The conclusion is that, by itself, long duration of illness should not weigh against performance of the operation. Freeman and Watts (1950) make this same point. The apparent discrepancy between the effects of length of illness and length of stay in hospital is probably to be explained by the view that the patient who is able to remain outside hospital, even though ill, does so because of his good retention of personality and his social adaptability.

Retention of Personality.—By this we understand that, despite his psychosis, the patient retains an interest in his appearance, in personal and topical affairs, and in social intercourse. Of those patients with good pre-operative retention of personality 46% made grade I or II recoveries. Of those who seemed deteriorated before operation 21%, less than half, made grade I or II recoveries. Even this 21% is quite a respectable figure, but then it is notoriously difficult, especially in schizophrenia, to determine the presence or absence of deterioration. We found that probably the best test is the response to electric convulsion treatment (E.C.T.), and we would now hesitate to stigmatize a patient as too deteriorated for operation until we had seen the response he made to a course of electroplexy.

Response to Electric Convulsion Therapy.—Of those who had made a good, albeit transient, response to E.C.T. given before leucotomy 22% made grade I recoveries, while of those who had shown no response to E.C.T. only 3.5% made grade I recoveries. Table IV illustrates these results.

TABLE IV.—*Relationship Between Response to E.C.T. and Condition at Time of Investigation*

Clinical Response to E.C.T.	Grade (see Table II)										Totals
	I	II	III	IV	Va	Vb	Vc & Vd	VR	VI	VII	
No improvement	2	11	6	2	5	5	16	8	2	0	57
Temporary improvement	33	19	8	13	13	13	23	22	6	1	151
No E.C.T. given	6	1	1	0	3	2	11	5	1	0	30
Totals ..	41	31	15	15	21	20	50	35	9	1	238

Response to Insulin Coma Therapy.—On the other hand, we found no significant differences after leucotomy between those schizophrenics who had made some response and those who had made no response to insulin coma therapy.

Emotional Tension.—It is generally agreed that the best results of leucotomy occur in those patients who still show a strong affective reaction to their psychosis. As the presence of this affective reaction or emotional tension was one of our main criteria of selection, there were only 16 patients in the series who showed no obvious tension: the figures are therefore too small for comparison. It is interesting, however, that even of these 16 patients five made grade I or II recoveries.

Diagnostic Categories.—The series included 35 cases of affective psychosis and obsessional neurosis and 194 cases of schizophrenia. In the former group 60% made grade I or II recoveries, while only 27% of the schizophrenics reached these grades. Surprisingly, all our five cases of mania made grade I or II recoveries.

Relapses.—It was found that of 115 patients who had improved enough to be discharged from hospital 22 relapsed after an average period of two and a quarter years free from symptoms. When this group of relapsed cases was compared with those who had maintained their recoveries the only significant factor found was that the pre-operative personality was more often intact in the recovered cases than in the relapses (Gillies and Mayer-Gross, 1950).

Summary and Conclusions

A follow-up study was made of 238 chronic psychiatric patients who had undergone the standard leucotomy operation some one to seven years previously. The best results occurred in those whose pre-operative personality

was more or less intact, who had well-adapted pre-psychotic personalities, and who had been only a short time in hospital. If these factors were present, long duration of illness did not worsen the prognosis.

In schizophrenia the best test for pre-operative deterioration is afforded by the response to electric convulsion treatment.

Of the psychiatric patients who have hitherto been regarded as hopeless hospital invalids the standard leucotomy can return one-third to a normal or almost normal social life and can fit one-quarter for gainful employment.

Broadly speaking, the prognostic criteria for leucotomy are still those well-tried criteria that hold for the untreated psychosis.

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FAMILIAL ERYTHEMA NODOSUM

BY

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(From a General Practice)

Erythema nodosum is a clinical entity with a characteristic skin eruption, usually accompanied by a general constitutional upset. Diagnosis of the eruption is easy, but there is still some uncertainty with regard to the aetiological aspects of this condition. The general consensus of opinion is that it is a non-specific reaction in a sensitive subject in response to a number of various allergens. These are best discussed under separate headings.

