dermically in ordinary doses will stimulate the sympathetic center sufficiently to arrest the propulsive activity of the arterioles, and, by thus reducing the caliber, limit still further the quantity of blood admitted into the capillaries. When, therefore, chloral is beginning to lose its effect an occasional injection of morphine may be used advantageously to sustain it. *Antipyrin* and *acetanilid* act in the same way.

It would appear as if the central erethism would render small doses of morphine adequate to *stimulate* the sympathetic center; but such is not the case. Trousseau and Pidoux[113] many years ago held that large doses were alone effective. This is readily accounted for, however, when the marked vascular tension present in tetanus is taken into account. Unless violently stimulated, the arterioles cannot contract upon the tense arterial column. Hence the advice I submit, to give it in ordinary doses, but only *after* the arterial tension has been already reduced.

EPILEPSY.

SYNONYMS.—*Falling Sickness, Falling Evil, Falling Fits, Morbus Sacer, Morbus Caducus.*

Definition.—Epilepsy, a chronic disease characterized by periodical convulsions accompanied usually by unconsciousness, is due to inherited or acquired hypoactivity of the adrenal system and to the resulting accumulation of toxic wastes in the blood. As this entails a marked rise of vascular tension, an excess of blood is driven into all capillaries, including those of the spinal system and cortex. Both the latter being thus rendered hyperexcitable, a fit occurs when this hyperexcitability is suddenly increased by the appearance in the blood of an excess of auto-antitoxin, the result, in turn, of a sudden resumption of defensive activity by the adrenal system when the blood becomes sufficiently toxic to enforce it. The fit lasts until the toxic wastes are converted more or less efficiently into harmless and eliminable end-products.*

Symptoms and Pathology.—Three types are recognized: minor epilepsy, or petit mal; major epilepsy, or haut mal, or grand mal; and Jacksonian epilepsy.

In *minor epilepsy* there may be a brief loss of consciousness, and perhaps slight clonic spasms of the face and limbs, but only entailing, as a rule, a temporary cessation of the conversation or occupation in which the patient may be engaged. He suddenly becomes pale, his face assumes a blank expression, but after a few seconds he recovers and resumes the sentence or act he had begun before the spell. Occasionally the patient falls into coma which is usually attended with stertorous breathing suggesting apoplexy. In minor epilepsy clonic convulsions are never witnessed.

* *Author's definition.*

[113] Trousseau and Pidoux: "Traité de thérapeutique," Paris, 1875.

An attack of *major epilepsy* is sometimes preceded by ringing in the ears, tingling, general malaise, epigastric uneasiness, etc., but a common prodrome is the *aura,* which occurs in about one-half of the cases. This may consist of sensory phenomena, *i.e.,* pain, sensations of heat or cold, or of a breeze striking an extremity and traveling upward towards the body; or of aural, visual, olfactory or gustatory hallucinations, such as roaring sounds, flashes of light, unpleasant odors, etc. Or again, the aura may manifest itself by motor phenomena, a marked tremor or an irresistible tendency to use the muscles, to gesticulate or to run, the so-called "procursive" epilepsy. Finally, it may be attended by physical phenomena; sudden terrors, mental exuberance or hallucinations as to the presence of strangers, or bearing upon long-past events, etc. The aura may be very short, a few seconds, or endure sufficiently long to enable the patient to protect himself against the oncoming convulsion, by sitting or lying down. In rare instances it lasts thirty minutes or more.

All these phenomena clearly betoken erethism, *i.e.,* undue stimulation of the motor or sensory organs involved. The aura is, in fact, the beginning of the convulsive paroxysm.

Spratling[114] states that "there is a growing tendency for some years past to regard the aura as essentially constituting a part of the epileptic fit," and considers it as such himself, advising, moreover, that such cases be treated accordingly. This conclusion was based on a study of 1325 cases at the Craig Colony. Of these 45 per cent. had auras.

When the fit begins the patient usually utters a loud cry, due to sudden contraction of the muscles of the chest and larynx. Three symptoms occur simultaneously at this time, *i.e.,* the "epileptic cry," unconsciousness and fall—the patient dropping like a log. A *tonic* spasm of all the flexors follows: the legs being extended, the fingers, hand, forearm flexed, the head

[114] Spratling: Med. News, July 18, 1903.

thrown back and turned to one side; the eyes also turn up or aside. This rigid state of all the muscles lasts usually but a few seconds.

The transition from the state of rigidity to that of *clonic* spasm is usually marked by a momentary tremor. When the true fit begins the extremities are thrown about violently, sufficiently so at times to produce dislocations. The head is tossed from side to side, the eyes roll in their orbits, the lids open and close rapidly and the tongue is protruded and withdrawn, provided it is not caught between the teeth by the jaws, whose muscles are likewise contracted with violence—causing disfiguring distortions. The bitten tongue often causes the saliva, itself converted into foam by the churning to which it is submitted, to become streaked with blood, and the patient is said to "froth at the mouth." The urine and fæces are sometimes involuntarily voided, owing to contractions of the intestinal walls. The pallor of the clonic stage has now disappeared and becomes replaced by a dusky, cyanotic hue, the features being swollen, and usually, as is the case with the rest of the body, covered with sweat.

