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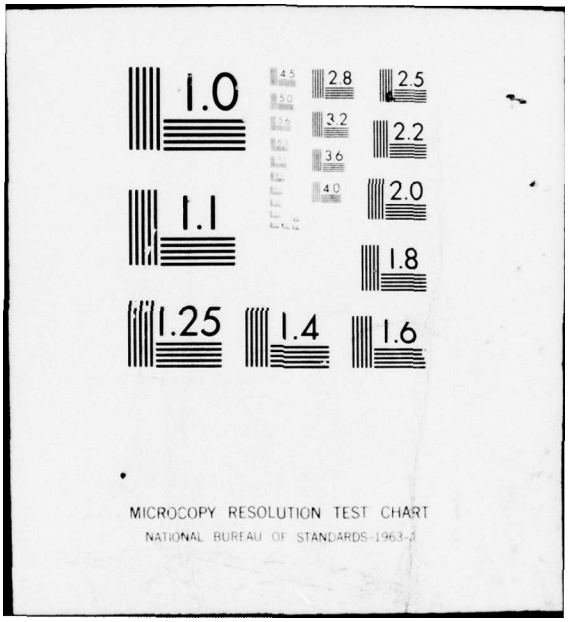
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12 pp

(14) USAMRIID

TRANSLATION NO.: -MUL-0532

(11) 2 Jun 77

(12) 19p.

(6) TITLE: Suprarenal Apoplexia in Small Children

(10) AUTHOR(S): C. Friderichsen

(21) Transl. from

REFERENCE: Jabrb. F. Kinderh., 87, 109-125, 1918.

(Denmark)

DISTRIBUTION STATEMENT

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distribution unlimited

U. S. ARMY MEDICAL RESEARCH INSTITUTE OF INFECTIOUS DISEASES

Fort Detrick, Frederick, Maryland 21701

405 039

SECURITY CLASSIFICATION OF THIS PAGE *(When Data Entered)*

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE *(and Subtitle)* Suprarenal Apoplexia in Small Children		5. TYPE OF REPORT & PERIOD COVERED Translation
		6. PERFORMING ORG. REPORT NUMBER MUL 0532 ✓
7. AUTHOR(s) C. Friderichsen		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS Jahrb. F. Kinderh. 87-109-125, 1918		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS USAMRIID Library ✓ Fort Detrick Frederick, Md. 21701		12. REPORT DATE 2 June 1977 13. NUMBER OF PAGES 26
14. MONITORING AGENCY NAME & ADDRESS*(if different from Controlling Office)*		15. SECURITY CLASS. *(of this report)* Unclassified 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT *(of this Report)*

Approved for public release: distribution unlimited.

17. DISTRIBUTION STATEMENT *(of the abstract entered in Block 20, if different from Report)*

18. SUPPLEMENTARY NOTES

19. KEY WORDS *(Continue on reverse side if necessary and identify by block number)*

Suprarenal Apoplexia
Hemorrhage
Addison's Disease

20. ABSTRACT *(Continue on reverse side if necessary and identify by block number)*

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SECURITY CLASSIFICATION OF THIS PAGE *(When Data Entered)*

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MUL 0532

Suprarenal Apoplexia in Small Children

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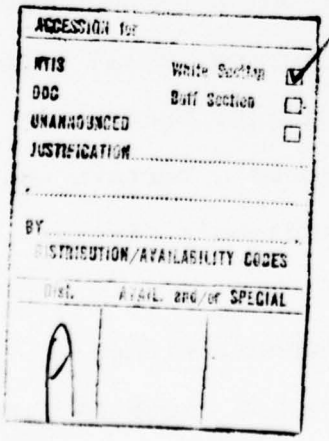

Jahrb. F. Kinderh.
87: 109 (1918)

MUL 0532

While, in recent years, a number of experimental and clinical observations have been made concerning the importance of the suprarenal glands to growth, as well as their relationship to problems of the central nervous system and the genital sphere, the pathology of the suprarenal glands today still concentrates itself, primarily, with the clinical picture of Addison's disease. Other than of this disease, we still know very little about other diseases that can occur in these organs. Hemmorrhagias, degenerations, inflammations, atrophy and tumors can attack it, destroy the parenchyma and destroy its physiological function. In spite of the fact that these various anatomical changes occur not very infrequently, the syndrome of Addison's disease can be proven only very rarely and experimental pathology still searches for the reason of this disagreement.

If, therefore, I have permitted myself to report on some suprarenal hemorrhages in small children (i.e. such that were older than a few months) is presented, this is done, on the one hand, because it appears that we are confronted with a group of suprarenal diseases, that do not present individual characteristic clinical symptoms. They may, in spite of their lack of being pathognomic in relation to the remainder of the clinical picture, still possibly be able to aid in its delineation -- partially, because it does present a symptom, in which there seems to be a certain analogy to the chronic suprarenal destruction: Addison's disease (bronzed skin disease).

