

ACUTE INSUFFICIENCY OF THE SUPRARENALS.*

R. S. LAVENSON, M.D.

PHILADELPHIA.

It is interesting that a condition looked on as one of considerable importance by the French clinicians is accorded but the most indifferent consideration by those of other countries. Hemorrhage of the adrenals has been generally recognized as a common pathologic finding in still-born infants or those dying shortly after birth, and the literature of Italy, Germany and England contains occasional references to hemorrhage or other acute destructive lesions of the adrenals in adults. In none of the countries outside of France, however, has acute insufficiency of the adrenals become a factor in medical diagnosis in advanced life as well as in infants. It might be suggested that this state of affairs is but the result of the conservatism of the American, German, English and Italian clinicians contrasted with the somewhat more unstable, fanciful attitude of their French brethren. That a symptom-complex dependent on acute insufficiency of the adrenals does occur, however, in such a striking form as to demand clinical recognition is well exemplified by the case which I have to bring before you.

Patient.—A woman, admitted to the University Hospital, where in the capacity of clinical assistant to Dr. Stengel, I had the opportunity of observing her during her illness and of subsequently performing the postmortem examination. She was a widow, 44 years of age, white, and a native of Ireland. The few elements of her family history that were obtainable had no bearing on her present condition. Her previous history revealed the fact that during the past seven years she had had infrequent attacks of asthma, and that during the past two years she had been subject to occasional attacks of abdominal pain with vomiting. During the past two years she had lost slightly in weight.

History of Illness.—On November 30, shortly after eating breakfast, and while in comparatively good health, the patient had an attack of vomiting, with some pain in the epigastrium, at the same time she felt weak and prostrated. A half hour later she drank a glass of water, when she again vomited. The pain in the epigastrium became more severe and the attacks of vomiting more frequent. During the afternoon there were frequent attacks of vomiting, and toward the evening the patient became slightly delirious. She was then seen by Dr. H. Kennedy Hill, who immediately sent her to the University Hospital. On admission to the hospital, temperature was 95, respiration 48, and no pulse could be felt. Vomiting had ceased by this time. The patient complained of pain in the epigastrium, and there was tenderness in this region and in the loins. The predominating symptoms were those of shock; the patient was extremely apa-

*Read in the Section on Practice of Medicine of the American Medical Association, at the Fifty-ninth Annual Session, held at Chicago, June, 1908.

thetic; her extremities were cold, the skin leaky and absolutely no radial pulse could be felt. During the earlier part of the next day the breathing became of the Cheyne-Stokes type.

Physical Examination.—The lungs were slightly emphysematous, and on respiration numerous dry râles could be heard. The upper border of the heart was on a level with the fourth rib; the right border at the right border of the sternum; the left border about a quarter of an inch outside of the left mid-clavicular line; the apex-beat was in the fifth interspace in the midclavicular; the cardiac sounds were weak and somewhat obscured by the respiratory râles; no murmurs could be detected. The tenderness in the epigastrium and in the loins persisted. There was slight rigidity of the abdominal wall, but no distention. The extremities were cold and slightly cyanosed.

Urinalysis.—Straw colored; slight brownish sediment; acid; specific gravity, 1002; no sugar or albumin; a small amount of mucus; a few leucocytes.

Blood Examination.—Hemoglobin, 61 per cent.; erythrocytes, 4,930,000; leucocytes, 52,800.

Clinical Course.—With vigorous stimulation during the day after admission, the patient reacted slightly, her temperature becoming 100 at noon on the day following admission. This reaction lasted for but a short time, the patient dying at 8 o'clock in the evening following her admission, or about thirty-six hours after the onset of the illness. Respiration had remained in the neighborhood of 48; the radial pulse had at no time become palpable. As counted by auscultation, the heart beat from 120 to 140 times per minute.

It is almost needless to emphasize how impressive a clinical picture the patient presented—the suddenness of onset, the vomiting, the epigastric pain, the lumbar tenderness, and, above all, the profound shock formed a most striking group of symptoms. In the light of our knowledge at the time, it resembled most acute hemorrhagic pancreatitis, though the shock was more profound and the vomiting and epigastric tenderness less marked than would have been expected in this condition.