Tuberculosis.—It is probable that erythema nodosum is most often associated with the primary tuberculous complex, particularly in children and adolescents. In these cases the eruption occurs when the patient first develops hypersensitivity to tuberculin. The time-interval for this to happen has been estimated at three to eight weeks from the time of infection. The frequency with which erythema nodosum is associated with primary tuberculosis apparently varies individually and also nationally. Thus Wallgren (1938) estimated that 30% of primary infections in Scandinavia were associated with the eruption; Dunlevy (1949), in Eire, found only a 2.8% incidence. In Scandinavia the average age of primary infection is much higher than that in Eire. Wallgren, in a series of 800 cases, reported that 95% had a positive tuberculin skin reaction. This is significant, because these Scandinavian children could normally have been expected to have a negative reaction. He also describes a number of cases in which the change of the skin response from negative to positive was definitely associated with the eruption.

Punch (1941) was able to show that in student nurses the change from a tuberculin-negative to a tuberculin-positive skin reaction was often accompanied by an eruption of erythema nodosum. Bruce Perry (1944), in a series of 112 cases, found a positive Mantoux reaction in 54%. In those under 15 the incidence was 75% and in those over 15 it

was only 25%. Doxiadis (1949) found 88% tuberculin-positives out of 100 children under 15 who developed erythema nodosum. There are relatively few reports on series of adult cases. Löfgren (1946) considers that a non-tuberculous cause is more frequent in adults.

Acute Rheumatism.—The usual view held in this country, until recently, was that erythema nodosum was a frequent accompaniment of acute rheumatism. All the latest papers discussing the aetiology of erythema nodosum stress the rarity of this association (Wallgren, 1938; Bruce Perry, 1944; Löfgren, 1946; Doxiadis, 1949). The points against the rheumatic theory are the absence of any signs of carditis in erythema nodosum, the different sex and age incidence, and the lack of response to salicylates. Although rheumatic fever as a common cause is discredited, it is certain that erythema nodosum may occasionally be a manifestation of acute rheumatism.

Streptococcal Infection.—It was Collis (1932) who first drew attention to the fact that tuberculin-negative cases of erythema nodosum had a markedly higher sensitivity to streptococcal nucleoprotein at the time of the eruption. It seems probable that erythema nodosum may be an expression of streptococcal allergy in certain cases. It is from this cause that cases of recurrent attacks occur. Rotnes (1936) reported a case in which there had been 14 attacks, usually after a pharyngitis or tonsillitis.

Sarcoidosis.—Erythema nodosum is occasionally met with as a sign of sarcoidosis (Kerley, 1942, 1943; Löfgren, 1946; Crawley, 1950).

Sulphonamide Hypersensitivity.—In the early days of sulphonamide therapy skin rashes of diverse types were common. At the present time, with compounds of lower toxicity, these rashes are much less frequent. Occasionally an eruption indistinguishable from erythema nodosum is found in these circumstances, and it disappears rapidly when the drug is stopped. It is difficult to know whether the eruption is the result of the primary condition or whether it is a complication of the treatment.

Coccidioidomycosis.—For many years a chronic granulomatous condition, due to infection by *Coccidioides immitis*, has been prevalent in the San Joaquin Valley in California. This condition has a number of features akin to tuberculosis. There is a mild primary stage of infection which is sometimes followed by a general blood-stream spread and a possible late occurrence of chronic granulomata in the lungs and other organs. About 5% of these cases have a typical eruption of erythema nodosum associated with the primary stage of infection.

Miscellaneous.—There are a number of other conditions with which erythema nodosum has been associated—for example, meningococcal, gonococcal, and staphylococcal septicaemias; lymphogranuloma inguinale; syphilis; lymphadenoma; and intoxication with bromides and iodides.

Question of Specificity.—The recognition of small epidemics of erythema nodosum gave rise to the theory that it is a specific disease (J. O. Symes, 1921; Lendon, 1925). The causal organism has, however, never been convincingly isolated. Further studies of these epidemics suggested that in the majority there was evidence of a recent simultaneous contact with the tubercle bacillus.