While suprarenal hemorrhages in the newborn, either directly after birth or shortly thereafter, are not uncommon find-

ings, they must be counted as rarities, when they occur at a later infant age. In that case, the disease is generally bilateral, symmetric and its course is so acute that we find oursleves confronted with a sudden case of death. It may also be of forensic importance to be able to interpret and diagnose these cases.

I. My first case was that of a 6 month old boy, who had been breast fed for three months and subsequently was given pasteurized milk. He had always been completely healthy; nothing was wrong with him yesterday, he played and drank well, twice had natural defection and slept through the night. Suddenly awoke this morning with a scream, first became pale and then cyanotic. Lay quietly whimpering, with obvious fear on his face. Twice during the course of the forenoon some thin saring defecation without visible blood. Had drunk well and was well wet. Temperature at 10 AM 41.3°. No cough. Cyanosis considerably on the increase and very changable, occasionally completely pale, at other times the body and face completely blue. Is admitted to the hospital on Jan. 22, 1917 at 12 noon under diagnosis of pneumonia.

The child is in good nutritional condition, strong and big. Face, hands and oral cavity completely blue, fontanel is slack. Respiration not increased, approx. 30, but very irregular, occasionally of a Cheyne-Stokes type. Pulse small and soft. Pulmonary stet. normal conditions. Thymus damping not increased. Stet. cord.: the action quite irregular, occasionally 60, sometimes 180. The limits are natural, the sounds pure, no echo, but both heart sounds present. Abdomen is soft and inflated,

percussion sounds tympanitic. No organ swelling no vein outlines. Is somewhat sensitive to deep pressure. Exploration shows no blood. Temperature 41.2. Scattered on chest and back one sees, along with strongly changing cyanosis some small petechiae; in short duration many and pea-sized purpura-sport appear all over the body, the extremities and the face. These gradually assume a black-blue coloring and expend into hand-sized suffusions. The child is unconscious. Temperature 40.1°-, he dies quietly two hours after admission, about three hours after the outbreak of the petechiae and 6 hours subsequent to the first sign of illness.

Autopsy: Nutritional condition good. No problems of the lowest epiphysis femoris. An exanthema is found, spread over the entire body, but more pronounced on the front- than on the back- side, especially expressed in the face. This consists of very small to penny-sized spots, bluish-red, some of which confluate. On the buttocks and the underside of the scrotum in the skin crusty, peasized deep-black areas. In the mouth and throat, no signs of angina, diptheria or any other infection. No indications of lymphadenitis. Neck organ normal. Thymus, large-30 grams. Lymphatic glands hyperemic. Chest organs: No adhesions nor fluids in the pleural space. The lungs swim with ease on water. Some serious foaming liquid in the bronchia. The bronchial-hilusmesenterial glands somewhat hyperemic. Heart, pericardium - Zero, esophagus, ventricles, intestine, liver, pancreas, kidneys - Zero. Both suprarenal glands enlarged and dark red. Connective tissue capsule in good condition, no signs of

rupture, nor of blood outside. Suprarenal vessels normal, no signs of thromboses.

Microscopy: In many sections, dyed with hematoxylin-Eosine and hematoxylin - van Gieson, the suprarenal glands are the seat of considerable bleeding, in which the blood corpuscles have stuffed, so to say, the entire suprarenal tissue. The blood shows the most in the reticular zone as well as in the medullary area, where the normal cells have been displaced, so that only small islets of nuclear stained material can be found. No indications of degeneration and no necrotic parts. The outline of the connective tissue is well preserved. In several places cut lumina can be seen, of apparently dilated capillaries some filled with blood corpuscles, some empty, while in the tissue all around, one can see, between the cells of the cortical substance, many blood corpuscles that appear to have been packed together. In cuts of the frontal portion of the suprarenals, one can see, in some places of the cortical substance, a hemorrhage to large, that the glandular tissues have been completely pushed aside, to that, in a manner, a blood cyst has formed itself, but without any indication of organization. No signs of pigment or old bleeding.

The apparently dilated vessels are found far towards the outside of the connective tissue capsule, whcih is ruptures in individual places, so that fine bodies of blood form themselves outside of it. While the capillaries of the medulla and of the cortex are dilated, the vessels on the outside of the cortex appear normal and do not seem to be surrounded by blood particles.

The skin: On cuts taken from the purpura eruption of the nates, the tela subcutanea is strongly vascularized. The vessels are dilated and filled with blood, on a single location, the vessel is ruptured and a small amount of blood has been pushed out into the tissue. On a transverse cut of one of the interpapillary vessels, this is ruptured and the surrounding area is filled with blood corpuscles. No indication of bacteria, neither in Gram's nor in Una-Pappenheim's coloring. No plasma cells, indications of inflammation nor degeneration. No thromboses nor indicia of organization.

The lungs: No indications of hemorrhaging or of pneumonic infiltration.

In a culture from the blood, one obtains a small gram-negative diplococcus, that does not take in mice.