The autopsy revealed the interesting and unexpected nature of the affection. The following brief notes are abstracted:

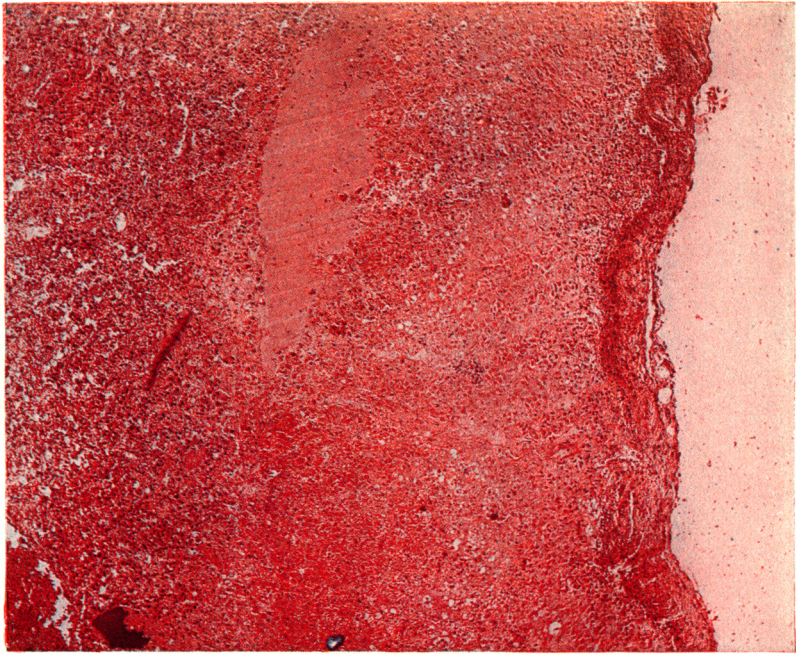
Pathologic Report.—The lungs showed, macroscopically and microscopically, a moderate degree of emphysema with slight hypostatic congestion. The heart was of normal size; both ventricles were relaxed; the cavities and walls were of normal proportions; the valves were soft and competent; the coronary arteries were slightly sclerotic; the muscle was somewhat grayer than normal. Microscopically, the heart muscle presented the picture of a slight, chronic fibrous myocarditis. The peritoneum was smooth and glistening. The uterus and appendages, aside from slight atrophy, presented no pathologic features. The kidneys were of normal size; their consistency considerably increased; the capsule stripped with some difficulty, but did not tear the kidney substance; the surface was slightly granular and showed a number of dark-based depressions and a few small cysts containing clear fluid. The microscopic features were characteristic of an arteriosclerotic, chronic interstitial nephritis of moderate degree. The stomach showed itself to be the seat of a chronic catarrhal gastritis. The intestines were without noteworthy characteristics, except for considerable venous congestion. The spleen was slightly enlarged and softer than normal. The liver was of normal size, its consistency slightly reduced; the organ was paler than normal, its structure somewhat obscured. The microscopic examination revealed fatty degeneration with early periportal fibrosis. The bile ducts were patulous; there

were no gallstones. The pancreas was of normal size, the consistency increased, the structure somewhat obscured; on squeezing the organ, a few droplets of turbid, yellowish fluid were expressed from the smaller ducts; several pinhead-sized areas of fat necrosis were found in the peri-pancreatic fat. Microscopically, a distinct interlobular and intralobular fibrosis was seen, with some atrophy of the secreting cells; there was no necrosis; in the interlobular tissue, especially in the neighborhood of the ducts, there was a diffuse, polynuclear leucocytic infiltration of moderate degree. Both suprarenals were enlarged and soft, and presented on section a dark-red, homogeneous appearance; both suprarenal veins were thrombosed. Microscopically, there was almost complete destruction of the gland substance; with the exception of small, scattered islands, the parenchyma of the cortex stained a homogeneous pink with hematoxylin and eosin. Nuclei of the connective tissue cells of the stroma were preserved here and there, but scarcely any epithelial nuclei were visible. Scattered throughout this necrotic tissue were hemorrhagic extravasations of various size. There was considerable hemorrhage into the medulla, but less cellular and nuclear destruction than in the cortex. Cultures from the pancreas showed staphylococci, colon bacilli, and a non-identified Gram-positive bacillus. Cultures from the suprarenals were negative.

