

CARDIAC DISORDERS.—Kothe,⁸⁶ Rothschild,⁸⁷ Crile,⁸⁸ and others have obtained prompt recovery (after all other means had failed in Kothe's cases) in surgical heart-failure from intravenous injection of adrenalin in saline solution. Mankowsky,⁸⁹ Bates,⁹⁰ Floersheim,⁹¹ Deeks,⁹² and Boy-Teissier⁹³ have urged the value of adrenal preparations in cardiac disorders accompanied by weakness, particularly when there is dilatation, cyanosis, or œdema. Voight^{93a} found 10 to 15 minims of adrenalin 1:1000 solution and 5-grain tablets of the gland valuable in cardiac dropsy and cardiac dyspnea.

In 1853 Brown-Séguard⁹⁴ found that the venous blood of the venæ cavæ contained some substance which contributed to the contractions of the heart. A contemporary promptly relegated this experimental fact to oblivion, by showing that carbonic acid, the only excitant credited to venous blood, failed to cause an exposed heart to contract. Had it not been for this misdirected experiment it is more than likely that Brown-Séguard, over fifty years before Oliver and Schäfer, would have discovered that, in Schäfer's words,⁹⁵ the adrenal extract produced "a powerful physiological action upon the muscular system in general, but especially upon the muscular walls of the blood-vessels, and the muscular wall of the heart." He would then, moreover, have reached the obvious conclusion to which I was subsequently led, that, inasmuch as the adrenal secretion passed by way of the adrenal veins to the inferior vena cava, it was inevitably carried to the right heart in the blood of this great channel, and that it was the adrenal secretion, therefore, which helped the heart to contract.

This explains the beneficial effects of adrenal preparations in adynamic heart disorders. Their active principle *via* the venæ cavæ excites *directly* the muscular elements of the right heart. Besides this, however, the entire cardiac muscle is also, from my viewpoint, excited *indirectly*. The adrenal

⁸⁶ Kothe: *Centralbl. f. Chir.*, Aug. 17, 1907.

⁸⁷ Rothschild: *Therapie der Gegenwart*, June, 1908.

⁸⁸ Crile: *Amer. Jour. Med. Sci.*, April, 1909.

⁸⁹ Mankowsky: *Russian Arch. of path., Clin. Med. and Bact.*, March, 1898.

⁹⁰ Bates: *Medical News*, March 2, 1900.

⁹¹ Floersheim: *New York Medical Journal*, Oct. 6, 1900, and May 4, 1901.

⁹² Deeks: *Montreal Medical Journal*, Nov., 1901.

⁹³ Boy-Teissier: *Arch. gén. de méd.*, Aug. 23, 1904.

^{93a} Voight: *British Med. Journal*, March 9, 1912.

⁹⁴ Brown-Séguard: "Experimental Researches Applied to Physiology and Pathology," p. 104, 1853.

⁹⁵ Schäfer: *Loc. cit.*, vol. i, p. 951, 1898.

active principle being carried by the venous blood from the heart to the pulmonary air-cells, it is added to that already in the blood, and becomes converted into the albuminous constituent of hæmoglobin, which, as we have seen, sustains oxidation. In this form it returns from the lungs to the left ventricle, with the arterial blood it has enriched, to be distributed to the body at large. When we recall that the first arteries given off by the aorta are the coronaries, whose branches supply the heart muscle proper, it becomes evident that the entire heart is the first to receive blood freshly laden with oxygen. On the whole, the adrenal secretion itself contributes to the heart's working power in two ways: (1) by enhancing directly the contractile power of its right ventricle, and (2) by sustaining oxidation and metabolism of the entire cardiac muscle.

