be overcome by introduction of air and heparin into the cerebrospinal canal, and it may be worth while to try her methods in such desperate cases. It need not be feared that children thus saved might prove to be crippled in one way or another for the rest of their lives. Regarding such consequences Alexander (private communication) states:

"The experience in this country when both sulphadiazine and type-specific rabbit antiserum are used in combination for the treatment of influenzal meningitis indicates that any residual damage to the brain is exceedingly rare following recovery. This appears to be true even in very chronic cases of the disease which recover over a long period of time. For example, I know, as a result of my own experience and by talking over the experiences of a number of others, of only one case in which residual damage to the brain followed a child's recovery."

In all, 5 out of 20 cases were treated with sulphonamides alone. Only one of these five recovered. Fifteen cases had combined sulphonamide–penicillin treatment and eight of them recovered. The total number of cases is too small and the methods of treatment varied too much to allow of statistical assessment. The only conclusion to be drawn is that the encouraging recovery rate suggests pushing to the limit the combined sulphonamide–penicillin treatment, perhaps supported by specific antiserum.

The sporadic occurrence of *H. influenzae* meningitis in this country makes it very difficult for any investigator, single-handed, to work out a satisfactory routine treatment. It seems reasonable to suggest that cases of *H. influenzae* meningitis of the non-fulminant type should be concentrated in a number of treatment centres. An adequate method of treatment, as in the case of subacute bacterial endocarditis, might be evolved for the majority of cases, and a substantial number of children's lives might thus be saved.

Summary

A survey of the various methods of treating *H. influenzae* meningitis is presented.

Clinical data are given of 19 cases of *H. influenzae* type b meningitis and of 1 case due to *H. influenzae* of the respiratory group. Of 5 cases treated only with sulphonamides, one recovered. Fifteen cases had combined sulphonamide–penicillin treatment. Eight of these recovered. It is suggested that the combined administration of these drugs should be used more energetically in *H. influenzae* meningitis. In view of the good therapeutic results reported from the U.S.A. specific *H. influenzae* type b rabbit antiserum, which is now available in this country, should also be given.

The establishment of a number of treatment centres to evolve a standard routine method of treatment is advocated.

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REFERENCES

Alexander, H. E. (1939). *Proc. Soc. exp. Biol.*, N.Y., **40**, 313.
—— (1943a). *Amer. J. Dis. Child.*, **66**, 160.
—— (1943b). Ibid., **66**, 172.
—— (1944). *J. Pediat.*, **25**, 517.
—— Ellis, C., and Leidy, G. (1942). Ibid., **20**, 673.
—— and Heidelberger, M. (1940). *J. exp. Med.*, **71**, 1.
—— and Leidy, G. (1943). *J. Pediat.*, **23**, 640.
Anderson, D. G., and Jewell, Marjorie (1945). *New Engl. J. Med.*, **233**, 485.
Cairns, H., Duthie, E. S., and Smith, H. V. (1946). *Lancet*, **2**, 153.
Drysdale, Constance F., McIntosh, D. G., and Brodie, J. (1946). *British Medical Journal*, **2**, 223.
Forgacs, P., Hutchinson, R. I., and Rewell, R. E. (1945). *Lancet*, **1**, 785.
Fothergill, L. D. (1937). *New Engl. J. Med.*, **216**, 587.
Gordon, J., Woodcock, Hester E. de C., and Zinnemann, K. (1944). *British Medical Journal*, **1**, 779.
Gordon, M., and Zinnemann, K. (1945). Ibid., **2**, 795.
Herrell, W. E., and Nichols, D. R. (1945). *Proc. Mayo Clin.*, **20**, 449.
Hewitt, W. L., and Pittman, M. (1946). *Publ. Hlth. Rep., Wash.*, **61**, 768.
Horsfall, F. L., jun., Goodner, K., and MacLeod, C. M. (1936). *Science*, **84**, 579.
Lindsay, J. W., Rice, E. C., and Selinger, M. A. (1940). *J. Pediat.*, **17**, 220.
McIntosh, D. G., and Drysdale, Constance F. (1945). *British Medical Journal*, **2**, 796.
Mutch, N. (1941). *Lancet*, **2**, 751.
Pittman, M. (1931). *J. exp. Med.*, **53**, 471.
—— (1933). Ibid., **58**, 683.
Smith, M. H. D., Wilson, P. E., and Hodes, H. L. (1946). *J. Amer. med. Ass.*, **130**, 331.
Straker, E. A. (1945). *Lancet*, **1**, 817.
Wilkes-Weiss, D., and Huntington, R. W., jun. (1936). *J. Pediat.*, **9**, 462.