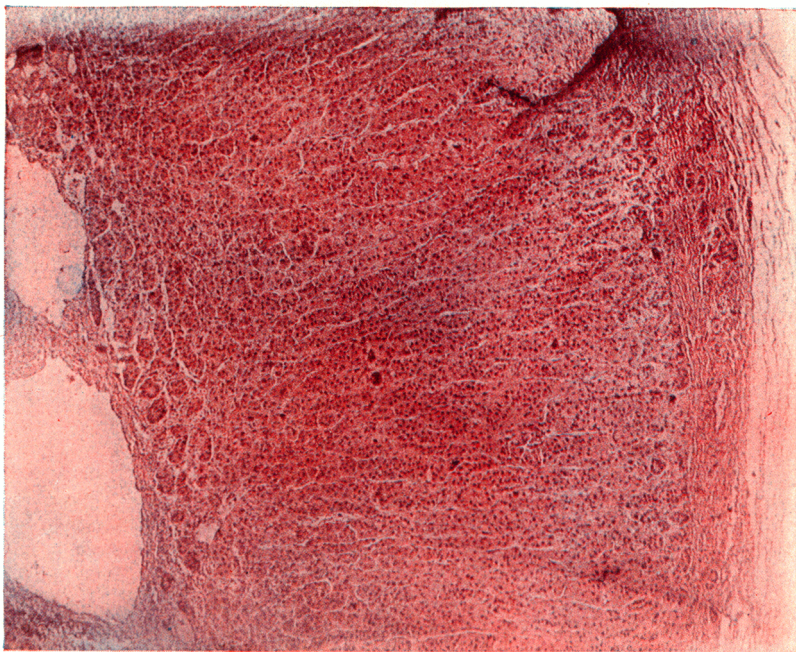
Pathologic Diagnosis.—Emphysema and hypostatic congestion of the lungs; chronic fibrous myocarditis, chronic interstitial nephritis; chronic catarrhal gastritis; acute splenic tumor; fatty degeneration of the liver, with beginning periportal cirrhosis; chronic pancreatitis, with acute interlobular suppurative pancreatitis; thrombosis of the suprarenal veins and acute hemorrhagic necrosis of the suprarenals.

My interpretation of these pathologic findings in their relation to the clinical phenomena is that the woman had a chronic pancreatitis of probably some years duration. Recently an acute suppurative inflammation was engrafted on this, the suprarenal veins became thrombosed as a result of this neighboring inflammation, and the hemorrhagic necrosis of the suprarenals resulted. The remaining pathologic features were for the most part the result of the existing arteriosclerosis.

Almost the only two conditions characterized by insufficiency of the suprarenals are hemorrhage and so-called adrenalitis. These two can be neither clinically or pathologically well differentiated in most cases. Adrenalitis is in the vast majority of cases not a true inflammation, as the term would imply, but a necrotic process, with which more or less hemorrhagic extravasation is always associated. When both necrosis and hemorrhage are present the two are generally the common results of the same condition, a vascular thrombosis. On the other hand, a number of the cases do present the clinical and pathologic features characteristic of simple hemorrhage. Many of these cases, by reason of the suddenness of the insult and the frankness of the hemorrhage, are appropriately termed adrenal apoplexies. The relation of suprarenal hemorrhage to acute hemorrhagic adrenalitis may be perhaps better understood by calling attention to the analogy that at least pathologically exists



Laminate photomicrograph of necrotic suprapneumal. Section stained with hematoxylin and eosin.



Laminate photomicrograph of normal suprapneumal. Section stained with hematoxylin and eosin.

between them and pancreatic hemorrhage and acute hemorrhagic pancreatitis.

I have been able to find but two cases in which insufficiency of the adrenals was dependent on other pathologic lesions than hemorrhage or necrosis. One is the case of Janowski,¹ in which the two adrenals formed small abscesses above the two kidneys. The other is the case of Stursberg,² in which suppuration was found in both suprarenals of a woman suffering from Pott's disease. It is not improbable that the glands in this case were tuberculous.