Emphasis must be laid upon an important practical fact in this connection, namely: that the obvious purpose of the direct aid the right ventricle receives from the adrenal secretion is to assist the walls of this ventricle in projecting the venous blood into the lungs. This explains the rapidity with which cardiac dyspnoea is relieved by adrenal preparations; they not only restore to the right ventricle its power to drive the venous blood adequately to the air-cells, but they supply it with the pabulum which enables it to absorb from the air enough oxygen to restore the general respiratory equilibrium. The increased metabolic activity in the vascular muscles being also enhanced, passive œdema is also caused to disappear, while the dilated heart tends to resume its normal dimensions.

Whether given orally, hypodermically, or intravenously, therefore, adrenal gland, through the agency of what active principle it happens to contain, enhances the contractile power of the heart. Mankowsky⁹⁶ found that its efficiency was best shown in cardiac weakness and threatening collapse, and all evidence available points in the same direction. Floersheim states that when powdered adrenal is placed on the tongue, mixed with saliva and masticated thoroughly, its effects appear within ten seconds. At other times it takes ten minutes to regulate a

⁹⁶ Mankowsky: *Russian Archives of Pathology*, March, 1898.

weak, irregular pulse, but the usual time has been between two and three minutes.

The dried gland in daily doses of 1½ to 3 grains (0.1 to 0.2 Gm.) is used in Europe. Whether our preparations are weaker or not I cannot tell, but the fact remains that such doses have not proven active in my practice, 2 grains (0.13 Gm.) three times daily, when a good preparation is available, being necessary to obtain appreciable effects, *i.e.*, such effects as can readily, and with more accuracy, be obtained with digitalis. Kothe⁹⁷ injects 20 drops (1.23 c.c.) of the 1:1000 solution of epinephrin in 1 quart of saline solution intravenously. John⁹⁸ injects slowly, in the same manner, 3 to 15 minims (0.18 to 0.92 c.c.) of suprarenin in 1½ drachms (5.55 c.c.) of saline solution. It has been used subcutaneously in 15 (0.92 c.c.) or more minims in ½ to 1 pint (250 to 500 Gm.) several times daily if necessary by Josué and others. Netter gives 10 to 20 drops (0.62 to 1.23 c.c.) or more by the mouth, but also subcutaneously in saline solution, when larger doses are required.

The contraindications are mainly: chronic nephritis, aortic lesions with tendency to anginal pains, angina pectoris, and arteriosclerosis, in all of which conditions a marked increase of the vascular tension would be harmful.

The indications of adrenal preparations are, as stated, those in which weakness of the myocardium exists, though I would fear their use when degeneration is present, owing to the marked increase of vascular tension they cause, and the greater resistance thus imposed upon the heart. Their value is manifest where marked and threatening cardio-vascular adynamia exists, and in cardiac collapse in the course of infections, which is due, as I have shown under "terminal hypoadrenia," to arrest of adrenal functions. In such cases, especially where urgency prevails, adrenal medication promptly restores the arterial tension; the cardiac beats become more ample and regular, and the—perhaps suspended—pulse resumes its normal strength and rhythm.

In the treatment of valvular and other cardiac disorders, digitalis is more reliable, and it can be adjusted to the needs of each case with greater precision.

⁹⁷ Kothe: Therapie der Gegenwart, p. 95, 1909.
⁹⁸ John: Münch. med. Woch., p. 1221, 1900.

RESPIRATORY DISORDERS.—We have seen that adrenal preparations enhance the vigor of the cardio-vascular contraction. The asthma often met with in elderly people is thus promptly relieved by these agents. This applies also to true asthma, as first shown by S. Solis-Cohen.⁹⁹ This result is explained, from my viewpoint, not only by the increased oxygen intake and the improved tissue oxidation just mentioned, but also by the more perfect hydrolysis of the toxic wastes to which the spasm of the bronchial muscles, and therefore the asthmatic paroxysms, are due. This introduces, however, an important feature of the problem, to wit, the participation of the whole organism in the improved oxygenation.