Section diagnosis: Exanthema cuteana (skin eruption), serous bronchitis of a low degree, suprarenal gland hemorrage. "utriusque" (?)

A survey of the case histories of the Queen Louise Hospital in Copenhagen resulted in:

II. Ten months old girl. Admitted May 14, 1909. Bottle baby. Was, ten days prior released after a 3½ months stay because of an exzema on face and on the scalp from the IV department of the Community Hospital. Since then complete well-being until this morning, when she was peevish and indisposed, and would not accept food. Vomited once. Temperature at 6 o'clock: 39.6°. Somewhat later in the day a sudden blue-red exanthema. Respiration 92, gasping; pulse not to be felt. Was admitted at

eleven o'clock as moribunda. Temperature 38.4^0. Fontanelle depressed. Tongue dry. No bleeding from the gums. Medium degree of rickets. Stet pulm. and cord. normal. Spleen: one finger, liver, two fingers below the curvature. Some edema on the left lower extremity. On the face, the upper portion of the body, the arms and the lower extremities as well as on the bottox, one can see many scattered, sometimes individual, sometimes confluent petechiae of the size of a pea, sometimes bulging from the level of the skin. The color of the smallest ones is a lighter red, that of the larger, dark black-violet, all intermediate colors are present.

Two hours after admission, the petechiae have considerably increased both in size and number, they have spread, but none are yet found on back or abdomen.

Death 3 hours after admission, 9 hours after the first signs of sickness.

Autopsy: Small for her age, but well-nourished. Everywhere on the skin a large number of hemorrhages of small petechiae to more than pea-sized confluent suggilations. On the costal cartilage, medium strong ricketts. Intestines pale, some inidvidual petechiae on the serosa; spleen hyperemic. Liver, pancreas, bile ducts normal. Hemorrhaging in both suprarenals, so that these are changed into walnut-sized hematomas. No change in the vessels to the suprarenals. Kidneys somewhat swollen with grey corticalis. Diagnosis: Hemorrhage of the suprarenal glands (utriuspue). Skin hemorrages.

In the review of the case histories of the last ten years

in the Community Hospital, I only found one case, and that in a 14-year old boy, whose case history shows a very similar course, in spite of his age. The case had been published by Borberg.

III. (Borberg, dissertation, 1913.). 14-year old boy, admitted because of coma. During the night, complaints of dizziness and nausea. Vomiting. Unconscious. Temperature 41.9°. Strong cyanosis all aver. Death, 12 hours after observation of the first symptoms. Autopsy diagnosis: Hematoma of the suprarenal gland(s) (? Tr.) (utriusque?). Skin hemorrhages, hemorrhages of the endocardium, and (minimal) of the intestines. Postmortem culture of the cerebro-spinal fluid in buillon: growth of gram-negative Diplococcus in pure culture. Inoculation to mice: living after 3 days. Culture from blood in buillon: growth of gram-negative, large diplococci in pure culture. Inoculation in mice: living after 3 days. Microscopy of the suprarenas: diffuse hemorrhagic infiltration of the cortex, the medulla relatively undamaged, with weak color-affinity.

While these three cases are the only ones that could be found in the larger Childrens Stations in Kopenhagen, I have found scattered in the Literature 25 cases whose case histories showed practically the same beginnings, course and the same symptomatology, as those mentioned here. They had been found either as illustrative cases or as post-mortem discussions.

IV. (Waterhouse; Lancet 577, 1911). 8 months old breast-fed infant. Boy. Appearance, suddenly very bad. No pain. Drinks well. 6 hours later into the hospital. Respiration 72, pulse 140, temperature 38°. In a state of collapse.

Two hours after admission, purpura spots on body, arms and legs. Strong syanosis. Death 4½ hours after admission, 10½ hours after the first indications of sickness. Autopsy: Hemorrhage of the cortex and the medulla of both suprarenals.

V. (Cannata: Dtsch. med. Wschr. 21 1911). 15 months old breast-fed infant, boy. Two months prior: measles, since then, coughing. Some time ago, suddenly developed hemorrhagic spots on the body. Is cyanotic. Autopsy: milary tubercules in lungs, spleen and kidneys. The suprarenals show point-shaped hemorrhagic foci in the medulla.

VI. (Langmead, Lancet, pg. 1496 1904). Two months old breast-fed baby, boy. Completely healthy. Suddenly, one morning difficult respiration. No cramps, will not drink. Apparently has pain. Prior to admission to hospital purpura spots show in the face and on the body. Autopsy: Hemorrhage in both suprarenals.

VIII. (Langmead, ibid.). 2 months old breast-fed infant, boy. Suddenly awakes, screaming. In the evening, cramps, purpura outbreak in the face and hemorrhagias of nose and mouth. Autopsy: Hemorrhage of the right lung and in both suprarenal glands.