INFECTIONS OF THE NERVOUS SYSTEM OCCURRING DURING AN EPIDEMIC OF INFLUENZA B

BY

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Influenza epidemics in the past have on occasion been associated with cases presenting evidence of cerebral or cerebrospinal infection, although the relationship is obscure. During the epidemic of influenza B at the beginning of 1946 nine cases of acute infection of the nervous system, occurring at three separate levels, were observed. Two of these presented signs of brain-stem encephalitis, two of myelitis, and five of generalized polyneuritis akin to the acute toxic polyneuritis of Guillain, Barré, and Strohl (1916).

Brain-stem Group

Case 1.—A girl aged 18 complained of diplopia and right-sided ptosis. She was well until May 14, 1946, when she developed a generalized headache and extreme lassitude. She had intense sleepiness, and found it difficult to remain awake. Her neck felt a little stiff. She was bad-tempered, and had one outburst of unreasonable rage. Three days before the onset of her symptoms she had been in close contact with a girl who had a severe attack of influenza. On the 18th her vision became blurred, and she noticed diplopia in all directions. Next day the right lid began to droop, and she experienced discomfort in the right supraorbital region. The headache persisted; there was no polyuria or polydipsia; the appetite was poor; and she still felt very sleepy. She had had diarrhoea off and on for the past nine to ten days. On May 24 she was admitted to the London Hospital under the care of Dr. Russell Brain.

Examination showed the following: Right pupil a little larger, and reacting a trifle more sluggishly to light than the left; equal brisk reaction to accommodation; right ptosis; weakness of elevation, adduction, and depression of the right globe; diplopia in all directions; all tendon reflexes depressed; knee-jerks obtained only on reinforcement; equivocal right plantar response. Lumbar puncture on May 25: C.S.F. pressure, 100 mm.; 8 cells, mainly lymphocytes; protein, 20 mg. per 100 ml.; W.R. negative; Lange, 222321000. On the 28th the white cell count was 6,700 per c.mm. (polymorphs 70%, lymphocytes 25.5%, large hyalines 4.5%). June 6: No diplopia; right ptosis; very slight weakness of elevation of right globe; pupils equal, reacting sluggishly to light. On the 8th there were full ocular movements and no diplopia. The tendon reflexes were sluggish and plantar responses flexor. The patient was discharged symptom-free.

Case 2.—A medical man aged 38 complained of headache, photophobia, diplopia, dizziness, and tingling in hands of five days' duration. On March 12, 1946, he had a sore throat, cough, and general malaise, but after sulphathiazole for three days he felt fit. About March 26 he developed dizziness and photophobia, followed 24 hours later by tingling in both hands and difficulty in focusing. On the 30th he had diplopia in all directions. The left pupil was larger than the right, and both pupils reacted only sluggishly to light. Next day there was an increase in the severity of all symptoms: tingling now present in feet; headaches more severe, mainly frontal aching pain; movement of eyes painful; diplopia in all directions except to the extreme right. Left ptosis was noticed by the patient on April 1. He felt extremely drowsy, and slept eleven to twelve hours. He was admitted to the London Hospital under the care of Dr. Clifford Wilson. The patient presented a difficult diagnostic problem, as he had suffered from Hand-Schüller-Christian disease since 1932 and had had five injections of "pitressin" daily to control his diabetes insipidus.

He was seen by Dr. George Riddoch on April 2. Examination showed: Pupils moderately dilated, regular, left larger than right; very feeble reaction to light and, on convergence, right more than left; gross paresis of all external ocular movements, left more than right; severe bilateral ptosis. Upper limbs; no weakness, ataxia, or dystonia; tendon reflexes absent. Lower limbs: no weakness, ataxia, or dystonia; knee-jerks just present; ankle-jerks absent; plantar reflexes flexor. There was no cutaneous sensory change. The abdominal reflexes were present and equal. B.P. 190/120. Urine normal. Lumbar puncture: pressure 240 mm.; 4 cells; protein, 30 mg. per 100 ml.; Lange 1222100000; W.R. negative. A radiograph of the skull showed nothing abnormal. The patient was considered to be suffering from an acute infection of the nervous system, chiefly affecting the brain-stem. Daily injections of 2 ml. of "hepolon" were advised. On April 3 the left pupil was larger than the right, both fixed to light; sluggish reaction to accommodation; ptosis more severe, left worse than right. The white cell count was 7,750 per c.mm. (polymorphs 69%, lymphocytes 25%, eosinophils