This paroxysm only lasts, as a rule, a couple of minutes. The violence of the contractions becomes gradually less, and the patient lapses into a comatose state attended by stertorous breathing. Finally he falls into a deep sleep. On waking, some lassitude and muscular pain may be complained of, but on the whole, the patient, recollecting nothing of the paroxysm, seems hardly to have suffered from the experience. Occasionally the full return to consciousness is preceded by "postepileptic states," during which the patient may perform automatic acts, undressing, etc., such as those ascribed to somnambulism. He may also become suddenly maniacal and violent, sufficiently so at times to commit murder. Marked weakness, paresis, tremor, aphasia and kindred nervous phenomena may also be witnessed, but these rarely last more than a few hours.

These attacks occur with more or less frequency. From the practically continuous paroxysms, lasting hours and even days, constituting the *status epilepticus,* during which the patient may die of exhaustion, to the rare instances in which years elapse

between the fits, there are gradations innumerable. In the majority of cases, however, they occur at intervals of a few days.

A *Jacksonian* paroxysm is often preceded by an aura, which may be motor, such as tremor or rapid contractions of the toe, thumb, etc., first affected, or sensory, tingling, paræsthesia, etc. The special senses may also be the source of phenomena such as those witnessed in the aura of major epilepsy. The tonic phase of the latter form is also present, but to a very limited degree, and may not occur at all.

While the spasm may be restricted to a limited number of muscles corresponding with a given cortical lesion, the irritation of the latter often spreads to contiguous motor areas, so that several groups of muscles may be involved. It may thus creep up the arm to the shoulder and face, and involve the whole side of the body; or up the leg, the body, and face; or, again, begin at the face and proceed downward. Finally, it may become general, when a typical attack of major epilepsy occurs. While this gradual progression occurs, the patient remains conscious and it is only when certain regions, including the face, are involved, that consciousness is lost. After the paroxysm, which lasts but three to five minutes, the region affected may be numb and paralyzed and remain so from a few hours to several days. After a time this may become permanent.

Etiology and Pathogenesis.—The *tonic* spasm is produced in the same manner as the corresponding though more severe spasm of tetanus* (*q.v.*). Instead of terminating as such, however, it soon lapses into the typical epileptic paroxysm, the clonic fit.

The impulses which cause *clonic* convulsions are primarily derived from the cerebral cortex, the spinal system being used as the mechanical intermediary for their production, and are of the nature of voluntary impulses to the spinal system.*

A striking feature of this stage is the similarity of the movements to those carried on voluntarily. Thus, to turn the eyes from one direction to the other, to throw the head backward, to bend and unbend the arm at the elbow, are all, at other times, voluntary movements. The performances during the postepileptic states, which M. Allen Starr termed "psychical equivalents," also point to the source of the impulses that evoke the movements, namely, the cortex. As I have pointed out elsewhere, the latter does this *only* by exciting the appropriate cells in the

* *Author's conclusion.*

spinal system, the sole source of motor impulses. Indeed, Prus[116] has shown that excitation of the cortex caused typical convulsions even after division of the pyramidal tracts, the impulses passing by way of the tegmentum and pons—a conclusion confirmed experimentally by Bischoff,[117] Hering[118] and others. Long before, in fact, Magnan[119] had caused epileptic seizures in animals deprived of their hemispheres, while Vulpian[120] had been led to conclude by a series of experiments that the center for epileptic convulsions was located at the *base* of the brain. It is evident, therefore, that the basal structures can provoke clonic as well as tonic spasms.

The persistence of clonic convulsions after division of the pyramidal tracts simply shows that these represent but a portion of the link-system between the brain and the spinal cord, and that impulses from the cortex can excite the upper extension of the cord in the third ventricle. Where they reach the basal cells is suggested by one of Bischoff's conclusions, namely, that "after destruction of the optic thalamus, the hypothalamic region and the pyramidal path on one side, faradic irritation of the homolateral motor cortex remains without effect." As we have seen, it is in the hypothalamic region that the cortical paths meet those from the pituitary body, which pass downward and finally reach the cord. In the normal animal, including man, of course, the entire spinal gray matter receives spasmogenic impulses from the cerebrum.

The clonic convulsions are the result of a temporary and intense hyperæmia of the cerebral cortex, due in turn to general vasoconstriction.* The cortex being a sensory organ, this marked congestion—during which the speed of the blood-streams is greatly increased—provokes a storm of impulses to the spinal system—itself hyperæmic and oversensitive—which the spinal motor cells convert into motor impulses and transmit to the muscles (which are also hyperæmic and overexcitable), thus inciting the clonic fit.*

The neuroglia being plasma capillaries,* they bear the brunt of the excessive blood-pressure to which the nervous elements are submitted,* and if the disease is not treated early, more or less extensive gliosis occurs and the chances of recovery are correspondingly reduced.

