It will be noticed that the principal objections to digitoxin are connected with its insolubility, and Cloetta has succeeded in preparing a soluble, amorphous digitoxin, which may be injected subcutaneously.

I have not been able to find an account of the process of manufacture, but his original article is usually quoted to the effect that it is prepared by a very complicated process, evolved after five years of effort. This preparation, called digalen, is marketed by the firm of Hoffmann, LaRoche & Co., which, so Cloetta states, despite the trouble and expense amounting to 11,000 marks per kg., has happily undertaken the preparation, selling it at but 2 marks (48 cents) for a small vial so that it may be universally used.

Quite a bit of philanthropy, it would appear, but when we reflect that a kg. costing 11,000 marks contains 3,000,000 doses and sells for 440,000 marks (\$105,600), the philanthropy becomes less obvious.

While clinical evidence seems to show that digalen is an effective substitute for infusion of digitalis, Karl Reitter, in Schrötter's clinic in Vienna, was unable to obtain the therapeutic effect with less than 6 c.c. (6 mg. daily), and finds it no better than the leaf and more expensive.

This preparation presents the anomaly of requiring a much larger dose when injected intravenously, presumably because of its rapid elimination by the kidney, and it will be interesting to know what the effect will be on that organ of the continued administration of so irritant a substance.

STROPHANTHIN.

Loeb found that strophanthin had much less constrictor effect on the coronary circulation than digitoxin has. This is of much importance, as it has been shown that the heart tension, or strength, is dependent on blood supply to an extraordinary degree. If an agent causes general vasoconstriction it means that the heart must contract against an increased resistance, and if the constriction of the coronary vessels is pronounced, the blood supply of the heart may be diminished despite high aortic pressure.

P. Maas has shown dilator and constrictor nerve fibers for the coronary vessels, but we can not study blood supply of the heart when the vessels are under central control in the mammal.

Strophanthin possesses the typical digitalis action; it can be prepared in constant and stable form, it is not expensive, it can be given for long periods without inducing cumulative effects (Fränkel having given it to a cat in just submaximal doses for ninety-two days). The effective dose lies much further from that which causes cumulative effects than in the case of digitoxin. It is quite soluble in water, hence much quicker to act. This occurred in three hours as against forty-eight hours for digitoxin. It is much more active and less irritant than digitoxin.

Sollmann has suggested that it probably deserves the preference over digitalis, and it has been used with satisfaction in France, Holland and Belgium, but for some reason many species of seed, many of them inert, have been brought into Germany and the United States, and some tinctures were found to be but one-sixteenth as strong as others. This has caused the crude drug, its preparations and its pure principle to fall into disrepute.

ANTIARIN.

This substance is of such extraordinary power that 1-10,000 of a milligram causes slowing of the frog's heart and 1-1,000 mg. causes systolic stand-still, being apparently 250 times as active as digitoxin.

Hedbom studied its action and that of antiarigenin—which he found but slightly toxic to the mammalian heart, though differing from antiarin only in the loss of a molecule of glucose. The extraordinary difference in the activity of these principles suggest that they possess an active nucleus so combined that it enters into more effective combination with the sensitive apparatus of the heart in some cases than in others, and it seems probable that further research may discover means of modifying some of the many more active principles of this type.

OBSTACLES TO USE OF DIGITALIS.

The greatest obstacle to the use of digitalis and its preparations arises from their variability, due to differences in methods of collection and preservation.

It has been shown that leaves gathered in the proper season quickly dried, cut up, dried thoroughly in a vacuum and hermetically sealed, will undergo but little change in a year. We should, therefore, demand leaves which have been thus preserved and physiologically tested on the frog's heart, with the date of the test stamped on the package, as is done with sera.

Kobert tested leaves which had thus been dried and made into tablets with sugar of milk and starch, finding them effective.

This may appear as too complicated for practice, but there is no reason why such leaves should not be sold very much cheaper than the nostrums which are being so much lauded as possessing all the virtues and none of the objectionable features of digitalis.

414 East Twenty-sixth Street.

PHARMACOLOGY OF VERATRUM.*

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PHILADELPHIA.

I firmly believe that if pharmacologists, instead of spending their time investigating commercial synthetics would direct their energies to more careful study of pharmacopoeial remedies, the world would be greatly benefited. A splendid example of the general ignorance concerning drugs which we call "well-known" is found in the case of the veratrums. When the statement is made in standard works on pharmacology, that the active principle of *Veratrum viride* is veratrin, and that this plant is useful only as a local application, it becomes evident that there is room enough for more accurate knowledge even among those who devote their attention especially to the study of drugs.