2.5%, large hyalines 3.5%). On the 5th there were almost complete ophthalmoplegia interna and externa; dilated fixed pupils; sensory change to cotton-wool and pin-prick below mid-forearm; vibration loss below the clavicles, and he still had marked photophobia. He was seen on the 8th by Dr. Russell Brain, who confirmed the above signs and noted, in addition, weakness of the hip muscles. Signs of recovery in the eyes were observed on the 12th—a little movement of the lids and some pupillary response to light. Vibration sense started to return in right leg on the 15th. On May 7 convergence was returning, the pupils reacted well to light, and the external recti were still weak. On June 1 he still had diplopia in all directions, except on looking upwards and to the right. The right pupil was a little larger than the left, both reacted sluggishly to light and briskly on accommodation. Left eye: defective elevation, abduction, and adduction. Right eye: defective elevation and adduction. He still had slight weakness of dorsiflexion of wrist and fingers, complete areflexia of upper and lower limbs, and weakness of hip flexors, abductors, and adductors. Plantar responses were flexor, and there was no sensory change.

Myelitic Group

Case 3.—A man aged 24 had an attack of influenza on Jan. 4, 1946, with fever, sweating, running nose, and sneezing, but he had no headache or sore throat. A slight cough and aching pain in the frontal region began on Jan. 7, and he was in bed for seven days. At the end of this time both lower limbs were stiff, the right more than the left, and the right lower limb felt numb. There was a little delay in initiating micturition. Past history: Pott's disease from 2 to 9 years of age; ? tuberculous left knee-joint, with eventual removal of patella, arthrodesis, and osteotomy; well since 1939. His father died of phthisis in 1929. The patient was admitted to the London Hospital under the care of Dr. George Riddoch on Feb. 1.

Examination on the 4th revealed a gibbus, D.7–D.8. C.N.S.: nil abnormal in cranial nerves and upper limbs; left lower limb—gross shortening, arthrodesis at knee, patella absent; bilateral lower-limb spasticity, right greater than left; lower abdominal reflexes absent; right knee-jerk and both ankle-jerks increased; left knee-jerk absent; bilateral extensor plantar responses; vibration sense impaired in both lower limbs; postural sensibility impaired in toes; patchy diminution to pin-prick and cotton-wool below D.6. Lumbar puncture on Feb. 11: pressure 80 mm.; no block; 2 cells; protein, 20 mg. per 100 ml.; W.R. negative; Lange 1122110000. A radiograph of the spine showed old tuberculous kyphosis but no sign of activity. During the following month the power of both lower limbs improved and the sensory changes regressed. On June 4 the lower-limb weakness had improved. There was moderate bilateral spasticity with loss of tickle sensation over the inner aspect of the right knee, relative analgesia below the right knee, and impaired vibratory sense in both feet. Sensory level to dragged pin at D.10.

Case 4.—A married woman aged 29 began to have backache, headache, and muscular aching in mid-February, 1946. Influenza was diagnosed, and she was kept in bed for seven days. On getting up she noticed weakness of both lower limbs and tingling in the toes, which persisted until the time of examination. There was occasional urgency of micturition. Examination on May 1 revealed nothing abnormal in the cranial nerves or upper limbs. There was moderate bilateral spastic weakness of both lower limbs, with extensor plantar responses. There was no sensory change and the abdominal reflexes were absent. On May 29 she was much improved symptomatically—the lower limbs were stronger, but the signs persisted unchanged.