Confining our attention then to necrosis and hemorrhage, let us determine what the factors are bearing on these two conditions. The extraordinarily rich vascularization of the organs naturally impresses itself as standing in some relation to the frequency of hemorrhage. The gland receives its blood supply from three sources, the aorta, the renal artery, and the arteries of the diaphragm. The arterioles and the capillaries from these sources form a dense network about the cells of the cortex, and the capillaries and venules finally unite in the inner cortical layers and medulla to form a single vein, which emerges at the hilus of the organ. The facts that such a large amount of blood unites to enter one vessel in the medulla, and that extensive hemorrhages usually seem to occur into the medulla, suggest that simple alterations in the blood supply or blood pressure of the organ may be the determining factors in the production of the hemorrhage. This hypothesis has been put forth as especially applicable to hemorrhage of the adrenals so frequently found in the new-born. The great increase in intra-abdominal pressure in the child, incident to the uterine contractions, and especially the pressure of the liver on the vena cava just above the suprarenals, have both been thought to be the direct cause of increasing the adrenal blood pressure sufficiently to induce hemorrhage. This view receives some support from the fact that when hemorrhage has occurred into only one of the suprarenals, it has been more frequently on the right than on the left (according to Hamill,³ fifteen times in twenty-four cases), and the right vein enters the vena cava directly, while the left enters it through the renal vein. These relations would naturally subject the vessels of the right gland to greater pressure than the left in the presence of any cause obstructing the return of venous blood.

Chronic heart disease associated with passive congestion has been observed in a number of cases, and has thus been looked on as a causal factor.

1. Janowski: *Gaz. lek.*, 1898, liv, 354.

2. Stursberg: *Deutsch. med. Wchnschr.*, 1904, xxx, 1406.

3. Hamill: *Arch. Pediat.*, 1901, xviii, 161.

Similarly, chronic pulmonary disease has been not infrequently found in these cases, and it is possible that the chronic passive congestion resulting therefrom has been an active factor in the production of hemorrhage.

A certain number of cases have been observed in which death has resulted after the occurrence of phenomena tending to a great increase in blood pressure, and in which, at autopsy, hemorrhage of the suprarenals was found. A striking example of this is a case reported by Ogle⁴ of an epileptic dying after two weeks of almost continuous convulsions. At the autopsy hemorrhage into both suprarenals was discovered. I believe that it is not improbable that in some of the cases said to have manifested themselves clinically by convulsions these were the cause rather than the result of the hemorrhage, induced by the great increase in blood pressure incident to the convulsions. Duckworth⁵ refers to a case in which the paroxysms of coughing in a child with pertussis apparently induced hemorrhages into both adrenals.

The great tendency to hemorrhage throughout the body in asphyxia, in all probability as the result of venous engorgement, has caused it to be looked on as one of the possible factors in the production of suprarenal hemorrhages, especially in the new-born. A factor emphasized by Spencer⁶ as responsible for the greater frequency of suprarenal hemorrhages in infancy is the normal delicacy of the blood-vessel walls in this period of life.

Thus far we have dealt with only passive congestions. It has been asserted that active congestion also plays a rôle in the production of adrenal hemorrhage. One of the functions attributed to the suprarenal capsule is that of neutralizing toxins, and it is said that the functional activity of the gland in the presence of a toxic agent in the body so increases its blood supply as to lead to hemorrhage.

It is doubtful, however, if it is alone by increasing the blood supply to the gland that infections and intoxications act in inducing insufficiency of the suprarenals. In a number of cases organisms have been isolated directly from the adrenal glands, the seat of hemorrhage and necrosis. Klebs and Eppinger⁷ isolated an organism in several cases of suprarenal hemorrhage in the new-born, which they called *Mona hemorrhagica*. Gaertner⁸ isolated a bacillus resembling the colon bacillus, and

4. Ogle: Tr. Path. Soc., London, 1863, xiv, 127.

5. Duckworth: Twentieth Century Practice of Medicine, ii.

6. Spencer: Tr. Obst. Soc., Lond., 1891, xxxiii, 203.

7. Klebs and Eppinger: Boston Med. and Surg. Jour., 1891.

8. Gaertner: Arch. f. Kinderh., 1895.

Riesman⁹ the *Staphylococcus albus* and *aureus* from four out of six cases occurring within a short space of time.

Experimentally, hemorrhage and acute destructive lesions of the glands have been produced by Roux and Yersin¹⁰ by inoculating rabbits and guinea-pigs with diphtheria bacilli; by Charrin and Langlois¹¹ with the *Bacillus pyocyaneus*; and by Roger¹² with the bacillus of Friedlander. Pettit,¹³ Pilliet¹⁴ and Wibaud¹⁵ have confirmed these results. Oppenheim and Loeper¹⁶ have produced similar results by injecting the toxins of Friedlander's bacillus, of the diphtheria bacillus and the tetanus bacillus, as well as by arsenic, phosphorus and mercury. Practically the same results were obtained by Bernard and Bigart¹⁷ in injecting various metallic poisons.