IX. (Dudgeon: Am. J. of med. Sci. pg. 134, 1904). 2 year and 9 months old girl. Very sick on admission. Temperature 39.6°. Abscess on the left side of the neck. Bilateral inflammation of the ears. Frequent attacks of pains with crying. No cramps. The condition worsenes very rapidly. Semicoma. Purpura eruption on the left leg. Autopsy: Thrombosis sinus longitudinal is sup. and of the cerebral and cerebellar veins. Diffuse purpura. Hemorrhage of suprarenal gland(s) (?, Tr.) without

absess of the thymus. Growth of staphylococcus aureus and albus from cardiac blood. Microscopy of the glands: multiple hemorrhages in the medulla of the suprarenal gland(s). The capillaries are distended everywhere and the vesicular walls are ruptured in many places.

X. (Dudgeon, ibid.). 1 year, 9 months old girl. Four days ago outbreak of chicken-pox. The condition deteriorated. Head, body and extremities are covered with" bluish-black ulcers." The floor of the ulcers was dry and glazed." Autopsy: Tubercular gl. in the mesenterium; tubercular ulcerations in the intestine. Small hemorrhagias in the pleura. Bilateral hemorrahe of the suprarenals.

XI. (Dudgeon: ibid.). 14 months old boy. Is admitted with bronchial pneumonia. Suddenly becomes sick in the morning. No vomiting, cramps or pain. Autopsy: Hemorrhage in both suprarenal glands in the cortex as well as in the medulla. Capillaries and veins considerably distended.

(The author here returns to "X" as subsequent number. Not the same case as "X." Tr.)

X. (Little: Brit. J. of Dermat. 13, 445 1901). (Blaker and Bailey: Brit med. Journ. III, pg. 75 1901). 11 months old breast-fed child, boy. Suddenly became ill with vomiting attacks. Strong cyanosis. Multiple hemorrhagic spots on the body. Died 4 hours after appearance of the first purpura spots, 13 hours after the first vomiting. Autopsy: bilateral hemorrhage of the suprarenals. Culture from the spleen: the blood produced a culture of Bact. coli, commun.; a saprophyte grew from the cardiac

blood. These, apparently, are based upon terminal infection without causality in connection with the disease. Microscopy of the skin showed that the main veins contained cocci in lumps and chains. The vessels were dilated.

XI. (ibid.) 12 months old boy. Suddenly sick in the evening. Feverish. In the morning hemorrhagic eruptions on the skin. They spread rapidly. Dead few hours later. Autopsy: bilateral hemorrhage of the suprarenals. Culture from cardiac blood: sterile. Multiple cocci in the vessels of the skin.

XII. (ibid.) 7 months old girl. Suddenly short of breath, cyanotic. Collapse. Temperature 40^{o}. During the course of the night purpura spots on the right ear and arm. Cyanosis increasing strongly. Autopsy: bilateral hemorrhage of the suprarenals. No bacterial findings.

XIII. (ibid). 12 months old girl. Suddenly ill. Vomiting. Temperature up to 41.2^{o}. Strong cyanosis. 4 times, thin slimy defecation without blood. Hemorrhagic spots on the arms. Autopsy: Hemorrhage of the suprarenal(s) in primis skin. Individual point-shaped, subperitoneal hemorrhagias.

XIV. (Quoted according the Graham Little) 4 months old girl. Suddenly high fever, indisposed. Pupura eruptions on body and lips. Death, approximately 12 hours after beginning of sickness. Autopsy: Bilateral hemorrhage of the suprarenals.

XV. (ibid.) 3 year old boy. Two days ago spots on the face and the arms. In autopsy these show to have been hemorrhagic bullae. Strongly cyanotic. Temperature 40.5^{o}. Death -

one hour after admission. Autopsy: bilateral hemorrhage of the suprarenals. No microorganisms.

XVI. (ibid.) 11 months old girl. Two weeks ago, measles and bronchitis. Three days prior to admission, bleeding from nose, ear and mouth; at the same time, the face was covered with purpura spots. Patient lived 8 days after outbreak of purpura spots. Temperature 38.9°. The autopsy revealed bronchopneumonia and extravasation of blood of the left suprarenal. Nothing is reported of the right suprarenal.

XVII. (ibid.) Two year old girl. During the night, sudden vomiting. No cramps. Temperature 40.5°. The skin, covered with petechiae. Died about 12 hours after beginning of the illness. Autopsy: bilateral hemorrhage of the suprarenals.

XVIII. (ibid.) 15 months old girl. In the morning, feverish with hemorrhagic spots on the chest. Refused by the hospital for fear of chickenpox. Died suddenly after hardly 2 days of illness. Autopsy: The cadaver was covered with purpura spots. Bilateral hemorrhage of the suprarenals. Cultures from various organs: sterile.

XIX. (ibid.) 13 months old, breast-fed infant. Suddenly became ill in the morning. Several hours later the face was covered with purpura spots that spread over the whole body. In the evening sharp cramps with penetrating crying. Temperature 42.3°. No blood in urine. Death, 24 hours after first attack. Autopsy: individual small sub-pleural hemorrhagias. Right suprarenal changed into a blood-cyst, left suprarenal: multiple hemorrhagias. No bacteria.