Before considering the properties of *Veratrum viride* I would like to discuss for a moment the question of the identity of *Veratrum album* with this plant. The Eighth Revision of the U. S. Pharmacopeia has recognized *Veratrum album* as equivalent to *Veratrum viride*, making one title, veratrum, to refer to both plants. I shall not go into the discussion of the botanical relations of green and white hellebore, as this question seems at present impossible of final decision. It may be dismissed with the

* Read in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.

statement that the majority of botanical authorities seem to hold the plants, not as specifically distinct, but as varieties; the differences between the two being only such as might be expected from different soils and climatic conditions.

While the alkaloidal contents of the two plants are in a general way very similar the alkaloid veratrin or cevadin, of which traces are discoverable in *Veratrum viride*, seems to be entirely absent from the European variety, so that it can not be claimed that their chemical compositions are identical. Moreover, it would seem that the relative proportion of the various alkaloids common to both plants is different. The reported cases of poisoning seem to show that vomiting and purging are more frequent and more pronounced after *Veratrum album* than by *Veratrum viride*; in other words, that the European variety contains more of the irritant principle, be it a resin or the acrid alkaloid rubijervin. In a study of the comparative effects of the two rhizomes, in 1899,¹ the conclusion was reached, that although, as a rule, the white hellebore was somewhat the more toxic of the two, the differences between them were no greater than might exist between individual specimens of *Veratrum viride*.

zero line; suddenly the pulse becomes enormously rapid and the pressure rises to a height very much beyond the normal and continues so for several minutes, until it rapidly falls immediately preceding death. During this period of elevation of pressure it will be noted that the respiratory movements, if present at all, are usually ineffectual, and there is very frequent asphyctic struggling of the animal. The rise of pressure is generally attributed to the asphyxia; I have, however, performed recently two experiments in which in spite of artificial respiration the same sequence of events occurred, so that I believe that there is another cause for this toxic rise of pressure which I shall mention later.

In view of the inequalities of the effects of veratrum evidently it would be preferable to employ its active principle were such principle known. There appear to be five alkaloids in the plant, of which veratrin is present in such small amount that it can have practically no part in the general effects of the drug; while pseudojervin seems practically inert. This leaves three alkaloids to which might be due the poisonous properties of the drug; these are jervin, rubijervin and protoveratrin.

In considering the question as to which of these alka-

Fig. 1.—Atypical effects of *Veratrum viride*. A. This shows the rise frequently seen after a large dose of *Veratrum viride*; (x) indicates injection of 1 c.c. 25 per cent. solution of *Veratrum viride* (0.25 gm.). Both pneumogastric nerves have been cut, the animal curarized and artificial respiration employed. H. Heart rapid. S. Slight convulsion. B. Five minutes later. C. Eight minutes later. D. Twelve minutes later. No drug has been given.

I believe, however, that the recognition of the two plants as identical was progressing backward.

Frequent observations of the effects of *Veratrum viride* on the circulation, as well as systematic studies of the drug, have impressed steadily on my mind the irregularity and uncertainty of the effects of this plant. Frequently have I been quite at a loss to explain to my classes the extraordinary effects which have followed the injection of this drug. These differences are very evidently to be explained by varying amounts of one or other of the several alkaloids; to this question I shall revert shortly.

The effects of veratrum on the circulation of the normal animal differ entirely according to the size of the dose which has been administered. If into a dog is injected what might be spoken of as the therapeutic dose of the drug ordinarily there is produced a distinct slowing of the pulse with a moderate fall of blood pressure (Fig. 1.). These conditions last for a considerable period of time and are followed by a gradual return to the normal. With the large toxic dose there is produced a marked slowing of the pulse, sometimes even complete arrest of the heart, with a fall of pressure almost to the

loids is due the activities of the plant, we must bear in mind the therapeutic use of the remedy. Although the eclectics attribute to American hellebore "adenagic" virtues, whatever that means, the regular profession employs it almost solely for its influence in reducing blood pressure and in quieting the heart. In other words, the therapeutic use of veratrum is to slow and soften the pulse and to lower the arterial pressure.