The prompt arrest of a paroxysm of asthma by the hypodermic injection of 5 to 10 drops (0.31 to 0.62 c.c.) of the 1:1000 solution of adrenalin chloride, first recommended by Kaplan, has been termed "inexplicable" and "marvelous"; but if the adrenal principle is considered as the active factor in general oxidation, and it is recalled that, according to Takamine, one two-hundred-thousandth of a grain (0.00000033 Gm.) of adrenalin (and this applies as well to other adrenal principles, such as suprarenalin, epinephrin, etc.) suffices to awaken physiological action, one can readily understand why many times this dose will produce therapeutic effects. Especially does this assert itself when we take into account a fact I have long urged, to wit, that we must look upon the active principle of the adrenal secretion not merely as a reducing agent, but as a *catalyzer* which, though remaining itself stable, can take up oxygen and transfer it with extreme rapidity, and in relatively enormous quantities, to the hæmoglobin, and from this compound to the tissue-cells. The adrenal active principle has not only been found in the red corpuscles by Mulon, as we have seen, but its catalytic action, first pointed out by Poehl, meets precisely the conditions deemed necessary by Moritz Traube, in 1858, to explain the massing of oxygen in the tissue-cells through its all-powerful catalytic action.

It has been noticed that a rise of blood-pressure does not always occur when epinephrin or adrenalin is injected into the tissues, but this is due to its slow absorption, though the asth-

⁹⁹ Solis-Cohen: Jour. Amer. Med. Assoc., May 12, 1900.

matic paroxysm is aided at once. The rise of blood-pressure is hastened, according to Miles and Mulleberg, when the area in which the remedy was injected is massaged. Spraying the nose with a 1:4000 or stronger solution of adrenalin or suppositories containing this agent has also been found capable of arresting paroxysms of asthma by Matthews. Aronsohn applies to the nostrils an ointment of vaselin and lanolin, of each, 1 drachm (4 grammes), containing 30 to 60 minims (1.85 to 3.7 c.c.) of 1:1000 solution of adrenalin chloride. Weiss^{99a} recommends an injection of adrenalin $\frac{1}{80}$ grain and pituitary extract $\frac{2}{3}$ grain in 15 minims of water. A second injection was required in only 10 out of 300 cases.

In hay fever the nasal spray referred to above was, at one time, used extensively, but it eventually proved more harmful than beneficial. By exhausting the contractile power of the nasal mucosa it caused the latter to relax and to block the respiratory area. If used at all, it should be only for a short time. Matthews^{99b} uses a 1:1000 solution in severe cases and 1:2000 or 1:4000 in milder ones. Far more efficient is the adrenalin ointment 1:1000, to reduce the turgescence of the nasal mucosa, keeping the latter down by means of a 10-grain to the ounce of liquid petrolatum spray, between times.

Solomon Solis-Cohen recommends the use of adrenalin tablets, beginning with $\frac{1}{50}$ -grain (0.00132 Gm.) doses, and increasing the latter, if need be, as the patient becomes accustomed to the use of the remedy until $\frac{1}{10}$ grain (0.0066 Gm.) is given. The tablets are allowed to dissolve on the tongue. If the patient can remain in a dark room to avoid the reflex excitation of the sensitive centers, the remedy is given less often.

ASCITES AND OTHER EFFUSIONS.—In this condition, there is a more or less great loss to the circulatory blood of its adrenal principle, owing to the accumulation in the peritoneal cavity of a more or less great volume of its serum. The latter being, as I have shown, the intermediary between the red corpuscles and the tissues for the transmission of the adrenoxidase to the latter, the ascitic fluid deprives the body of part of its oxidizing principle, *i.e.*, transfers a given proportion of it where it cannot carry on its normal functions. In some cases, in fact,

^{99a} Weiss: Deutsche med. Woch., Sept. 19, 1912.
^{99b} Matthews: British Med. Jour., Feb. 19, 1911.

as in one recently observed by Bean,¹⁰⁰ the serum may be bloody. The marked anæmia and asthenia which complicate these cases speak in favor of this view.