XX. (Garrod and Drysdale: Path. Soc. Trans. pg. 257, 1898). 4 months old girl. No clinical information. Autopsy: Body is covered with purpura spots. Bilateral hemorrhage of the suprarenals. Cultures from various organs are sterile.

XXI. (Volker: Middlesex Hosp. Rep. pg. 95, 1894. Quoted by Dudgeon). Two years old. Suddenly falls ill. Temperature 40.5°. Wide spread petechiae on all of the body. Death 24 hours after beginning of the attack. Is considered a dubious smallpox case. Autopsy: bilateral hemorrhage of the suprarenals.

XXII. (Talbot: St. Bart. Hosp. Reports 36: 207 (quoted according to Little)). Five months old. In the morning, suddenly vomiting, pains and cramps. Temperature 38.5°. No objective findings. Death, about 6 hours later. Autopsy: bilateral hemorrhage of the suprarenals in both, cortex and medulla.

XXIV. (Batten: Path Soc. Trans. 1898). 2 years, 3 months old. Admitted because of papillar urticaria. Approximately 1 month later suddenly ill with vomiting and diarrhoeha. The following night, coma and cramps. Pulse 200, temperature 41.2°. There was staining of the skin, something that was attributed to earlier skin problems. No purpura was, apparently, present. Autopsy: bilateral hemorrhage of the suprarenals.

XXV. (Still: Path. Soc. Trans. 1898). 14 months old, died of miliary tuberculosis. Had been ill for some months. In the last 6 days heavy diarrhea and vomiting attacks. Autopsy: Other than the acute miliar tuberculosis only suprarenal hemorrhage, sin.

XXVI. (ibid.) Child, died after 2 weeks of illness of

bronchopneumonia. Stong cyanosis, no purpura. Obduction Hemorrhage of the right suprarenal.

XXVII. (ibid.) 4 years old. Sick for two weeks. No clinical information. The autopsy showed a definite bronchopneumonia and hemorrhage of the right suprarenal gland.

XXVIII. (Marchand: quoted according to Thomas in "Handbook of Pathology of children, Vol. II). Nine months old girl. Died of a morbus maculosus. During the autopsy, one found, along with a tumor, possibly originating from the symphicus part of the right suprarenal gland, a widespread hemorrhagic destruction of the suprarenal gland.

Since these case histories appear to form a specific type of their own, that differs somewhat from the suprarenal gland hemorrhages in newborn as well as from those of adults and since it is not mentioned in any of the larger handbooks, I want to discuss the primary characteristics briefly.

The illness appears to occur with equal frequency in boys as in girls. The largest part of the patients are, originally, breast-fed children, who had been converted to mixed feedings at a later date. 18 of the cases fall into the age group between 2 months and 1 year, 6 cases below 2 years, 3 cases between 2 and 3 years and one has the age of 14 years. The infant-age, in other words, has the majority of the cases and appears to be expecially predisposed.

It is always a matter of healthy, well-nourished children, who have not had any difficulties before and who had offered no indications of illness during the course of the day and evening.

Towards morning, they awake suddenly, with a scream or with vomiting, occasionally with thin, sparse defecations. Occasionally, there is a mention of cramps. The sickness quickly develops a disquieting form. They are brought to the hospital, in almost moribund condition with very strong and constantly changing cyanosis and paleness, without greater Dyspnoa of indices of lung affection, with high temperature of 39 to 41°, with small, soft, and very irregular pulse, some unconscious, others, visibly tortured with fear. The objective examination presents normal conditions for lungs and heart. On the body, the extremities and the buttox, now appear scattered uprpura efflorescences, initially as small reddish-blue petechiae with serrated or star-shaped edges, which, quickly spread into hand-sized suffusions of a round shape with spreading and, towards the end, confluent limits and convex blue-black surfaces. These appear along with strong cyanosis, generally several hours after beginning of the sickness and often only a few hours before death. Death occurs shortly, after the 6th to 24th hours after inception of the illness without successful determination of other symptoms or a specific cause.

In the autopsy, it is shown constantly that it is always a matter of skin hemorrhages and hemorrhages of both of the suprarenal glands, in the medulla as well as in the cortical zone.

Let us consider the etiology and the pathology more closely for a moment.

Several theories have been established concerning the causes of suprarenal hemorrhages in the newborn (traumas during

birth, in Schultze's fluctuations, the change in blood circulation infections, thromboses and embolisms, congenital suprarenal hyperplasia (Lundsgaard), fatty degeneration(Virchow) parenchymatous degeneration(Droubaix) -- the survey of the present case histories and autopsy reports, exclude the majority of the mentioned factors.