Of the three alkaloids which contribute to the action of the crude drug, protoveratrin is undoubtedly the most actively poisonous. According to the experiments of Eden,² the fatal dose for the rabbit of this alkaloid is 0.11 milligrams per kilo, approaching, therefore, aconitin in its toxicity. The symptoms produced by it are muscular weakness, a peculiar dyspneic type of respiration and frequently convulsions. The blood pressure, following the intravenous injection, may undergo a temporary reduction but eventually rises to a point very much above the normal, the pulse rate, in the meanwhile, being markedly reduced. If the vagi have been previously divided the primary fall of blood pressure does not occur, so that it is evidently due to the slowing of the pulse. If the dose has been large enough the stimulation of the inhibitory mechanism gives way later to a

1. H. C. Wood and H. C. Wood, Jr.: Amer. Jour. Med. Sci., May, 1899.

2. Arch. f. Exper. Path. u. Pharm., 1892, vol. xxix, p. 440.

paralysis. These changes in the circulation occur in curarized animals, with artificial respiration, and therefore, and quite independent of any disturbance either of the respiratory center or of the motor apparatus. Late in the poisoning there occurs a stage in which asphyxia fails to produce a rise of pressure, so that it would seem that finally the vasomotor centers become paralyzed.

In experiments in which the spinal cord was previously divided the drug was still able to produce marked elevation of the blood pressure. To sum up, protoveratrin is a primary stimulant to the pneumogastric nerve, to the cardiac muscle, and probably to the vasomotor center. A toxic dose paralyzes the peripheral vagi and the vasomotor centers and produces a peculiar arrhythmic condition of the heart. It is evident, therefore, that although this alkaloid is the most poisonous substance found in the plant it can not be held responsible for the therapeutic uses of the drug, since, in therapeutic dose, it is a stimulant to the heart, rather than a depressant. I believe that the peculiar elevations of pressure sometimes seen after the injection of large doses of *veratrum viride* may probably be attributed to the stimulant effects of protoveratrin; when only a moderate dose has been employed the proportion of this alkaloid is so small that it fails to modify the action of the drug and

facts would seem to indicate that it is to jervin that veratrum owes its therapeutic value (Fig. 2).

A study of the comparative power of the alkaloid and the crude drug, however, throws grave doubt on this conclusion. Jervin appears to be present in the root of *Veratrum viride* in the proportion of from 0.1 to 0.13 per cent. If it were principally to this alkaloid that the circulatory depressant influence of the plant is due jervin must be a substance of marked power. Such, however, is not the case. In my own experiments the intravenous injection of 0.02 Gm. of the alkaloid produced in a moderate-sized dog a fall of pressure amounting to only 10 millimeters of mercury, a drop almost negligible. The injection of 0.05 Gm. in two doses produced a fall from 180 to 155 millimeters, or a drop of about 15 per cent. In another animal of about the same size the intravenous injection of 0.25 c. c. of fluid extract of *Veratrum viride* produced a fall of from 200 to 160 millimeters. So far as my present evidence allows me to conclude, I believe that the quantity of jervin required to effect the circulation is about one-fifth of the dose of the rhizome of *Veratrum viride*. Evidently there must be some other principle which shares with jervin the responsibility for the action of this plant.

It is impossible for me to compare the fatal doses of this alkaloid and the rhizome because I have been unable

Fig. 2.—The physiological action of jervin. A, Five c.c. of 0.5 per cent. jervin (0.025 gm.) injected intravenously. B, One minute later. C, Fifteen minutes later, 12 c.c. of jervin solution injected. A total of 0.15 gm. has been injected. D, Fifteen minutes later, total of 0.18 gm. has been injected. V, Irritation of vagus. This shows the slight irritability of the vasomotor center on stimulation of the vagus.

may even favor the fall of pressure by slowing the pulse rate.

In 1874, an exhaustive study of jervin and veratroidin was made by H. C. Wood.³ The substance known at that time as veratroidin seems to have been an impure form of rubijervin. Rubijervin is a comparatively feeble substance, present in very small quantities. Its dominant action is on the respiratory center, although it appears also to have some depressant influence on the heart muscle, as well as slowing of the pulse through stimulation of the inhibitory mechanism. It is present in the plant in the amount of 5 parts in 100,000.

Of the five alkaloids which have up to the present time been found in veratrum, we have excluded all save jervin as of therapeutic use. In the studies made by H. C. Wood, in 1874, it was found that this alkaloid produced a primary slowing of the pulse which later became rapid, with a progressive fall of the arterial pressure, due, he believed, in part to an action on the cardiac muscle and in part to the depression of the vasomotor centers; there was also a simultaneous or subsequent failure of respiration. These experiments I have very recently repeated with essentially similar results. These

to kill a dog with it. In one experiment I injected into a dog weighing 9.6 kilos, 0.2 gm. of jervin (which was all of the alkaloid I had at my disposal) intravenously; it produced a very decided fall of pressure, from 180 millimeters to 65, but with no symptoms suggesting a probable fatal issue.