Three cases of erythema nodosum which occurred simultaneously in one family are described.

Case Reports

The family, in October, 1950, comprised the parents and three young children: Mary aged 7½, Janet 5, and Roger 3½. They lived in a house of three bedrooms on the outskirts of South-east London. The parents slept in one bedroom, the two girls shared a double bed in the second, and Roger had a small room to himself. The father, a builder's decorator aged 30, had been unwell for some weeks with a cough, and on October 21 bilateral open pulmonary tuberculosis was diagnosed. He was at once

ordered to bed. The mother then slept with her two daughters in their double bed, and the father had a separate room. He remained there until November 29, when he was admitted to a sanatorium. When tuberculosis was diagnosed the rest of the family were investigated at the local chest clinic. Chest radiographs showed no signs of any disease, and tuberculin tests on the children were all negative.

On December 1 the mother was seen on account of a sore throat, of three days' duration, and a painful eruption on her legs, which she had noticed for 12 hours. She was a healthy young woman of 28. She had a clean medical record, and was at this time four months pregnant. There were no cough, joint pains, or any digestive upset. The whole family had had a meal of prawns on the previous day. Examination at this stage revealed a normal temperature—98.2° F. (36.8° C.)—and pulse rate 81. The fauces were hyperaemic, but there was no exudate. On the extensor aspects of both legs there were about a dozen typical areas of erythema nodosum. Over the next four days her general condition became a little worse, with a fever up to 100° F. (37.8° C.), and increasing pain in the legs. On the fifth day she began to improve, and the eruption had disappeared by the tenth day. She received no specific treatment.

On December 1 Mary, aged 7½, began to feel unwell with vague dull mid-abdominal pain and fever—99.5° F. (37.5° C.)—and a pulse rate of 92. She showed no abnormal physical signs at this stage. There was no sore throat, no vomiting or diarrhoea, or any joint pains. On December 4 the characteristic eruption of erythema nodosum appeared on the anterior aspects of both legs. By this time she felt better and there was no abdominal pain or other constitutional upset. The eruption persisted for eight days. She, too, had no specific therapy.

Janet, aged 5, was quite well in spite of the appearance of typical areas of erythema nodosum on her legs on December 6. There was no fever or tachycardia. Her eruption had disappeared within seven days.

Roger, aged 3½, had during all this time remained in his usual good health and continued to do so.

All four were further investigated. Chest radiographs of the mother, Mary, and Roger on December 21 were considered to be within normal limits. Janet's radiograph showed a slight degree of left hilar enlargement. Further radiographs on June 4, 1951, were all regarded as within normal limits. A tuberculin patch test was performed on all four on December 15, and Janet showed a positive response. A Mantoux, 1/1,000, however, resulted in a positive reaction in the other three. The family has remained well since December, 1950, until the time of writing (July, 1951). The mother was delivered of a normal healthy boy in April, 1951; he is Mantoux-negative (1/1,000), and is about to have B.C.G. vaccinations. Janet and Roger had measles in March, but have otherwise remained well. The father is still in a sanatorium, but is due for discharge soon.

Discussion

It seems certain that in the two girls the development of a positive tuberculin skin reaction accompanying a primary tuberculous infection was associated with an eruption of erythema nodosum. This is also likely to be the case in the mother, but it is inconclusive, as a previous skin test was not done.

A number of previous reports describe similar series of cases. The most remarkable of these was an "epidemic" which occurred in the Welsh town of Mynyddislwyn in the summer of 1920. It is reported by J. O. Symes (1921), quoting R. E. Roberts, who was then the local M.O.H. Over a period of five weeks 50 cases of erythema nodosum were seen in an area enclosing three streets. There had been no cases in this town for the previous 15 years. There is no mention of any search for a tuberculous cause. W. L. Symes (1907) reported 12 cases occurring over a period of four weeks in a girls' residential school of 100 pupils.

Robinson (1926) described three cases. Lendon (1925), in a survey, quoted 10 instances of outbreaks of erythema nodosum; in two of these there was a subsequent tuberculous infection. Demole (1933) reported three cases in a dressmaking school where a tuberculous source was found. He also states that in the nineteenth century there were widespread epidemics of erythema nodosum in Bosnia, Jutland, and Turkey.