That, in addition, the adrenal principle should prove useful in these cases, suggests itself, since they would restore to the organism that which is so essential to its physiological welfare. Fleischer and Loeb¹⁰¹ found that injections of adrenalin not only improved the general condition, but also that they increased the rapidity of absorption of the fluid from the peritoneal cavity. Tyson and Jump¹⁰² resorted to this measure in 3 cases. In the first patient ascites was due to chronic parenchymatous nephritis associated with moderate regurgitation at the mitral valve. Tapping had already been performed three times. Nine injections of adrenalin chloride were then given in the space of about two weeks, the original dose used being $7\frac{1}{2}$ minims (0.5 c.c.) of a 1:1000 solution, rapidly increased to 30 minims (2 c.c.). The first 5 injections were given on successive days. After the third injection the line of dullness in the abdomen began to descend, and after the sixth ascites was barely demonstrable. The patient had two attacks of pulmonary œdema during the treatment, but stated that he had had previously several such attacks. The quantity of urine passed gradually rose during the treatment, the daily output at its termination being from 70 to 80 ounces (2100 to 2400 c.c.). Progressive improvement followed. As to the question whether the adrenalin had some influence upon the kidneys in addition to that on the absorptive power of the peritoneum, the fact that the patient had already been under treatment for a long time, which treatment had apparently been beneficial, leads to a conclusion in the negative.

The third patient was suffering from an abdominal carcinoma, probably arising in the stomach and extending to the omentum. The first injection of 30 minims (2 c.c.) apparently diminished the amount of fluid. The injections were gradually increased to 60 minims (4 c.c.), 12 in all being given, after which, no improvement being noted, paracentesis became necessary. The character of the causative disorder, however,

¹⁰⁰ Bean: Chicago Medical Times, Sept., 1910.

¹⁰¹ Fleischer and Loeb: Jour. Exper. Med., vol. xii, No. 3, 1910.

¹⁰² Tyson and Jump: Therapeutic Gazette, Jan., 1911.

could but defeat the curative value of the adrenal principle. In Bean's case, from which nearly sixty gallons of fluid, sanguinolent at times, we have seen, complete recovery occurred.

Satisfactory results have also been obtained in serous effusions in the pleura and tunica vaginalis after aspiration, by injecting into the cavity from 8 minims (0.5 c.c.) to 2 drachms (8 Gm.) of adrenalin in four times the quantity of saline solution.

GENERAL INDICATIONS OF ADRENAL PREPARATIONS.—The list of disorders in which adrenal preparations have been, and are being, employed could be greatly extended, but I have limited myself to those in which their use has proven advantageous in the hands of a sufficiently large number of practitioners to warrant their being added to our trusted remedial agencies. In a certain number of diseases they may even be said, interpreted from my viewpoint, to exceed other means at our disposal in value. These are:—

1. Addison's disease. In this affection adrenal preparations compensate for the deficiency of adrenal secretion, and, therefore, for deficient general oxidation, metabolism, and nutrition. The dosage should be adjusted to the needs of each case. Beginning with 3 grains (0.2 Gm.) of the desiccated extract three times daily after meals, the dose should be gradually increased until the temperature and the blood-pressure become normal, when the last dose should be maintained. (See page 103.)

2. Surgical heart-failure; collapse from hæmorrhage, shock, asphyxia, and submersion. Here the adrenal active principle (suprarenalin, adrenalin, etc.), as a catalyzer and a constituent of the hæmoglobin, promotes energetically the intake of oxygen and its utilization by the tissue-cells, including the muscular elements of the cardiovascular system, and thus causes them to resume their vital activity.

3. The toxæmias, including bacterial infections, surgical septicæmias, etc., when collapse threatens, especially when a persistently low blood-pressure, hypothermia, and cyanosis are present. Besides enhancing pulmonary and tissue respiration, the adrenal principle, administered in the same way, enhances the efficiency of the immunizing process. (See pages 113 and 124.)