Adrenal hemorrhage associated with a general purpuric eruption can be looked on only as a visceral manifestation of a general hemorrhage tendency. As the purpuras of childhood are practically always infectious, the functional activity of the gland as the result of the infection, according to the above-mentioned hypothesis, probably increases its predisposition as a seat of hemorrhage.

Trauma does not seem to play a very important rôle in the production of acute destructive suprarenal lesions. In but two cases, those of Canton¹⁸ and Mattei,¹⁹ does trauma seem to have been the cause of the adrenal hemorrhage found subsequently at autopsy. The secluded, well-protected position of the adrenals is probably the cause of its being so infrequently affected by trauma.

In the cases of Arnaud,²⁰ Churton²¹ and Dudgeon²² adrenal hemorrhage was apparently induced by severe surface burns. In Dudgeon's and Arnaud's cases there were symptoms of adrenal insufficiency before death. This association suggests that which exists between surface burns

9. Riesman, quoted by Hamill: Arch. Pediat., 1901, xviii, 161.

10. Roux and Yersin: Ann. de l'Inst. Pasteur, 1889.

11. Charrin and Langlois: Compt. rend. Soc. biol., 1896, Series 10, iii.

12. Roger: Presse méd., 1894, i, 35.

13. Pettit: Thèse de Paris, 1896.

14. Pilliet: Arch. de physiol. norm. et path., Series 5, F. 7.

15. Wibaud: Etude des capsules surrénales dans les maladies infectieuses expérimentales, Brussels, 1897.

16. Oppenheim and Loeper: Arch. de méd. expér., 1901, xiii, 332.

17. Bernard and Bigart: Jour. de physiol. et de path. gén., 1902, iv, 1014.

18. Canton: Tr. Path. Soc. Lond., 1863, xiv, 257.

19. Mattei: (Case 2) Sperimentale, 1883, li, 386.

20. Arnaud: (Case 1) Arch. gén. de méd., 1900, clxxxvi.

21. Churton: Lancet, London, 1886, i, 245.

22. Dudgeon: (Case 2) Am. Jour. Med. Sc., 1904, cxxvii, 134.

and duodenal ulcer. Whether the adrenal lesion results from internal congestion, toxic products or embolism is quite as much open to question as the pathogenesis of duodenal ulcer.

Suppurative inflammations of adjacent organs has apparently been the cause of necrosis and hemorrhage of the suprarenals, with the clinical signs of insufficiency in three cases—my own and two of Arnaud's.²³ In one of Arnaud's cases the neighboring lesion was an abscess of the liver, in the other a suppurating hydatid cyst of the liver. In all three cases thrombosis of the adrenal veins was apparently the immediate cause of the changes in the glands. It is possible that pneumonia acts in the same way in producing acute insufficiency of the adrenals as to these lesions of neighboring abdominal viscera.

The appearance of the gland varies with the nature and extent of the lesion. Simple hemorrhages usually occur into the medulla of the organ. If of small size the hemorrhage merely distends the cortex slightly, producing but little destruction of its cellular elements. If of larger size it may so distend the organ that the cortex forms but a thin shell enclosing a large blood cyst. Rayer²⁴ records a case in which hemorrhage into a suprarenal gland resulted in a blood cyst weighing two kilos. Carrington²⁵ reports a case in which the suprarenals were transformed into cysts the size of large oranges, and in Routier's²⁶ case 1,600 cubic centimeters of a blackish-brown fluid were evacuated from a suprarenal, the seat of hemorrhage. At times the capsule of the gland ruptures, permitting the escape of blood either into the surrounding retroperitoneal tissues or into the peritoneal cavity itself.

When hemorrhages are multiple and small they are usually found in the cortex rather than in the medulla. In such cases more or less necrosis of the epithelial elements of the cortex is usually present. The necrosis and hemorrhage may be the common result of the same cause, thrombosis, or the necrosis may be either the cause or the result of the hemorrhage. Judging from the pathologic features of my case, venous thrombosis results in extensive necrosis with but slight hemorrhage. In such cases the gland presents macroscopically a homogeneous, reddish-brown appearance and a microscopic picture similar to that described in the above pathologic notes of my case.