As I have pointed out,[121] the neuroglia fibers and cells are channels for blood-plasma containing adrenoxidase granules. Pierce Clark and Prout[122] recently wrote: "The neuroglia hyperplasia in epilepsy is now almost constantly found. With improved methods and technique it will probably be demonstrated in every case of considerable duration." Chaslin,[123] who first pointed out this condition, ascribed it to a constitutional vice of development, but the identity of neuroglia fibers as capil-

* *Author's conclusion.*
116 Prus: Wiener klin. Woch., Bd. xi, S. 857, 1898.
117 Bischoff: *Ibid.*, Bd. xii, S. 961, 1899.
118 Hering: *Ibid.*, Bd. xii, S. 831, 1899.
119 Magnan: Arch. de physiol. norm. et path., vol. v, p. 115, 1873.
120 Vulpian: C. r. de l'Acad. des sci., Apr. 27, 1885.
121 *Cf.* this vol., chapter fifteenth.
122 Pierce Clark and Prout: Amer. Jour. of Insanity, vol. lx, p. 645, 1904.
123 Chaslin: Arch. de méd. exper. et d'anat. path., vol. iii, p. 305, 1891.

laries alone accounts logically for it. Many investigators, Féré, Koppen, Hohne, Bratz, Anglade[124] and others, have confirmed Chaslin's observation. Victor Horsley has[125] emphasized the importance of congestion of the cortical mantle in the production of fits. Féré and Chaslin, Pierce Clark and others found diffuse gliosis in cases of long standing. Ito[126] produced typical fits in guinea-pigs by causing traumatic hyperæmia of the cortex.

The participation of the vasomotor system, as shown by the general vasoconstriction, is as clear. Spitzka, in 1881, attributed the fit to the "explosive activity of an unduly irritable vasomotor center," and epilepsy is now commonly referred to as a "functional vasomotor disease." A continuous rise of pressure during the fit was noted by François-Franck and Pitres. The speed of the blood-stream is greatly increased at this time—three to five times in the muscular vessels, according to Hill[127]—an index of the violence of the cortical circulation. Even the skin shows evidence of this sometimes by minute capillary hæmorrhages, as observed by Aldrich[128] and others. Weber,[129] moreover, found vascular lesions and extravasations in the cortex and medulla of cases of status epilepticus, so great had been the capillary pressure—the identical pressure which projects the blood-plasma into the neuroglia fibers.*

Chaslin always found the hyperplasia most advanced in the *superficial* layer of the cortex, though it involved the subjacent strata. Blocq and Marinesco[130] found as the most constant lesion in the psycho-motor zone of nine cases, vascular alterations and hyperplasia of the neuroglia, associated with punctiform hæmorrhages in other parts of the nervous system in every instance. The cortex being regarded as a sensory organ, its uppermost layer thus becomes the most active in the production of the convulsions. Indeed, Prus[132] found that even electrical excitation of the cortex could not provoke fits after the application of a cocaine solution had anæsthetized its surface, thus identifying the cerebral gray matter as the source of the spasmogenic impulses.

The excessive vasoconstriction and rise of blood-pressure which gives rise to this cortical hyperæmia, is due to irritation of the vasomotor and sympathetic centers by toxic waste-products.* Epileptic convulsions differ from convulsions produced by many exogenous poisons (strychnine, for instance) in that they are due to poisons formed in the body.*

"Certain drugs, notably absinthe," writes Schäfer,[133] "produce, when injected into the vascular system, convulsive attacks which are scarcely distinguishable from the epileptic fits provoked by stimulation of the cortex cerebri." That all such drugs provoke a marked rise of the blood-pressure may be shown by comparison with a few of the many other spasmogenic agents. Thus, while absinthe was found to cause intense congestion of all organs examined by Pauly and Bonne,[134] Wood[135] states

* *Author's conclusion.*
124 Anglade: Arch. de neurol., 2 série, vol. xiii, p. 418, 1902.
125 Victor Horsley: Brit, Med. Jour., Apr. 2, 1892.
126 Ito: Deut. Zeit. f. Chir., Bd. lii, S. 417, 1899.
127 Hill: Schäfer's "T. B. of Physiol.," vol. ii, p. 155, 1900.
128 Aldrich: Med. News, May 26, 1900.
129 Weber: Wiener med. Woch., Bd. xlix, S. 158, 1899.
130 Blocq and Marinesco: Semaine méd., vol. xii, p. 445, 1892.
132 Prus: *Loc. cit.*
133 Schäfer: "T. B. of Physiol.," vol. ii, p. 721, 1900.
134 Pauly and Bonne: Gaz. hebd. de méd. et de chir., May 13, 1897.
135 Wood: *Loc. cit.*, thirteenth edition, p. 217, 1906.