4. Capillary hæmorrhage from the pharyngeal, cesophageal, gastric, or intestinal mucous membrane. The mastication of tablets of adrenal substance, or the oral use of powdered adrenal substance in 5-grain capsules, arrests the flow by causing active metabolism in the muscular elements of the arterioles of the mucosa and constriction of these vessels.

5. Asthenic cardiac disorders with dilatation of the right ventricle, dyspnœa, and possibly cyanosis and œdema, owing to the direct action of the adrenal principle on the right ventricle and improved oxidation and metabolism in the cardiovascular muscles and the tissues at large. Tablets of from $\frac{1}{2}$ to 2 grains (0.033 to 0.13 Gm.) of the desiccated gland can be taken after meals.

6. Asthma, to arrest the paroxysms, by augmenting the pulmonary and tissue intake of oxygen and the cardio-vascular propulsion of arterial blood. From 5 to 10 minims (0.31 to 0.62 c.c.) of the 1:1000 solution of suprarenalin or adrenalin in 1 drachm of saline solution should be injected, drop by drop, into a superficial vein, or hypodermically.

7. To prevent the recurrence of serous effusions in the pleura, the peritoneum, the tunica vaginalis, etc., after aspiration, by reducing the permeability of the local capillaries and restoring the circulatory equilibrium.

8. In neuralgia or neuritis, as pointed out by Carleton, applied to the cutaneous surface over the diseased area to produce ischæmia of the hyperæmic nerves and thus arrest the pain. One to 2 minims (0.12 c.c.) of a 1 to 1000 adrenalin ointment should be applied by inunction.

PITUITARY ORGANOTHERAPY.

I have submitted elsewhere in this work the many reasons which have led me to differ from those who consider the pituitary body as a secreting gland, and to attribute to this organ the functions of a composite nerve-center. Pituitary organotherapy, though of marked value, does not mean to me, therefore, as did the organic preparations reviewed so far in the present chapter, the scientific use of a substance which carries on well-defined functions in the body, but rather the use of a

tissue rich mainly in *chromaffin substance* and nucleins, or at least in substances capable of producing jointly the effects of adrenal preparations (a generally recognized fact) modified, and indeed improved, through their combination with other components of the pituitary body. I may recall in this connection that of the two lobes, as shown by Howell, Silvestrini, Thaon,¹⁰³ and others, the posterior is the only one whose extracts are active therapeutically, but that, as shown by Crowe, Cushing, and Homans,¹⁰⁴ it is not removal of this lobe which causes death in animals—as it should, were it like the adrenals and the thyroparathyroid body, a secreting gland important to life—but removal of the anterior, which therapeutically is inert.

What explanation of the rôle of pituitary preparations I will offer, therefore, will not take the so-called secretion into account; it will utilize the only certain fact we have at our disposal for this purpose, viz., that, as shown by Wiesel, the posterior lobe is rich in chromaffin substance—the active component of adrenal tissue—and that it is mainly the physiological effects of this substance—though advantageously modified as a therapeutic agent through its combination with other constituents of the same tissue, I repeat—that we witness.

The phenomena awakened by pituitary are strikingly those of adrenal preparations. Mairet and Bosc¹⁰⁵ found, in 1896, that subcutaneous injections of pituitary extract produced a rise of temperature which lasted but a couple of hours. An intravenous dose produced marked myosis, slowing of the respiration, powerful cardiac beats, and hyperthermia as main signs, the animals recovering, however. Schäfer and Vincent¹⁰⁶ then found that pituitary substance raised the blood-pressure—besides containing a depressor substance—and that this substance when applied to mucous membranes caused blanching, as is the case when a solution of adrenalin is applied. They also noted that in small mammals it caused, in toxic doses, paralytic symptoms which they also consider analogous to those caused by adrenal extracts. According to Jas. Barr,¹⁰⁷ pituitary extract actively produces

¹⁰³ Thaon: *L'hypophyse*, p. 99, 1907.