The fact that the hemorrhage is almost always bilateral and generally symmetrical, could indicate that one may be confronted with a universal illness, and, since many cases indicate an elevated temperature and follow a very acute course, it appears close at hand, to assume an infection to be the direct cause.

The experimental investigations that have been carried out appear to support the possibility of an infection or intoxication. Roux and Yersin found, on inoculation of guinea pigs with diphtheria, almost constantly a dilatation and congestion of the suprarenal vessels. Langlois and Charrin found hemorrhages in the medulla as well as dilation of the vessels in guinea pigs which had died of acute pyocyaneus infection. They further showed that hemorrhages in the glands develop both, when bacteria are injected and after injection of their toxic products. Roger found, on the injection of Friedländer's bacillus in guinea pigs, that the entire suprarenal gland was suffering from a diffuse hemorrhagia that occurred 24 to 36 hours after injection. Pilet has confirmed this susceptibility to toxic influences by showing that suprarenal hemorrhages could be produced even in subcutaneous injection of bacterial as well as chemical toxins. Later, Oppenheimer and Loeper have shown, among others, that sub-

sequent to experimental injection of diphtheria-, anthrax-, tetanus- and pneumo- bacilli, suprarenal hemorrhages are almost always present.

These experimental studies that show the susceptibility of the suprarenals to infection are also confirmed by clinical observations in the specific infectious diseases. Thus, Ricker and Auerbach have told of cases of death of measles in children, where hemorrhagias of the suprarenals were found; Comby, Hutinel, Tixier and Troisier, Olaf, Scheel, as a result of scarlet fever; and Moltschanoff has constantly found, in 29 children who had died of diphtheria, small bleeding in the medullar substance and the zona reticularis.

One has also felt, in connection with suprarenal hemorrhages in newborn infants, in a number of cases, that it was a matter of infection. Klebs and Eppinger have isolated a microorganism, which they call noma haemorrhagica; Gaertner has reported on a coli-type bacillus, that produced visceral hemorrhages in dogs upon injection and could be found in their blood. Merceles, Brehns, Kilhann, Babinski and Langmead confirm these findings by isolating one or the other microorganism.

In surveying the above as well as the following case histories, it can be seen that blood examination was carried out in only 12 of the cases.

Of these, in 7 cases, the cultures were sterile, in one case, staphylococcus aureus albus (Dudgeon), in one spermococci (Dudgeon) were determined. Little found streptococci in the skin vessels of two cases with purpura eruptions. In the cases of the

Reichs - and the Community - hospitals, a gram-negative diplococcus was found that did not grow in mice.

The fact that it did not succeed in the few bacteriological studies that have been carried out to prove bacteria need in no way contradict the bacteria theory. In none of the cases, the bacteriological examination was carried out in vivo. The total of the intense acute course as well as the high temperatures appear to indicate that one is confronted with a universal infection or intoxication that, in the first instance, concerns the suprarenal parenchyma.

The predisposition that the suprarenals appear to have, is being considered to be a pathological weakness of the vessels by the author. The anatomical arrangement of the blood vessels of the interior cortical zone, appears, however, as Arnaud and Alexais have shown, to be able to be predisponable to hemorrhaging. While, histologically, this zone is part of the cortical area, it differs in its reticular structure from the stratum glomerulosum and the stratum fasciluare. The zone is the softest part of the gland, in that it is composed of cellular trabecula and a large number of anastomosing capillaries, that rupture easily, partly because of the thin cell wall, partly because of lacking support of the glandular substance, since the individual cell elements lie in a more scattered manner and do not provide sufficient support substance, especially not for the flaccid and dilated vessels. It is for this reason, that the hemorrhage more likely hits this zone and then spreads to the adjoining areas. It cannot be determined with certainty, what the reason may be that the hemorrhage occurs here. It has been assumed that an active

congestion starts, at the moment that the gland is attacked by toxic materials while the gland attempts to porduce antitoxic materials. Perhaps, another hypothesis is closer: In the moment that the toxic materials begin to act of the suprarenal parnchyma, which, on the basis of experiments, we must consider to be especially susceptible, the secretory nerves become paralyzed. The stop of suprarenal activity concerns, initially, the neighboring capillaries of the suprarenal gland itself, which are accustomed to be exposed to the vascular-tonic in the suprarenal secretion continually and in high concentration. A sudden vesicular dilation then occurs which easily results in a diffuse hemorrhage because of the lack of support by the surrounding cell tissue.

On the other hand, the question as to whether the vessels of the suprarenals are dilated or not will require very large amounts of control material and it is always necessary to count with the potential source of error in post-mortal changes.

That the loss of blood should be the cause of the sudden death cannot be assumed; in none of the cases was the hemorrhage so great that it had ruptured the capsule and entered into the peritoneum. The anemia that had been observed is caused by other factors.