that "the full dose of strychnine produces a rise of the arterial pressure which is enormously increased during the convulsion." He also refers[136] to the observation of Bezold and Bloebaum, "that when a small dose of atropine is injected into the carotid artery—that is, near the vasomotor centers—," he adds, "there is an instantaneous rise of blood-pressure"—"a great rise," as he afterwards says. Cocaine, as shown by Von Anrep, causes "convulsive movements of cerebral origin," which "are arrested by section of the spinal cord;" Wood also says: "Certainly the evidence is overwhelming that cocaine directly increases the blood-pressure." The fits are precisely those of epilepsy; the syndrome is known as "cocaine epilepsy." Alcohol can likewise produce both minor and major epilepsy. Wood and Hoyt[137] concluded, after a recent experimental study, that the excitement it caused was due to the "enormously increased flow of blood running riot through the cerebrum."

L. Pierce Clark,[138] after a study of 150,000 seizures, we have seen, concluded that "we must see the principle of pathogenesis in an initial toxin or autointoxication," *i.e.*, "an accumulation of waste-products." Van Gieson[139] and other authorities have also noted greater frequency of fits during gastro-intestinal disturbances and constipation, the blood at the time being especially toxic. This view, which has a large number of supporters, is sustained by the beneficial effect of appropriate dietetic measures. The relation between epilepsy and other disorders attributed to toxic wastes points in the same direction. Spiller,[140] Bernhardt[141] and others have laid stress on its relationship with migraine, Trowbridge[142] with chorea, etc.

When the antitoxic powers of the blood are taken into account, however, it becomes evident that only very toxic fluids derived from epileptics will prove pathogenic in experimental animals. Herter,[143] for instance, obtained results in rabbits differing but little, if at all, from those produced by normal blood, with defibrinated blood taken from epileptics, but when he used blood-serum of exceptional toxicity obtained from an epileptic with prolonged headaches, habitually an overfeeder at meals and with *congested face and conjunctivæ*, 10 c.c. ($2^1/_2$ drachms) sufficed to kill rabbits in 45 minutes, after the animals had had tonic and clonic spasms and become somewhat cyanotic. Kraïnsky[144] produced characteristic seizures in rabbits in two and three minutes, and several recurrences, with blood-serum obtained by cupping from a case in status epilepticus. Savary Pearce and Boston[145] found that several injections of blood from an epileptic into rabbits caused an enormous leucocytosis, reaching in one instance 162,800 per cm.—a proof that the adrenal system was violently stimulated.

The toxic substances which incite the convulsions are formed when the breaking down of the worn-out chromatin of tissue-cells, the tissue-proteid, etc., is not carried to a finish, *i.e.*, when this process is not sufficiently active to lead up to the formation of benign, eliminable substances—urea and uric acid, etc., the normal end-products.* But it is only when this accumulation

* *Author's conclusion.*

136 Wood: *Loc. cit.*, thirteenth edition, p. 171, 1906.
137 Wood and Hoyt: Memoirs National Acad. of Sci., vol. v, 1905.
138 L. Pierce Clark: Med. News, July 18, 1903.
139 Cited by House: Buffalo Med. Jour., June, 1898.
140 Spiller: Amer. Jour. Med. Sci., Jan., 1900.
141 Bernhardt: Deut. Aerzte Zeit., July 15, 1900.
142 Trowbridge: Alienist and Neurologist, Jan., 1892.
143 Herter: Jour. of Nerv. and Mental Dis., Feb., 1899.
144 Kraïnsky: Wiener klin. Woch., Bd. xi, S. 185, 1898.
145 Savary Pearce and Boston: Medicine, Feb., 1904.

has reached a certain degree that epileptic seizures occur; thus, it may only be sufficient to give rise to the tonic spasm, *i.e.*, minor epilepsy; or it may exceed this limit and produce clonic convulsions, major epilepsy.*

Such being the case, it is evident that the cause of the disease is deficient activity of the process through which the worn-out living tissues are broken down. This process being carried out by trypsin, whose activity is governed by the heat-energy it receives through the interaction of nuclein and adrenoxidase, it follows that insufficiency of either of these bodies underlies the morbid process. It cannot be the nuclein, since this is derived from the food. The production of the tissue-ferment—or rather of the proferment—by the pancreas being proportionate with the secreting activity of this organ, and this function in turn being governed by the proportion of adrenoxidase in the blood, we are brought to *inadequate activity of the adrenal system as the primary cause of epilepsy.**

This insufficiency of the adrenal center is thus pathogenic in two ways: it entails (1) imperfect catabolism and the resulting accumulation of toxic wastes in the blood; (2) inadequate conversion of these poisons in the blood and liver into eliminable products, *i.e.*, imperfect protection of the organism.*