¹⁰⁴ Crowe, Cushing, and Homans: *Bulletin of the Johns Hopkins Hospital*, May, 1910.

¹⁰⁵ Mairet and Bosc: *Arch. de physiol.*, p. 600, 1896.

¹⁰⁶ Schäfer and Swale Vincent: *Jour. of Physiol.*, p. 87, vol. xxv, 1899.

¹⁰⁷ Barr: *Lancet*, Nov. 13, 1899.

arteriosclerosis, and it is also known to produce glycosuria. In other words, it awakens all the typical phenomena, physiological and pathological, to which the adrenal product gives rise.

The marked advantage of pituitary—owing, doubtless, to the fact that it is bound up in organic combination with other components of the organ—is that it sustains the rise of blood-pressure to which it gives rise much longer than does adrenalin, thus being more reliable in shock and other emergency cases. It seems also to sustain the temperature and the muscular tone, cardiac, vascular, intestinal, and uterine, longer than the adrenal active principle. It possesses also a great practical advantage over adrenalin and other adrenal principles in that it can be administered by the mouth without compromising its effects.

A product called "puitrin" by its manufacturers, in the form of a powder, is available on our market for oral use, the dose of which is given as 10 to 30 grains (0.66 to 2 Gm.). But this dose is too large, 5 to 10 grains (0.33 to 0.66 Gm.) being sufficient in most cases.

There is also a liquid extract of the posterior lobe, wrongly termed "infundibular extract," the infundibulum being the pedicle which unites both lobes of the pituitary to the base of the brain. This infundibular extract affects mucous membranes precisely as do adrenal extractives, and should be applied only when diluted in eight or ten times the same quantity of saline solution. It may be given orally in 10- to 30- minim (0.62 to 2 c.c.) doses, or intramuscularly in 3- to 15- minim (0.2 to 0.92 c.c.) doses.

Another liquid preparation is also available, *i.e.*, "vaporole," in small flasks containing 15 minims (0.92 c.c.) of a 20 per cent. extract, the quantity for one injection representing 3 grains (0.2 Gm.) of the posterior lobe, which contains the active agent. The injection should be given intramuscularly in the gluteal region, under strict antiseptis.

CARDIAC DISORDERS.—As shown by Rénon and Delille,¹⁰⁸ pituitary gland raises the depressed arterial tension and corrects purely functional disorders of rhythm.

It is recommended in doses ranging from 3 to 6 grains (0.2

¹⁰⁸ Rénon and Delille: *Soc. de Thérap.*, Jan. 22 and April 23, 1907, and *Congrès de Médecine de Paris*, Oct., 1907.

to 0.4 Gm.) of the whole gland, in myocardial weakness, particularly in that due to infections when the blood-pressure is receding, the pulse is becoming more rapid, and the urine scanty. While less active than digitalis as a diuretic, it nevertheless serves a valuable purpose in this connection. It is advantageous in mitral disorders when there is hyposystole and in chronic myocarditis, particularly that due to alcoholism. It is also useful in the tachycardia of certain neuroses and during menopause. These results have been confirmed by Trerotoli,¹⁰⁹ Parisot,¹¹⁰ and others.

It is contraindicated in aortic affections in any disorder in which high vascular tension prevails, and where there is a tendency to anginal pains, which it tends greatly to aggravate.

Pituitary gland is preferred to adrenal and particularly adrenalin, as stated above, when the action is to be sustained, the former being useful in urgent cases. Rénon and Delille, however, prefer digitalis, and recommend pituitary gland only when the latter fails. Leonard Williams,¹¹¹ on the other hand, deems it superior to digitalis, strophanthus, strychnine, and other classic tonics in what he terms the "runaway heart of toxic states," influenza, pneumonia, bronchitis, etc., with tachycardia, but low blood-pressure, and in all cases in which there is post-toxic cardiac debility. In these cases—which, from my viewpoint, are instances of pure hypoadrenia—Williams regards pituitary preparations superior to any remedy at our command.