Polyneuritic Group

Case 5.—A married woman aged 46 had lassitude and anorexia in mid-December, 1945. On Jan. 24, 1946, she had slight sore throat, pyrexia of 101° F. (38.3° C.), and aching in the lumbar region. The pyrexia continued for 25 days, and on Feb. 17 was followed by photophobia and left facial weakness, which rapidly spread to the right side of the face. At this time she noticed paraesthesia in the left thumb. She was admitted to the London Hospital under the care of Dr. George Riddoch on Feb. 21. The temperature was 98° F. (36.7° C.), pulse 80. She had complete facial diplegia, with loss of taste. There was no other nervous abnormality. Lumbar puncture: pressure 70 mm.; no excess of cells; protein, 120 mg. per 100 ml., W.R. negative. Next day a blood count showed: Hb, 88%; W.B.C., 7,600 (polymorphs 45%, lymphocytes 48%, basophils 2.5%, large hyalines 5%). On the 23rd she had paraesthesiae along the ulnar border of the left forearm and hand; the left lower limb felt weak; both ankle-jerks were sluggish; and vibration sense was a little impaired in the left big toe. Two days later the frontalis was working—on the left side more than the right. On the 27th all facial muscles responded to faradism. She was treated by galvanism to the face and given 2 ml. of "hepolon," intramuscularly, twice weekly. The signs were unchanged on March 11.

Case 6.—A married woman aged 54 had diarrhoea on March 13, 1946; this lasted for seven days. Her daughter also suffered from this complaint. The patient was admitted to Haymeads Hospital under the care of Dr. Leiper on the 20th, complaining of backache and vomiting. There were no abnormal physical signs in any system apart from a blood pressure of 200/110. All tendon reflexes were present. Dimness of vision started on the 27th, beginning with a left homonymous defect and progressing within 24 hours to complete blindness. She became drowsy and confused; the left optic disk was blurred; the tendon reflexes were absent, and the plantar responses flexor. Lumbar puncture: pressure 300 mm.; no increase in cells, protein, 288 mg. per 100 ml.; W.R. negative. After a few days the vision began to improve, and she was found to have a left lower homonymous quadrantic field defect. Plantar responses were flexor. She was seen by Dr. Russell Brain on July 3. The blood pressure was 210/95. The disks and fundi were normal. There was no field defect or any abnormality in the cranial nerves. Upper limbs: power good, no dystonia or ataxia; tendon reflexes present and equal; no sensory change to pin-prick, cotton-wool, vibration, or posture. Lower limbs: power good, no dystonia or ataxia; knee- and ankle-jerks absent on reinforcement; plantar responses flexor; no sensory change to pin-prick, cotton-wool, posture, or vibration. Abdominal reflexes present and equal.

Case 7.—This patient, a man aged 46, developed a cough during the first week of March, 1946. There was no pyrexia or sore throat, but he felt tired and ill. A fortnight later he noticed weakness of the lower limbs, which gradually increased, and three days later it involved the hands. Within a week he was unable to walk more than 400 yards or to shave. On April 1 he was admitted to the London Hospital under the care of Dr. George Riddoch.

Examination revealed no abnormalities in the cranial nerves. There was weakness of the whole of the upper limbs, most marked distally, and in the flexors and extensors of the wrist and fingers. The tendon reflexes were depressed. In the lower limbs the power was good in all groups save the dorsi- and plantar-flexors, especially the former. The knee-jerks were sluggish and the ankle-jerks much diminished. There was no sensory change to pinprick, cotton-wool, posture, or vibration in upper or lower limbs. The abdominal and intercostal muscles were strong. The abdominal reflexes were present. Lumbar puncture on April 6: pressure, 200 mm.; cells less than 1; protein, 20 mg. per 100 ml.; W.R. negative. He was given 2 ml. of "hepolon," intramuscularly, on alternate days, and he slowly recovered. On May 20 the power was greatly improved and he walked unaided.

Case 8.—A Wren aged 19 had a very mild cold early in December, 1945, which lasted for a week. On Dec. 22 she noticed weakness of both shoulders and weakness of flexion of arms on shoulders, which progressed until Jan. 2, 1946. She remained on duty, but on Jan. 12 she had weakness at the hips, and this increased during the next three weeks until she was unable to stand. There were no other symptoms. She was admitted to the London Hospital under the care of Dr. George Riddoch on Feb. 18.