This does not mean, however, that the test-organ does not respond to the stimulating influence of the circulating poisons: it only fails to do so adequately.* Accustomed to the presence of tissue-wastes, and even to that of these particular poisons in the blood circulating through it, it responds only when these have accumulated in great quantities, and then, by a spurt of activity which soon recedes, relieves the blood of at least some of its spasmogenic toxics by increasing markedly the production of auto-antitoxin.* These exacerbations of activity coincide with the convulsions.*

Briefly, the accumulation of toxic wastes in the blood violently stimulates the *three general centers of the blood-vascular system*, the sympathetic, vasomotor and adrenal centers, *simultaneously*, and although the rôle of the adrenal center is a protective one, it is to this collective action that the convulsions are due.*

* *Author's conclusion.*

Waste-products, we have seen, are thought by many observers to provoke epileptic seizures. The identity of the specific agent is not established, however. Hajg incriminated uric acid, but his view has not been sustained. As previously stated, uric acid is a benign end-product. Kraïnsky[156] attributed the fits to a diminution of the uric acid formed, the true spasmogenic substance being an intermediate product essential to the formation of uric acid, *i.e.*, ammonium carbonate. It proved not only highly toxic, but it produced, when injected in animals, typical epileptic seizures. Inouye and Saiki[147] attribute them to a dextro-rotatory lactic acid found increased in the blood after severe attacks, and which unites with urea to form dialuric acid, then uric acid. Both these views are sustained by an exhaustive study of Herter and Smith,[148] in which they found an excess of uric acid in the urine only *after* the convulsions. Teeter[149] also found that it contained a larger amount of urea than during the intervals, when it was very low. Rachford, in 1895, ascribed migraine, "migrainous" epilepsy and other periodical affections to paraxanthin poisoning. The poisonous ptomaine cholin, found by Mott and Halliburton in blood and cerebro-spinal fluid in cases of nervous disease, has also been considered as the spasmogenic agent by Donath,[150] Coriat[151] and others. When we consider that nervous, hepatic, muscular and other heterogeneous tissues are all the seat of imperfect catabolism and other facts, however, it is probable that the convulsions are caused by several poisons acting more or less collectively.* Thus, Ohlmacher[152] found a persistent thymus in several cases; Murdoch[153] and others have cured cases that were clearly due to gastro-intestinal disorders, etc.

The connection with the anterior pituitary body, as adrenal center, is suggested in various ways. We have seen that removal of the pituitary or of the adrenals provokes convulsions. Langlois[154] long ago showed that the adrenals, in some unexplained way, "annihilated the toxic substances produced in the course of chemical exchanges." He concluded that "there was every reason to suppose, however, that it was through an oxidation process." With adrenal secretion as the basis of oxidase, we have a clear index in the fact that while there are frequently abnormally low temperatures during health, as observed by Lemoine and others, a rise occurs during seizures which sometimes is very great. Charcot, Bourneville and others have laid stress on this feature. Clark and Prout[155] found that in status epilepticus, the height of the curve corresponded with the severity of the attack, sometimes reaching 107° or 108° F. (41.6° or 42.2° C.). This applies to ordinary cases as well; thus Benedikt[156] reported a case in which it sometimes rose to 109.4° F. (42.8° C.). If this is connected with an antitoxic process, an intercurrent disease, by raising the functional activity of the test-organ (which fails to respond promptly *only* to the physiological poisons to which it has become habituated), should prove beneficial. Hippocrates, Van Swieten, Esquirol and other masters have laid stress on the favorable influence of various diseases on epilepsy. Recent writers, Féré, Voisin, Lannois, Lenoir[157] and others have done likewise. Hessler[158] and Lannois[159] have even used bacterial injections on this plea. Pierce Clark and Sharp[160] have found, however, that a temporary improvement is all that is obtained by an intercurrent disease—which means, interpreted from my standpoint, that the adrenal system, whipped up for a while, soon lapses again into its lazy habits.

* *Author's conclusion.*

146 Kraïnsky: *Loc. cit.*

147 Inouye and Saiki: Hoppe-Seyler's Zeit. f. physiol. Chemie, Bd. xxxvii, S. 203, 1903.

148 Herter and Smith: N. Y. Med. Jour., Sept. 3, 1892.

149 Teeter; Amer. Jour. of Insanity, Jan., 1895.

150 Donath: Hoppe-Seyler's Zeit. f. physiol. Chemie, Bd. xxxix, S. 526, 1903.

151 Coriat: Amer. Jour. of Physiol., Dec. 1, 1904.

152 Ohlmacher: Amer. Jour. of Insanity, Apr., 1900.

153 Murdoch: Med. News, July 15, 1905.

154 Langlois: Richet's "Dict. de Physiol.," vol. i, p. 145, 1895.

155 Clark and Prout: Med. Record, Nov. 24, 1900.

156 Benedikt: Intern. klin. Rundschau, Nu. 46, 1891.

157 Lenoir: Thèse de Paris, 1901.

158 Hessler: Jour. Amer. Med. Assoc., May 14, 1898.

The main predisposing causes of idiopathic epilepsy are such as tend to inhibit the functional efficiency of the anterior pituitary body's test-organ.* The preponderance of this disease during youth is due mainly to one of two causes: (1) numerous diseases during childhood, which tend to debilitate this organ by stimulating excessively the pituitary body and through it the adrenals during development; (2) inherited general debility through the presence in parents of diseases or habits, such as tuberculosis, syphilis, alcoholism, etc., which tend to impair to a marked extent the test-organ's sensibility.* Epilepsy may also follow typhoid fever, influenza and other diseases, owing to this morbid influence on this organ.