Death must be originated by the acute insufficiency of the suprarenals. This is confirmed by the many suprarenal extirpation experiments that have been carried out. The suprarenals are necessary for the maintenance of the organism. The extirpation experiments have shown, amoun others, that death will

occur within a very short time. Strehl and Weiss found that in cases of bilateral suprarenal extirpation, death in rats, mice and guinea pigs occurs in the course of 4 to 19 hours. Biedl shows that dogs, cats and rabbits died, in this case, within 2 to 4 days.

As concerns the symptomatology, only the two most obvious symptoms are to be mentioned here, that of the cyanosis and the purpura, that, possibly are originated from the same cause.

While purpura does not appear to be a generally observed sign in the suprarenal hemorrhages in the newborn (among Hamill's approximately 70 cases, it only occurs once) and is also not pointed out in the cases that have been published on suprarenal hemorrhages in adults (where, according to the opinion of Simon, the hemorrhages are caused by marantic thromboses), the mentioned case histories showed that in infants and small children, it is a constantly observed sign in suprarenal hemorrhages. Little, in 1901, has already pointed that out.

That purpura in children is a sickness of its own cause, any more than it is in adults, but that it is a symptomatic complex, that can originate through a variety of etiological and pathogenetic conditions, is confirmed by a multitude of reports. As is known, it appeared in many specific infectious diseases: (Typhus, scarlet fever, measles, cerebrospinal meningitis, angina and pneumococcal infections) as well as in diseases of the blood. It has, therefore, been assumed that purpura originates from an affection of the vasimotor nerves (Jackson), or from a paralytic dilation of the finest vessels (Henoch) or from the fragility or

the changes of the vesicular walls (Leloir, Casel, Riegel) or, perhaps from diseases of the endothelium, that must be caused by a change in the blood and Sortaix has pointed to the role, that the liver plays in the coagulation processes.

While Conty, who in 1876 established the "nervous purpura theory," and pointed out that the disease were originated by a sympaticus affection, it was rightfully pointed out to him that the theory at that point in time was clearly lacking any certain basis. I feel that it is worth pointing the attention to the unique relationships that exist between the purpura outbreak and the suprarenal hemorrhage in the case histories that have been mentioned.

On the basis of the results that have been obtained by experimental suprarenal research in respect of the secretions of this endocrine gland, the presence of adrenalin can be recognized as a necessary condition for the maintenance of the peripheral vesicular tone. If the secretion is reduced or stops altogether, then a slackening of the peripheral vessels will necessarily occur. That the secretion is reduced by hemorrhages was shown by Luchsch, who found that the blood of the suprarenal vein of animals treated with diphtheria toxin, contained less adrenalin than normal blood. The universal dilatation of the blood vessels will lead to a drop in blood pressure as well as a peripheral stasis that can possibly be the causes of the strongly changing and fierce cyanosis and the subsequent transudation, which occurs most spectacularly in those areas, where the surrounding tissue is loose.

It is difficult to provide proof that acute suprarenal insuffieiency is, in fact, the cause of the purpura outbreak. It is possible that this skin affliction is caused by the fact that one is confronted with a universal infection or a form of a hemorrhagic diathesis. Especially in childhood, sepsis shows itself often through skin hemorrhages. Thus, the morbus Buhli in the newborn is characterized by multiple hemorrhages and a fat degeneration of the inner organs, that remind of those encountered in arsenic- and phosphorus- intoxication. Cyanosis is, in those cases, the general rule; on the other hand, fever is usually absent. The same thing applies to "Winkel's disease" (Jaundiced syanosis with hemoglobinuria).

In addition, as has been mentioned, purpura has been described in many cases of infection without indices of suprarenal disease. But it is not clear how the infections are to be a direct cause for purpura outbreaks. It is generally assumed that embolisms or thromboses are the cause. Unna, on the other hand, points out that these alone cannot explain purpura. Many infectiou thrombi do not produce any hemorrhagia at all. He feels that, in addition, there must be some sort of chemical influence involved.

If the purpura eruption of the case histories mentioned, were to be seen as common skin hemorrhages on the basis of a universal sepsis, or a hemorrhagic diathesis, then it would be reasonable to expect to find hemorrhages especially in the serous skins and mucous membranes, that generally are the first predilection locations; but this is the case only in a few of the men-

tioned section reports.

That a purpura eruption may have been caused by a suprarenal insufficiency could be supported, perhaps, by the fact that it occurs only late in the clincial picture and that the strongly changing cyanosis and the state of collapse show shortly before the beginning of the attack. Unfortunately, it was impossible to derive any blood pressure data from any of these cases.

But in those cases, in which experimental, as well as clinically acute suprarenal insufficiency of other causes is discussed, (Helly, Hornowsky, Hart), one finds purpura mentioned as little as in the suprarenal hemorrhages of adults. On the other hand, both Legrain and Fournier have shown that in typhus exanthematicus, the only available post-mortem finding is an acute surarenal inflammation, and they assume, on the basis of the greatly reduced blood pressure, that a relationship exists between suprarenal insufficiency and death in typhus. Sergent also sees a great part of the symptoms in abdominal typhus, and Khouri in the dengue fever, in the changes in the suprarenals.