In heart-failure and shock, it has been highly recommended by Mummery and Lymes and Bell and Wray, 15 minims (0.92 c.c.) of the extract being injected intramuscularly. While its virtues would seem to recommend it for the perpetuation of the effects of adrenalin, which are, at best, but temporary, the number of cases in which it has been tried has been too limited so far to warrant an opinion as to its actual value.

OBSTETRICS.—Dale¹¹² found experimentally that extract of pituitary caused "direct stimulation of involuntary muscle without any relation to innervation." Fröhlich and Frankl-Hochwart¹¹³ then ascertained that it caused contractions of the preg-

¹⁰⁹ Trerotoli: *Rivista critica di clinica med.*, Nos. 32 and 33, 1907.

¹¹⁰ Parisot: *Pression arterielle et glandes à sécrétion interne*, Paris, 1908.

¹¹¹ Williams: *Clinical Journal*, May 18, 1910.

¹¹² Dale: *Biochemical Journal*, 1909.

¹¹³ Fröhlich and Frankl-Hochwart: *Wiener klin. Woch.*, No. 27, 1909.

nant uterus in rabbits, while Foges and Hofstetter¹¹⁴ resorted to this property to check post-partum and other uterine hemorrhages in 63 cases. The extract proved worthless by the mouth; but when injected intramuscularly, marked uterine contraction appeared within five minutes and lasted a long while in most cases. Voigts^{114a} found pituitrin most satisfactory in 60 cases; 1 c.c. (15 minims) sufficed. Pouillot and Vayssières^{114b} give 7½ minims intramuscularly several times daily in all adynamic or hemorrhagic conditions. Trapl^{114c} recommends it in placenta previa of the marginal type. A number of authors have recommended it for menorrhagia and metrorrhagia. Pituitary is useful, in fact, in all forms of hemorrhage of the genital system.

Norris^{114d} never uses pituitary extract without exhausting his abilities in obstetric diagnosis. He considers that healthy multiparas with relaxed birth canals offer the widest and safest fields. For inertia in the early stage of labor, the sleep of morphine, chloral, or scopolamine is preferred; in the advanced stages of labor, pituitary extract, he says, often will wisely keep forceps innocuous. The uterus, after the tumultuous visitation of pituitary extract, usually needs the steadying hand of ergot. Half doses are more often to be employed than full doses.

A large number of observers have, however, brought out some dangerous features. Nagy¹¹⁵ observed that it decreased the action of the fetal heart. Spaeth^{115a} had 2 cases of death in the newborn which are ascribable to this cause. Various authors have noted tetanoid spasm of the uterus. J. Clifton Edgar^{115b} states that both small and large doses have caused, through this defect, fatal compression of the fetus, premature separation of the placenta, and deep rupture of the cervix, his experience being based on 70 cases. In 39 of these in the first and second stages there were 2 and probably 4 still-births, and 3 instances of deep laceration requiring sutures to control the bleeding.

¹¹⁴ Foges and Hofstetter: *Zeitschr. für Gynäk.*, No. 12, 1910.

^{114a} Voigts: *Deut. med. Woch.*, Dec. 7, 1911.

^{114b} Pouillot and Vayssières: *Presse médicale*, No. 4, 1913.

^{114c} Trapl: *Monats. chr. f. Geburtsh. u. Gynäk.*, Oct., 1912.

^{114d} Norris: *Amer. Jour. of Obstetrics*, May, 1915.

¹¹⁵ Nagy: *Zentralbl. für Gynecol.*, March 9, 1912.

^{115a} Spaeth: *Ibid.*, Feb. 1, 1913.

^{115b} Edgar: *New York Med. Jour.*, p. 150, July 19, 1913.