Over twenty years ago I[161] emphasized, after studying 40 cases, the predisposing importance of numerous children's diseases to hay-fever, a disease due also to the accumulation of toxic wastes in the blood. Out of 19 of these cases in which no heredity could be traced, 82 per cent. had had four children's diseases, while many of these, *i.e.*, 55 per cent. of the total, had had six. Bessière,[162] in a series of carefully analyzed cases of major epilepsy, could only ascribe one-sixth to hereditary influence, while in the other 152 cases infectious diseases and convulsions showed "an enormous preponderance in the antecedents." . . . . "The infectious process," says this observer, "leaves on the organism a profound impression, the nature of which is still to be determined." Out of 2000 cases studied by M. Allen Starr,[163] 68 per cent. had epilepsy before twenty years of age, *i.e.*, "during brain development." The neural portion of the pituitary body being an embryological offshoot of the brain-segment, it follows that it must participate in the morbid process. Indeed, the relationship between this organ and the osseous system is well shown by the overgrowth of bones attending its overactivity in acromegaly; that the opposite condition exists in epilepsy is evident. Gowers[164] found a history of rickets in nearly 75 per cent. of 100 cases studied.

The transmission of epilepsy has been affirmed by Obersteiner[165] and others, but, from my viewpoint, the patient inherits only a depraved condition of the test-organ. Hence the fact that experimental epilepsy in guinea-pigs, as noted by several investigators, has failed to sustain Obersteiner's view. The predisposing influence of debilitating diseases, tuberculosis, syphilis, alcoholism, etc., in parents is generally acknowledged, and is readily accounted for by the morbid action of such diseases (*q.v.*) on the pituitary body. Examples in which various diseases

* *Author's conclusion.*

159 Lannois: Lyon médical, vol. xcv, p. 37, 1900.

160 Pierce Clark and Sharp: Med. News, Dec. 1, 1900.

161 Sajous: "Lectures on Dis. of the Nose and Throat," p. 176, 1885.

162 Bessière: Thèse de Paris, 1895.

163 M. Allen Starr: Med. News, Jan. 9, 1904.

164 Cited by Ohlmacher: Amer. Jour. of Insanity, Apr., 1900.

165 Obersteiner: Neurol. Centralbl., Bd. xix, S. 498, 1900.

started epilepsy are numerous. Bourneville and Dardel[166] observed a case in which typhoid fever caused both epilepsy and idiocy in a previously normal subject. In one of Gélineau's[167] it followed influenza. In one reported by Clark and Sharp[168] measles converted an ordinary epilepsy into status epilepticus, etc.

Emotional shock and fright, by imposing too suddenly a severe stress upon the cellular elements of the posterior pituitary (as *sensorium commune*), may also provoke typical epilepsy, by impairing permanently their sensitiveness.* A constant flow of impulses from the periphery may initiate the form known as "reflex" epilepsy by fatiguing the organ's nerve-cells and similarly depressing its sensibility to impressions received through the anterior lobe and awakened by blood containing physiological waste-products.* The convulsions are caused by these wastes precisely as in typical cases of epilepsy, both in the reflex form and in that due to emotions, the former ceasing when the peripheral exciting cause is removed.*

Spratling[169] states that emotional shock and fright as causes of epilepsy do not receive the attention they should. In 1323 cases he traced 62 to this cause, some supervening immediately. Females around puberty predominate. In the 2000 cases studied by M. Allen Starr,[170] 119 were due to fright. The intense pallor, the relaxation of sphincters, the fainting, etc., often witnessed under such conditions exemplify the intensity of the shock upon the true *sensorium commune, i.e.*, the neural lobe of the pituitary, especially its sympathetic center.