Examination revealed no abnormality of the cranial nerves. There was considerable weakness of all muscles, particularly of the shoulder-girdle muscles. The triceps and the brachioradialis were weaker on the right than on the left. There was slight weakness of the muscles of the forearms and hands, the intercostal and abdominal muscles, the extensors of the trunk, and all hip-girdle muscles, especially the flexors. The flexors and extensors of the knees were somewhat impaired, but the leg and foot muscles were good except for weakness of dorsiflexion on the right due to old peroneal-nerve injury. The abdominal reflexes were brisk and equal. All tendon reflexes were present and equal. There were bilateral flexor plantar responses. No sensory abnormality was noted. Lumbar puncture on Feb. 23: pressure 60 mm.; 1 cell; protein, 20 mg. per 100 ml.; Lange 0111000000; W.R. negative. During the next eight weeks the left lower lobe of the lung collapsed and she had to be placed in a Drinker respirator. Plugs of mucopus were sucked out on two occasions, with eventual re-expansion of the lung. Her neurological condition, which had been slowly improving, relapsed as the result of the pulmonary complication. On June 6 she was transferred to another hospital for swimming-bath treatment. She was then as weak as when first seen.

Case 9.—A married woman aged 54 developed a sore throat, cough with greenish sputum, and pyrexia at the end of January, 1946. Three days later the temperature rose to 104° F. (40° C.), the sputum increased, and bronchopneumonia was diagnosed. Sulphathiazole and systemic penicillin were given. On Feb. 16 she was afebrile; rales were heard at both bases. On the 22nd she had weakness in both shoulders, which increased during the following 24 hours. Next day she had tingling in the finger-tips, and the lower limbs felt weak. On the 28th she was seen by Dr. George Riddoch. Moist sounds were heard at both bases. The cranial nerves were normal. There was weakness of all the upper-limb muscles, especially the scapular group, the deltoid, the flexors of the elbow, and, to a less extent, the extensors of the wrists. The supinators were more affected than the pronators, and the extensors of wrist and fingers more than the flexors. There was no weakness of the trunk, but moderate weakness of hip flexors and adductors of thighs was noted. The dorsiflexors

of the feet and toes were weak. Good power remained in the lower-limb muscles. Tendon reflexes were absent in the upper and lower limbs, save a much diminished left knee-jerk. Plantar responses were flexor. Abdominal reflexes were present and equal. There was no sensory change in the upper limbs; vibration was absent in the feet. On March 7 moist sounds were still heard at both bases. The physical signs in the central nervous system were unchanged, apart from diminution to pin-prick below the elbows and mid-calf. The patient was given 2 ml. of "hepolon," intramuscularly, daily. There was increased power in the affected muscles on March 23, and considerable improvement in the power of all affected muscle groups on May 2. The knee-jerks were just present.

Discussion

The brain-stem group is remarkably reminiscent of encephalitis lethargica, although it differs greatly from the haemorrhagic influenzal encephalitis first described by Leichtenstern (1890). Drowsiness, with the rapid development of nuclear midbrain lesions, occurred in both cases. The fleeting abnormal plantar responses in one patient and the weakness of proximal muscles groups, with areflexia and peripheral sensory change, in the other indicate a more widespread attack on the neuraxis. Complete recovery ensued within three weeks in Case 1; and equally striking, although slower, was the improvement in Case 2, following a total ophthalmoplegia interna and externa. Unfortunately, it is a matter for speculation whether the condition can be identified with encephalitis lethargica. Von Economo (1931) considers that the somnolent-opthalmoplegic type is the true basic form of this disease, and is the type that occurs sporadically. Certainly Case 1 might be regarded as a classical example of this variety.

Signs of a transverse or patchy myelitis affecting the lower thoracic cord occurred in two patients after an influenza-like illness. Recovery was slow, and, again, in the absence of pathological material, it can only be suggested that this group corresponds to the two patients described by Greenfield (1930), in whom histological examination disclosed evidence of an acute disseminated encephalomyelitis.

Of the polyneuritic group, Case 5 conforms to the classical type of acute toxic polyneuritis of Guillain, Barré, and Strohl (1916)—a febrile illness for three weeks being followed by facial diplegia, with an increase in the protein content of the cerebrospinal fluid. In Case 6 the patient, after an attack of diarrhoea, became drowsy and confused, with rapid visual failure of a cerebral type. All tendon reflexes disappeared, and the C.S.F. contained 288 mg. of protein per 100 ml., with no increase in cells. During recovery, which occurred rapidly and completely, a homonymous quadrantic field defect was observed. The tendon reflexes in her lower limbs were still absent three and a half months after the onset of symptoms. Case 7 developed a subacute weakness of the dorsiflexors of the wrists and ankles, without sensory change and with a normal C.S.F., three weeks after the onset of symptoms. Case 8 was in every way atypical, a slowly progressive weakness of hip- and shoulder-girdle muscles developing over six weeks and then becoming stationary, with no sensory change and a normal C.S.F., two months after the onset of symptoms. In Case 9 weakness of hip- and shoulder-girdle muscles developed following a 23-day pyrexia, associated with a basal bronchopneumonia. Recovery occurred slowly over the two months she was observed.

