800 000 units + (450 000 units)[1]	4	Disappearance of erythema 5 days after the 1st injection (penic. administered on four consecutive days).

Of the six patients treated solely with bismuth (Group I), two defaulted after two injections. At that moment their erythema did not show any effect of the treatment. Of the remaining four, two presented quite inconspicuous residues of the erythema 7 and 13 days respectively after a single injection. In the two other patients treated with 3 and 6 injections respectively, the erythema had disappeared definitely 13 respectively 37 days after institution of treatment. In the latter cases temporary disappearance during treatment was observed to precede the definite subsidence of the erythema.

Group II comprises three patients initially treated with bismuth salts. The bismuth doses being small in relation to the body weight and the treatment interrupted for considerable periods, only a partial and temporary disappearance resulted of the erythema. Neoarsphenamine or mapharside was then resorted to. Not until 6 $^1/_2$ and 2 months respectively after institution of treatment was freedom from symptoms attained in two of the cases. As regards the third patient (Case 7), there was marked improvement after the first bismuth injection and temporary freedom from symptoms after the second one administered 6 weeks later; when recurring, however, the erythema was more extensive than previously, an observation made also in another case or two. Neoarsphenamine and, subsequently, mapharside were adopted as supplementary treatment but owing to intolerance symptoms had to be abandoned. 6 $^1/_2$ months after the first bismuth injection the patient still presented a small remnant of the erythema.

Group III consists of just one case with three erythema-migrans circles. At the outset we had intended to use neoarsphenamine treatment only. However, after the first injection the patient defaulted, returning two months later on being requested to do so. The erythema circles had somewhat migrated. Vomiting ensuing from a single neoarsphenamine or mapharside injection, this type of treatment was discarded. Three days after the latter injection two of the circles had disappeared, a penicillin injection then being given. Four days later there was complete freedom from cutaneous symptoms.

Six cases, Group IV, were treated with penicillin alone, viz. from 600 000 to 10 000 000 units. In one case complete freedom from symptoms did not ensue until 2 months after institution of treatment, but four patients were rendered symptom-free within 3 weeks, whereas one after this period presented a coin-sized remnant of the erythema. Of particular interest is the action of penicillin on the neuro-meningeal symptoms sometimes associated with erythema migrans. In one patient (Case 12) who during the last few months

[1] Injection given on last day of observation or after disappearance of erythema.

before treatment had suffered from headache but did not present C. S. F. changes, the headache yielded to the first injection of penicillin. Another patient (Case 16) complained of weakness in one arm; there was a decrease in muscular force in the arm affected and a rise in cells in the C. S. F. After four penicillin injections (1 800 000 units) the subjective discomfort and objective brachial symptoms had entirely subsided (the C. S. F. was not re-examined). The only patient who was hospitalized and thus could be carefully observed, and who presented frank symptoms of meningitis, under penicillin treatment (10 000 000 units) showed an extraordinarily prompt, both subjective and objective, improvement (see Case 13).

The therapeutical results achieved indicate that in cases of erythema migrans disappearance or improvement of cutaneous symptoms can be brought about by bismuth salts alone. If the dosage is insufficient, the erythema may pale down only partly or disappear temporarily. This seems to apply also to the arsenicals. The most rapid therapeutical effect will apparently be attained by administering penicillin. According to the experience derived from the treatment of early syphilis, penicillin seems to be our most powerful spirochaeticide. The prompt effect of each separate injection was frequently striking, considering all the types of penicillin. In the few cases of erythema migrans presenting symptoms of neuro-meningeal involvement and treated with penicillin, the action of the drug was highly gratifying on both the C. S. F. changes and other signs of meningeal and nervous disease, objective symptoms as well as subjective discomfort.

The erythema itself may be allergically conditioned. Evidence in favour of this conception is afforded by the positive result of intradermal tests with tick extract as obtained by Hellerström and subsequently verified by Dalsgaard-Nielsen and Kierkegaard, and by the observation that the erythema is apt to disappear within an area exposed to quartz light, and to become visible again when it has migrated beyond the limits of the area irradiated.

The idea of the condition being purely allergic, however, is discouraged by the satisfactory therapeutical action of the drugs used in the present case series, since these drugs are devoid of anti-allergic properties.

The therapeutical results achieved with penicillin indicate that erythema migrans is infectious in nature, and the effects of all the drugs used in treatment, in particular the bismuth salts and neoarsphenamine, tend to suggest a spirochaete as the causative organism. Definite evidence is still lacking in this respect, but the therapeutical results in conjunction with Lennhoff's findings of spirochaetes in histological sections prepared from lesions of erythema migrans and with the demonstrated presence of spirochaetes in ticks, render probable that a spirochaete is the infective agent.

The infectious aetiology of erythema chronicum migrans, on the other hand, is not definitely adverse to the possibility of the cutaneous lesions being allergically conditioned. The erythema is perhaps due to an organism, most frequently deriving from ticks and possessing sensitizing power, which is introduced into the skin.

The negative results of inoculation tests may be due to the material for inoculation having been taken from the circumference of the erythematous

circle possibly arising through an allergic mechanism; in addition, the infection may require a certain predisposition.

SUMMARY

An account is given of sixteen cases of erythema chronicum migrans Afzelius treated with bismuth, neoarsphenamine, mapharside, and penicillin, either separate or in various combinations. In 14 cases (two patients defaulted) the therapeutical action upon the erythema was unmistakable and sometimes very rapid. If the dosage was insufficient, or if there were long intervals between the injections, the erythema was apt to pale down only partly or disappear temporarily. Penicillin appeared somewhat superior to the other drugs used, entailing a highly gratifying curative effect in a case with frank meningitis. The aetiology is discussed of the condition, special attention being given to the conclusions possibly to be drawn from the good therapeutical results.

ZUSAMMENFASSUNG

Verf. berichtet über 16 Fälle von Erythema chron. migrans Afzelius, welche mit Wismuth, Neosalvarsan, Mapharside und Penicillin, allein oder in verschiedenen Kombinationen behandelt worden waren. In 14 Fällen (2 Patienten entzogen sich der Behandlung) war die therapeutische Einflussung des Erythems unverkennbar und manchmal sehr prompt. Bei ungenügender Dozierung blasste das Erythem nur teilweis ab oder verschwand vorübergehend. Penicillin schien den anderen verwendeten Mitteln einigermassen überlegen zu sein, indem es in einem Fall mit ausgesprochener Meningitis einen ausgezeichneten Heilungserfolg bewirkte. Verf. bespricht die Aetiologie der Erkrankung und geht besonders auf die Schlussfolgerung ein, die sich womöglich aus den guten Behandlungsresultaten ziehen lassen.

Grev Turegatan 38, Stockholm, Sweden