As to reflex epilepsy, Brubaker[171] collected 15 cases in which irritation of the dental nerve, diseased or misplaced teeth caused epilepsy. Cases cured by the removal of aural growths or carious ossicles, etc., have been numerous. Ranney,[172] Gould[173] and others have reported cases cured by correcting defects of accommodation. Kafemann[174] found adenoids frequently in epileptics. Recently, St. Clair Thomson[175] reported a case six years after cessation of the seizures, cured by the removal of adenoids. Intestinal worms, phimosis, vesical and renal calculi, scars, etc., and many other morbid conditions may thus provoke epilepsy by control irritation transmitted by afferent sensory nerves, the fifth pair in the case of the head. A typical form of reflex epilepsy is that due to nasal exostoses, hypertrophies, etc. We have seen that Prus, by anæsthetizing the cortex with cocaine, prevented the fits caused by local excitation. Ten Siethoff[176] arrested oncoming fits in a man who had had epilepsy 20 years, by applying a 10-per-cent. solution of cocaine to the nasal mucous membrane; removal of neoplastic tissue therein cured the

* *Author's conclusion.*
[166] Bourneville and Dardel: Progrès médical, vol. xxvi, p. 26, 1898.
[167] Gélineau: Indépend. médicale, Mar. 21, 1900.
[168] Clark and Sharp: *Loc. cit.*
[169] Spratling: Amer. Medicine, Sept. 16, 1905.
[170] M. Allen Starr: *Loc. cit.*
[171] Brubaker: Jour. of Nerv. and Mental Dis., Feb., 1888.
[172] Ranney: N. Y. Med. Jour., Feb. 3, 10, 17, 1894.
[173] Gould: Amer. Medicine, July 5, 1902.
[174] Kafemann: Sarasohn: Dissert. Königsberg; Inter. Centralbl. f. Laryn., Rhin., u. verwandte Wissen., Nov., 1895.
[175] St. Clair Thomson: Practitioner, May, 1905.
[176] Ten Siethoff: Ann. des mal. de l'oreille, du larynx, etc., July, 1895.

case. Similar instances have been reported by others. Now, Cyon, we have seen, observed that immediately after removal of the pituitary body any amount of irritation, even ammonia, failed to excite reflex reactions which before the operation were readily obtained.

Jacksonian epilepsy differs from major epilepsy in that the cortex is the seat of a circumscribed lesion which, when hyperæmia of the brain of the kind just described occurs, serves as a local excitant. The cerebral lesion being localized, the impulses transmitted to the cord cause it to provoke clonic convulsions only in the group of muscles over which the area involved presides. So true is this that if the starting point of the premonitory tingling or numbness be carefully noted, *i.e.*, a toe, the fingers, the face, etc., Seguin's "signal symptoms," the location of the cerebral lesion may be exactly determined (cerebral localization), and the offending structure—a glioma, sclerotic patches, tumors, a syphilitic gumma, depressed bone, etc., in the motor zone in the great majority of instances.

In such cases the lesion acts as a foreign body, against which, when undue hyperæmia of the brain occurs, the cortex is projected and subjected to localized pressure and irritation—the spasmogenic factor.*

The evidences of secondary hyperæmia are also present in such cases at the site of the cortical lesion. Thus Joseph Collins[177] found in excised cortical tissue not only distention of the vessels with thickening and infiltration of their walls, but also proliferation of neuroglia. That marked vascular tension prevails is shown by occasional occurrence of cerebral hæmorrhage in young subjects, as in a case reported by Struppler;[178] the presence of congestion is shown by the choked disk, as in cases reported by Burr and W. J. Taylor,[179] evidence that we have here also the required pressure to engorge the neuroglia. From this to the formation of sclerosis there is but a step. Thus, Anglade[180] never found the neuroglia normal, and in some regions it had proliferated in the form of plaques, *i.e.*, areas of sclerosis.

Treatment.—The prevailing medicinal treatment of epilepsy may be said to resolve itself into the use of depresso-motors to prevent the convulsions. In the light of the foregoing evidence these agents, while reducing the number of seizures, simultaneously aggravate the morbid process.*

Measures Which Tend to Enhance the Accumulation of Waste-products in the Blood.—*Bromide Salts.*—The pri-

* *Author's conclusion.*
[177] Joseph Collins: Brain, vol. xix, p. 366, 1896.
[178] Struppler: Deut. med. Woch., Bd. xxvi, S. 191, 1900.
[179] Burr and Taylor: Amer. Jour. Med. Sci., July, 1902.
[180] Anglade: *Loc. cit.*

mary action of these salts is to depress the functional activity of the general vasomotor center, producing thereby relaxation of all the arteries.* By thus causing the blood to accumulate in the great central trunks, the proportion of blood circulating in the capillaries of all organs and the periphery is correspondingly reduced and the activity of intracellular metabolism is lowered in proportion.* This morbid process is aggravated by the fact that the bromides simultaneously reduce the sensibility of the adrenal center.* By thus diminishing the quantity of adrenal secretion supplied to the blood, they impair its catabolizing properties, and inhibit, therefore, the conversion of toxic wastes into eliminable products.* These pathogenic influences are proportionate, all else being equal, with the quantity administered in a given time.