The fact that the lesions are at times limited more or less to either cortex or medulla has led to an attempt to classify the symptomatology

23. Arnaud: (Cases 2 and 3) *Arch. gén. de méd.*, 1900, clxxxvi, 5.

24. Rayer: (Case 1) *Journal de l'expérience*, 1837.

25. Carrington: *Tr. Path. Soc., London*, 1885, xxxvi, 454.

26. Routier: *Bull. Soc. d'anat. de Paris*, 1895, 73.

according to the involvement of one or the other of these parts. Experimental evidence indicates that the functions of the cortex and medulla are different. The medulla seems to supply the elements having to do especially with the preservation of vascular tone, while the function of the cortex, aside probably from acting to an extent in a compensatory way for the medulla, appears to be the furnishing of an antitoxic agent to the body. In the majority of the cases of sudden death in adrenal insufficiency the hemorrhage does seem to have occurred into the medulla, but we are hardly justified in deducing from this fact the conclusion that this result attends destruction of only this portion of the gland. The functions of the adrenals are as yet too little understood and the limitations of the pathologic lesions involving them too poorly defined to warrant more than the statement that insults to the glands, regardless of their location or extent, may call forth certain profound symptoms such as will be described in the clinical discussion.

A study of the literature reveals a number of apparently incongruous relations requiring discussion. Numerous cases have been observed presenting the symptoms of acute suprarenal insufficiency in which only one of the glands was involved, the other being apparently normal. Why the compensatory action of the normal gland should not be capable of abolishing these symptoms is beyond the limitations of our pathologic knowledge to say. It is not improbable that our means of study are incapable of discovering lesions which, without destroying the morphologic integrity of the apparently normal organ, yet seriously interfere with its functions. A number of cases (those of Addison,²⁷ Goolden,²⁸ Carrington,²⁵ Greenhow,²⁹ and Mattei³⁰) have been reported in which the symptoms of Addison's disease were presented and in which at autopsy acute adrenal lesions were found. In all of them the diagnosis of Addison's disease, as judged by the reported symptoms, is open to doubt, but even were it authentic it is rational to consider that a chronic degenerative process would only predispose the gland to hemorrhage or other acute process which by its prominence could obscure the recognition of the chronic changes. An interesting group of cases is that in which the signs of acute suprarenal insufficiency occur, followed shortly by death, and at autopsy the destructive lesions of a chronic process are found in the suprarenals.

27. Addison: On the Constitutional and Local Effects of Disease of the Suprarenal Bodies (Case 10), London, 1855.

28. Goolden: *Lancet*, London, 1857, ii, 266.

29. Greenhow: *Lancet*, London, 1877, i, 349.

30. Mattei: (Case 3) *Sperimentale*, 1883, li, 386.

In regard to such cases it must be emphasized that the degree of tissue destruction is not always a measure of functional incapacity, and it is very possible that only when the destructive process has reached a certain degree, or involved certain elements, does it manifest itself clinically.

Since, as above stated, hemorrhage of the suprarenals and acute hemorrhagic adrenalitis can not be strictly differentiated either clinically or pathologically in the majority of cases, I shall not employ these two conditions as a basis for classification. The symptoms presented result from interference with the function of the adrenals, regardless of the agent inducing it. Even on the basis of the clinical phenomena I hesitate to attempt a classification for fear of confusing the reader in a maze of artificial grouping, for few of the cases conform to one type entirely distinct from the others. However, on the basis of the preponderance of one or another group of symptoms, I think that the following classification will serve as a basis for clinical consideration.

1. Cases of sudden onset with epigastric pain and tenderness, vomiting, profound prostration, feebleness and rapidity of pulse, coldness of extremities, lumbar tenderness, and at times diarrhea, and abdominal distention, followed within a few days by death. This is the symptom-complex that at times is called the peritoneal type of acute insufficiency of the adrenals, of which my case is a striking example. The literature of the subject contains a number of similar instances, among the most impressive of which are those of Stursberg,² Pritchard,³¹ Mattei,³² Arnaud,³³ Janowski¹ and Sotti.³⁴ The occurrence of the same group of symptoms in children is well exemplified by such cases as those of Batten,³⁵ Dudgeon,²² and the two cases of Talbot.³⁶ There is a striking resemblance between the cases of this type and many cases of acute hemorrhagic pancreatitis. Judging from the one case that I have observed, the shock is more profound, the lumbar tenderness more acute, and the epigastric pain and vomiting less pronounced in adrenalitis than is usually the case in acute hemorrhagic pancreatitis.