Wallgren investigated an outbreak which occurred in a class of 34 girls: 18 suffered simultaneously from a febrile condition. On follow-up 12 of these subsequently developed erythema nodosum within 6 to 10 weeks. Three months previously there had been an open case of pulmonary tuberculosis in the class. Further small series with a tuberculous aetiology are reported by Lannois (1892), Ledoux (1932), Parisot and Saleur (1933), Bertoye and Bernheim (1935), and Mouriquand and Weill (1937). Cibils Aguirre (1933) has collected a number of series of "familial erythema nodosum" cases with a probable tuberculous cause.

It seems likely that most of these multiple cases of erythema nodosum have been associated with a primary tuberculous infection. It is true that a definite tuberculous contact has not been found in some of these, but perhaps the contact was of a transient and elusive nature.

Summary

The possible aetiology of erythema nodosum is discussed. It is a non-specific reaction to a variety of allergens. The most important of these is the association of erythema nodosum with a primary tuberculous infection.

A report is given of three cases occurring simultaneously in one family. In these there was a definite tuberculous cause.

Previous reports of similar cases are reviewed.

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According to the Hungarian News and Information Service the first Congress of the Hungarian Microbiological Society was held in Budapest during January, and was attended by 250 Hungarian scientists, and 26 scientists from eight other countries, including the Soviet Union, China, and Korea. Eighteen lectures were delivered to plenary sessions of the Congress, and nearly 150 to meetings of its eight sections. The society was formed during 1951, and the congress was the first public presentation of the work of Hungarian microbiologists. Dr. Károly Rauss is engaged on research into a preventive vaccine for dysentery. Professor Rezső Manninger is working on vaccines against fowl pest, swine fever, and other animal diseases. Typhoid fever carriers, antibiotics, and the manufacture of penicillin are all being investigated. The Parasite Section of the National Institute of Public Health is working on the prophylaxis of malaria. Messrs. Kardos, Kiss-Bagoly, and Deutsch discussed the question of the formation of bacteria from non-cellular protein.

A NEGATIVE BENZODIOXANE TEST IN PRESENCE OF A PHEOCHROMOCYTOMA

BY

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Four cases of phaeochromocytoma have been reported which gave a negative response to the benzodioxane (piperoxane) test before operation. Prunty *et al.* (1950) described the case of a man, under the care of Professor Pickering, in whom a large phaeochromocytoma was removed at operation, despite a pre-operative negative benzodioxane test. Smithwick's case, described by Goldenberg and Aranow (1950), was that of a middle-aged woman with persistent hypertension and a negative benzodioxane reaction who was found to have a large phaeochromocytoma at operation. Calkins and Howard (quoted by Goldenberg and Aranow) described a similar case. Beyer *et al.* (1951) reported a negative benzodioxane test in a woman aged 40 in whom a phaeochromocytoma of the left adrenal was removed at operation.

The following case report concerns a woman with sustained hypertension and a negative benzodioxane reaction, who at necropsy was found to have a phaeochromocytoma.

Case Report

A woman aged 25 was admitted in September, 1950, for gynaecological investigation following a prolonged history of menstrual disturbances, anorexia, and loss of weight, with associated attacks of blurred vision and frequent night sweats. Routine examination revealed a sustained hypertension ranging from 240/130 to 220/120 and a persistent tachycardia (88–120), although she was a psychologically stable patient. She had a large hypertensive heart but no congestive lung changes. Retinoscopy revealed gross papilloedema with haemorrhages, exudates, and attenuated arteries.

Investigations.—Sodium amytal test (see Fig. 1). The benzodioxane test, carried out as described by Goldenberg, with a calculated dose of 17 mg., gave a negative result (Fig. 2). An electrocardiogram showed gross left ventricular stress. Renal function tests showed a normal blood urea; albumin, red cells, and granular casts in all urine specimens; and imperfect function. An intravenous pyelogram was normal.

FIG. 1.—Graph showing results of the sodium amytal test.