The action of the bromides on the vasomotor center has been shown in the department of Pharmacodynamics. The paralyzing action on the adrenals is sufficient in some instances to cause bronzing similar to that of Addison's disease. Bourneville and Chapotin[181] refer to Echeverria,[182] "who saw a case in which the brow and neck were markedly pigmented brown," and to cases witnessed by Voisin; in one of these "the skin of the face was a dark, dirty yellow," in the other it was "covered with bronze patches having no connection with the acne." The harmful effects of the bromides are being generally recognized. F. Peterson[183] has reported 11 cases in which withdrawal or marked reduction of the drug was followed by great diminution of the number of seizures. "In some of these cases," says this neurologist, "the improvement is startling." Spratling,[184] after close study of the results in several thousand cases at the Craig Colony, concludes that "we must not only regard the bromides as powerless to cure epilepsy," but also "as capable of doing as much harm as they do good, as they are ordinarily administered." Moreover, as Percy Bryant[185] rightly states, the bromides have added another disease in many epileptics, *i.e.*, bromism.

The bromides have been administered with *adonis vernalis*, as Bechterew's method, and with *digitalis*, as recommended by Huchard; but the recession of the blood from the tissues, caused by the bromides, thwarts the effects of these agents, and the cases on record do not seem to have afforded results other than those afforded by the salts themselves in corresponding doses.

Other Drugs Which Tend to Inhibit Tissue Metabolism.—Many such have been and are being used. Their main action is alone given in this connection, the reader being referred to the department of Pharmacodynamics for additional details and evidence. *Chloral, chloralose* and *paraldehyde* are even more pernicious than the bromides, since they depress primarily the adrenal center and therefore the activity of tissue metabolism and oxidation in the blood-stream. *Sulphonal* and *trional* produce similar effects in a different way: being active reducing agents, they diminish the oxygenizing and oxidizing (antitoxic) power of the blood, by robbing it of its oxygen. They inhibit the seizures by reducing the vital activity of all organs, including the nerve-centers.

Opium, used in increasing doses, as in Flechsig's method, sometimes diminishes the number of seizures. It does this by causing constriction of the arterioles, thus reducing the speed of the blood supplied to the nervous system, as well as to other tissues. Cellular metabolism, as observed by Reichert, is reduced from 26 to 62 per cent. *Antipyrin, acetanilid* and kindred coal-tar products reduce the fits in some cases. They do so, however, as do opium and morphine, by causing constriction of the arterioles. The lowered metabolism induced by these agents is shown by the effects of large doses, *i.e.*, cyanosis.

The bromides and other depressants have their place in the treatment of epilepsy, however, as shown below, but only to counteract the excessive irritability of the general vasomotor center, while other measures are employed to antagonize the pathogenic elements in all idiopathic cases, *i.e.*, the poisons in the blood-stream.*

Dechlorinization.—Withholding common salt from the diet of patients (used to render them more susceptible to the effects of the bromides) is not to be recommended, even though temporary benefit follow, this benefit being due to impairment of the osmotic properties of the blood and of the vital processes in which sodium fulfills an important rôle. Metabolism being retarded, nutrient materials accumulate in the blood and ultimately lead to additional disorders.*

The influence of common salt on osmosis is well known; Jacques Loeb[186] has shown that "the Nations of the blood as well as of the sea-water are essential for the maintenance of life-phenomena." Dechlorinization cannot, therefore, but deteriorate the body. This was illustrated in 30 cases carefully studied five months by J. Voisin, R. Voisin and Krantz.[187] At first the seizures were fewer, but the patients relapsed into their usual state. Marked anorexia appeared, the patients having to force themselves or be forced to take food. Then followed melancholia, confusion, hallucinations of sight, taste, etc., the patients fearing that they were being poisoned. In addition, there were dyspepsia, fatigue, lumbar and muscular pain. Schlöss[188] and others had already observed that under this treatment the patients became weaker. Conversely, Enriquez and Grenet[189] found that the addition of large doses of sodium chloride during four months diminished the intensity and number of attacks. C. H. Hughes[190] has, however, correctly emphasized the fallacy of dechlorinization as a therapeutic measure.

* *Author's conclusion.*

[181] Bourneville and Chapotin: Progrès méd., vol. xxix, p. 1, 1900.

[182] Echeverria: Phila. Med. Times, Nov. 23, 30; Dec. 7, 14, 1872.

[183] F. Peterson: N. Y. Med. Jour., Sept. 25, 1897; Amer. Medicine, June 24, 1905.

[184] Spratling: N. Y. Med. Jour., Aug. 19, 1905.

[185] Percy Bryant: State Hosp. Bull., Oct., 1896.

[186] Jacques Loeb: Studies in General Physiol., Pt. ii, p. 556, 1905.

[187] J. Voisin, R. Voisin and Krantz: Bull. et mém. de la Soc. méd. des hôp. de Paris, vol. xxi, p. 1215, 1904.

[188] Schlöss: Wiener klin. Woch., Bd. xiv, S. 1124, 1901.

[189] Enriquez and Grenet: Arch. gén. de méd., vol. cxciii, p. 380, 1904.

[190] C. H. Hughes: Med. Fortnightly, Feb. 11, 1907.