2. The asthenic type, in which the predominant feature is a profound asthenia ending within a few days in death. Instances of this

31. Pritchard: *Lancet*, London, 1890, i, 750.

32. Mattei: *Sperimentale*, 1863, ii, 3.

33. Arnaud: (Case 1) *Arch. gén. de méd.*, 1900, clxxxvi, 5.

34. Sotti: *Policlinico*, 1908, xv; *Sem. méd.*, 1.

35. Batten: *Tr. Path. Soc.*, London, 1893, xlv.

36. Talbot: *St. Barth. Hosp. Rep.*, 1900, xxxvi, 207.

type have been reported by Greenhow,²⁹ Murray,³⁷ Sicard³⁸ and Voisin and Norero,³⁹ all occurring in adults. In Sicard's case the asthenia was so pronounced as to give the case the appearance of an acute bulbo-spinal myasthenia. Interesting cases resembling those included in this group, except for their duration, are those reported by Marchand,⁴⁰ and Bernard and Heitz.⁴¹ In Marchand's case the duration was three months, in Bernard and Heitz's case five months. In both of them there was an extreme degree of asthenia, and at autopsy simple atrophy of the adrenals was found in both cases. Bernard and Heitz employ their case to justify them in originating a condition which they term subacute insufficiency of the suprarenals.

3. The nervous type, in which the predominant symptoms have been either convulsions, as in the cases of Portal,⁴² Valleix,⁴³ Parrot⁴⁴ and Droubaix;⁴⁵ or coma, as in the cases of Arnaud,⁴⁶ and Laignel-Lavastine;⁴⁷ or delirium, as in the cases of Mattei⁴⁸ and Ribadeau-Dumas and Bing;⁴⁹ or a typhoid state, as in the cases of Virchow⁵⁰ and Kohler.⁵¹ These varied symptoms have been noted in children, as well as in adults. In some of the cases in which convulsions have been a predominant feature I think it not improbable, as mentioned above, that they were the cause rather than the result of the injury to the adrenals.

4. Cases of sudden death. In this group I include the cases of sudden death in which at autopsy nothing except a destructive lesion of the adrenals, usually hemorrhage, has been found. It may be thought presumptuous in such cases to conclude that the sudden death was due to the adrenal lesion, but realizing from experimental evidence and from the clinical evidence of the more protracted cases how profound an influence destruction or injury of the suprarenals has on life, I think that it

37. Murray: Tr. Path. Soc., London, 1870, xxi, 395.

38. Sicard: Bull. Soc. méd. d'hôp. de Paris, 1904, xxi, 848.

39. Voisin and Norero: Bull. Soc. d'anat. de Paris, 1906, lxxxi, 320.

40. Marchand: Deutsch med. Wehnschr., 1903, xxix.

41. Bernard and Heitz: Tribune méd., 1904, New Series ii, 325.

42. Portal, quoted by Lieutaud: Historia anatomica, 1769, i, 285.

43. Valleix: Clinique des maladies des enfants nouveau-nés (Case 22). Paris, 1838.

44. Parrot: (Cases 10 and 11) Arch. gén. de méd., 1872, xix, 257.

45. Droubaix: Thèse de Paris (Case 1), 1887.

46. Arnaud: (Case 4) Arch. gén. de méd., 1900, clxxxvi, 5.

47. Laignel-Lavastine: Bull. Soc. anat. de Paris, 1902, lxxvii.

48. Mattei: (Case 1) Sperimentale, 1883, li, 386.

49. Ribadeau-Dumas and Bing: (Case 2) Bull. Soc. anat. de Paris, 1904, lxxix, 477.

50. Virchow, quoted by Lancereaux: Dict. encycl. d. sc. méd., 1875, iii, 155.

51. Kohler: Dict. encycl. d. sc. méd., 1875, iii, 155.

is a justifiable inference. This I believe to be true of still-born infants in whom this lesion is found, as well as in cases of advanced life. Instances of this type have been reported by Rayer⁵² and Goodhart,⁵³ and Hamill³ has collected the cases occurring in still-born infants and children reported up to the year 1900.