On the basis of presently available information, it does not appear to be possible to prove a direct relationship between the purpura outbreak and suprarenal insufficiency. It is also difficult to explain why not all cases discussed in the literature resulted in purpura. In tow cases (Talbot) it is pointed out that the skin was normal, in three others (Dudgeon and Sill) there is no mention of a purpura eruption. It is possible that this may be caused by the fact that the children were so seriously intox-

prognosis towards restitution in an acute suprarenal hemorrhage does not always have to be the worst (pessima), a case of Vollbracht may be mentioned in which a 15-year old girl, one year prior to an eruption of Addison's disease, had a purpura eruption over her entire body. Addison's disease in this case continued very acutely with death after 3 months. The post-mortem showed a hemorrhagia and acute tuberculosis of the suprarenals. On the basis of that which has been developed here, one feels tempted to place the suprarenal hemorrhage and the purpura eruption into the same point in time.

As concerns the therapy, in those cases where the hemorrhages in the suprarenals were so strong that the child died immediately thereafter, there was hardly anything to be done.

On the other hand, when the case is less acute, and the blood pressure, changing cyanosis and asthemia of the child, perhaps, permit the assumption of a suprarenal hemorrhage, it would be appropriate to start adrenaline treatment. The adrenalin must be given subcutaneously in large and frequent doses and under constant control of the blood pressure.

The good results that have been obtained in cases of diphtheria with adrenalin injections, where we know, on the basis of the studies of Roux, Yersin, Luchsch and others, that the suprarenals are attacked especially seriously by the diphtheria toxin, could demand that also in alimentary and infectious toxicoses, the measurement of the blood pressure be introduced as a control over the condition of the child and to try, on this basis, along with other stimulants, also an adrenalin treatment.

in the suprarenals, which can often be reduced to a difficult birth and, therefore, belongs into that group of suprarenal hemorrhages that we find in the newborn. At the same time, one must assume that even a very small suprarenal hemorrhage will considerably reduce the resistance of the child.

As example for this, one may point to the following:

I. 1 month old; bottle baby treated in the children's section of the Reichshospital. Diagnosis: Stenosis pylori cong. haematemesis, Melaena. Started vomiting 6 days ago, two days ago, scattered petechiae on body and abdomen. Died, 2½ months old. Autopsy: Old hemorrhage in the left suprarenal. Stenosis pylori congenita.

II. Five week old bottle baby. Admitted to Koenigin-Louisen Hospital because of invaginatio, where it was treated because of pyloric stenosis. Slow and slack since birth. During the hospital stay, explosive vomiting attacks, ventricular peristaltis, high retention, palpable pylorus tumor. Feverish. Strong cyanosis without dyspnoa. Melaena. A hematoma the size of a Two-Mark piece at the os sacrum. Died 7 weeks old. Autopsy: a walnut-sized hollow space in the left suprarenal, filled with old blood. Stenosis pylori congenita, general organ anemia.

Aside of the reduction of the resistence of the child towards later illnesses, suprarenal hemorrhage also seems to provide an increased dispostion towards diseases of the suprarenal parenchyma. Thus, Rolleston indicates suprarenal hemorrhagis with fibrous organisation as a rare cause of Addison's disease. As an interesting example of this and the proof of the fact that the

icated, that they died, before an effect on the peripheral vessels became obvious. The purpura eruption often only occurs a few hours before death.

One can, however, not ignore, on the basis of that which has been presented here, the comparison between the prupura eruption and the acute suprarenal insufficiency, with the pigmentation that is the cardinal symptom of the chronic suprarenal destruction in Addison's disease. As a result of the experimental results, one feels tempted to assume that a cessation in the suprarenal function will cause a slackening of the vessels, which, in the chronic, and more slowly progressing disease, results in an increased disposition to pigmentation (Borberg), while skin hemorrhages occur in the acutely appearing vesicular dilation. And, as we can find in cases of Addison's disease without pigmentation (Lewin has found 44 cases without bronzed skin out of 329 cases), so we can also find suprarenal hemorrhages without purpura. But, while Addison's disease is very rare in children, it appears that their suprarenal glands are especially predisposed to hemorrhages, perhaps because of their greater susceptibility to infections and intoxications.

As concerns the prognosis for this suprarenal hemorrhage, the case histories, referred to, indicate a fatal outcome. On the other hand, the hemorrhage can be so insignificant, that it results only in transient symptoms and this would be especially possible if only one of the suprarenals were attacked. As is known, it is not an uncommon autopsy finding, where a child died of an intercurrent sickness, to find signs of an old hemorrhage

There seem to be no studies concerning the pathology of the color-affinity tissues in these conditions, but, perhaps, the various hemorrhages of the skin and the mucous membranes, that we find in this, as well as in septic conditions, are related to a temporary insufficiency of the chromaffine system that could possibly be regulated.

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