This small epidemic of nervous diseases, while of such varied types, appears to be related to some common factor. Whether the prodromal illness was in fact an attack of influenza B is unknown, but the incidence of the cases is related to the peak period of this 1946 epidemic. Certainly, too, it seems that the type of case described above has been unusual during the past few years, as have epidemics of influenza B, sporadic cases of which appeared in England for the first time in 1939. In 1943 only a minor outbreak occurred, but in 1946 the death rate from influenza rose to a higher level than for the two previous years.

Whatever the relationship, however, the three groups seem to be the result of a virus attack on the nervous system, producing either polioclasis or myelinoclasis. It would appear likely from the known characteristics of the viruses which attack the nervous system that two separate viruses are thus concerned.

Summary

A small epidemic of nervous diseases coinciding with an epidemic of influenza B is described.

It is suggested that a myelinoclastic virus and a polioclastic virus are concerned.

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REFERENCES

Von Economo, C. (1931). *Encephalitis Lethargica*, London.
Greenfield, J. G. (1930). *J. Path. Bact.*, **33**, 453.
Guillain, G., Barré, J. A., and Strohl, A. (1916). *Bull. Mém. Soc. méd. Hôp. Paris*, **40**, 1459.
Leichtenstern, M. H. (1890). *Dtsch. med. Wschr.*, **16**, 212, 388.

ALLERGIC REACTIONS TO PENICILLIN

BY

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Reports on allergic reactions to penicillin are increasing in number. This is becoming an important problem as more and more patients are receiving penicillin therapy. Evidence is accumulating that the offending agent is the active principle of penicillin. Theoretically, therefore—and actual practice has shown this to be true—reactions may arise with any commercial preparation of the drug. The route of administration has in the majority of cases a bearing on the clinical features and site of the allergic reaction. Local use of penicillin will give rise predominantly to contact or sensitization dermatitis, while parenteral administration is more likely to produce immediate or delayed reactions resembling anaphylaxis.

Review of the Literature

Pyle and Rattner (1944) and Kolodny and Denhoff (1946) reported cases with skin lesions due to penicillin sensitivity. The latter found among dermatological patients treated with parenteral and local penicillin a 25% rate of skin complications as compared with 6% among non-dermatological patients. Especially in cases of fungous infection was contact dermatitis liable to develop, and skin tests were positive to penicillin and to trichophytin. From the study of their cases they concluded that there is no clear-cut relationship between the antigenic substances common to some of the pathogenic fungi (Hyphomycetes) and antigens of *Penicillium notatum* (Ascomycetes), but clinical observations are suggestive. Goldman *et al.* (1946) found 16 instances of contact dermatitis among 350 cases treated with penicillin locally. Vickers (1946) described a case of penicillin sensitization dermatitis; a patch test with penicillin solution was strongly positive. Hellier (1946) stressed the rarity of contact dermatitis due to penicillin as compared with that due to sulphonamides.

More characteristic are the manifestations described since 1943; they are practically always due to intramuscular penicillin and resemble severe urticaria or serum sickness. Lyons (1943), when reporting on penicillin therapy of surgical infections in the U.S. Army, found that there were urticarial reactions not attributable to particular batches of the drug. Of 209 cases 12 (5.7%) had an urticarial reaction, of which he described three types: (*a*) without fever; (*b*) with fever to 101° F. (38.3° C.); (*c*) with fever to 103° F. (39.4° C.) and abdominal cramps. The urticaria appeared as early as the first day or as late as the fourth week. Fever was present only if urticaria was severe, and normally did not exceed 101° F. Skin tests were negative. No precipitins were found in the serum of patients tested during the phase of urticaria, and heterophil agglutinins were not significantly and constantly increased. Criep (1944) reported a case in which a massive generalized urticaria appeared on resumption of a second parenteral course of penicillin. This persisted for six days. He made special laboratory investigations which showed the presence of some immune substances (reagins and precipitins) in the patient's serum. According to Criep the following takes place: First penicillin administration—drug discontinued—second penicillin administration → allergic reaction.