5. Cases occurring in association with a purpuric eruption or hemorrhages into the abdominal viscera. Numerous cases of this type occurring in children are reported in the literature. I have been able to find none occurring in adults. Undoubtedly the hemorrhage into the suprarenals in these cases is but a manifestation of the general hemorrhage tendency as a result either of infection, or, in some cases, possibly of asphyxia. The English clinicians have been inclined to look on these cases as possible instances of hemorrhagic smallpox, especially by reason of the fact that many of the affected children have been unvaccinated. As there is little else than this one fact in support of their view, I think it can not be looked on as a probable one.

Though the majority of cases permit themselves to be classified in one or another of the above groups, many are characterized by symptoms common to more than one group. The cases in which purpura is a prominent feature may present symptoms characteristic of the peritoneal or nervous type, and cases of the asthenic or nervous type may in addition present some symptoms belonging to the peritoneal type. Of all the symptoms the most constant and one of the most characteristic is a greater or less degree of asthenia. The occasional occurrence of two other symptoms is worthy of mention. They are tumor and the *ligne blanche* of Sergeant.⁵⁴ A tumor, the result of suprarenal hemorrhage, is mentioned as having been determined during life in three instances. In one of Rayer's²⁴ cases it involved the right suprarenal and presented itself in the epigastrium. In Routier's²⁶ case a hemorrhage into the left suprarenal formed a palpable tumor in the left hypochondrium. In Leconte's case there was a fluctuating tumor on each side of the mid-line extending from the hypochondrium to the iliac fossa. The *ligne blanche*, or white lines produced by stroking the skin with the finger, are looked on by Sergeant as being of great diagnostic value in suprarenal insufficiency. They result from the temporary constriction of the relaxed vessels. As the majority of observers agree that they can be produced in various conditions attended by vasomotor relaxation, I can not agree with Ser-

52. Rayer, quoted by Roger: Jour. de l'expérience, 1837.

53. Goodhart: New Sydenham Society's Atlas of Pathology, 1879, ii, 50.

54. Sergeant: Bull. Soc. méd. d'hôp. de Paris, 1904, xxi, 380.

55. Leconte: Thèse de Paris (Case 48), 1897.

gent in looking on them as diagnostic of adrenal insufficiency. As clinical investigation has as yet advanced no pathognomonic signs of the condition, it is only when the symptoms observe a sufficiently characteristic grouping that the possibility of diagnosis during life can be entertained. Attention should be paid to the relative frequency of the condition in the purpuras of childhood and during or shortly after the acute infections. An interesting case occurring subsequent to an acute infection is that reported by Sicard of a woman 33 years of age, who shortly after the crisis in Friedlander's pneumonia suddenly manifested a most profound asthenia; death occurred within a few days, and at autopsy hemorrhage and necrosis of both adrenals was found. Bousset⁵⁶ asserts that he has recognized acute insufficiency of the suprarenals as indicated by asthenia, arterial hypotension, nausea, vomiting and diarrhea eight times in the course of various acute infections and that he has caused their subsidence by hypodermic injections of adrenalin. Due consideration must be paid to the apparent etiologic relationship that exists between acute suprarenal insufficiency and inflammations in the neighborhood of the suprarenals, surface burns, chronic heart or pulmonary disease, and any phenomenon tending to a great increase in internal blood pressure.

Such cases as those of Laignel-Lavastine and Arnaud claim for acute suprarenal insufficiency a rôle of some importance as a possible factor in apoplectiform deaths. Both of the patients were men, respectively 36 and 47 years of age, apparently previously in good health, who suddenly fell unconscious and died in coma, one twelve hours, the other forty-eight hours after the onset. At autopsy the only finding of note was hemorrhage into the suprarenals. When physiology has taught us more of the functions of the suprarenals, and when they are subjected to a more rigid routine postmortem examination, and when clinicians pay more attention to the facts already determined, I have no doubt that acute suprarenal insufficiency will assume a position of greater clinical importance than it has maintained in the past.

328 South Sixteenth Street.

56. Bousset: *Gaz. hebdomadaire de médecine de Bordeaux*, 1904, xix.