According to Eden, the minimum fatal dose of protoveratrin is 0.5 milligrams. Supposing that this alkaloid was present in the proportion of 0.03 per cent. in the rhizome of *Veratrum viride*, it would require 1.5 gm. of the crude drug to produce the fatal dose of protoveratrin. On the other hand, from the comparative studies already quoted, made by H. C. Wood and myself some years ago, we found the minimum fatal dose from hypodermic administration of the rhizome to be about 0.2 gm. In other words, if protoveratrin is the chief active toxic principle of *Veratrum viride* the quantity present is so small that the alkaloid would have to be seven times as active as even the extraordinary figures given by Eden.

From the above evidence it seems to me the following conclusions may safely be drawn:

First.—Neither veratrin nor rubijervin are present in *Veratrum viride* root in sufficient amount to be held responsible in any degree for the activity of the drug.

3. Phila. Med. Times, vol. iv.

Second.—Protoveratrin, although an extremely poisonous substance, differs essentially in its effects from the veratrum rhizome, and, therefore, is not to be considered its active principle. Moreover, the proportions of it are too small to permit of its being considered the toxic ingredient.

Third.—Of the known proximate principles, jervin most nearly corresponds in its physiologic action to the crude drug, but is present in too small amount in proportion to its toxicity to be considered the chief active ingredient.

Fourth.—The evidence, therefore, seems to me conclusive that there is in *Veratrum viride* some active substance as yet undiscovered.

DISCUSSION

PAPERS OF DRS. HATCHER AND WOOD.

DR. S. P. BEEBE, New York, said that Dr. Hatcher spoke of Cloetta having prepared a preparation of digitalis, apparently a very effective one, which has most of the advantages and very few of the disadvantages of other extracts, yet there has been no detailed publication of the method by which this substance is made. A publication which says that it is made by a very complicated process after investigations lasting five years, Dr. Beebe thinks is a very flimsy excuse for not publishing full details. It is treating the pharmacologists of the world as if they were children. He thinks that Cloetta should receive a rebuke. He thought that the Section on Pharmacology and Therapeutics might pass a vote condemning Cloetta for doing what would be condemned among its own members.

DR. HENRY R. SLACK, La Grange, Ga., said that he had tried thyroid extract in a great many diseases, but in only two has he gotten any good results, in cretinism and in myxedema. Digitalis, he thinks, is the surest of all therapeutic agents. It is to be hoped, he said, that the investigation of the different alkaloids will continue and that it will finally be decided which one is the best to employ. Up to this time his experience with any individual alkaloid has been thoroughly disappointing. The clinical results obtained in his practice have come from the use of powdered leaves or from the infusion and some tinctures. The alkaloids, without exception, have been disappointing. In acute diseases strychnin, in his hands, has been of much more benefit. In chronic diseases of the heart digitalis has been and is the sheet anchor. Brilliant results are obtained from its use in chronic forms of heart disease, with general anasarca. Veratrum, he said, is used in the South very extensively in pneumonia. When there is high fever, flushed face, bounding pulse, doses of veratrum act like a charm to reduce the temperature.

DR. WILLIAM F. WAUGH, Chicago, regretted that Cloetta did not make plain his process of producing soluble digitoxin because in it he seems to have made two very remarkable discoveries. He has found the means of making digitoxin soluble, and effects are gotten within an hour. Dr. Waugh has not yet been able to make out any difference in the effect of digitoxin and digitalin. The two apparently are identical in effect. He agrees with Dr. Wood that veratrin is not the only active principle of veratrum. There is a decided difference between the action of veratrum and veratrin. Veratrin increases, to a certain extent, vascular tension by way of increasing directly the muscular force of the heart; but the two are identical in one action, that is, in opening the eliminants. In their effect of stimulating elimination Dr. Waugh has not been able to find any distinction between veratrin and veratrum. In the stomach and bowels, in doses far below the amount necessary to produce the toxic effect, either will irritate the stomach. Veratrin has a more powerful effect on the respiration. That might be a desirable thing in treating pneumonia. It remains for the clinicians to say how best to use it. Practically no difference is found in the clinical applications of the two. While veratrin is not the active principle of veratrum, over a great part of the field of action veratrin can be used as a substitute for the other.

DR. W. J. ROBINSON, New York City, was of the opinion that papers of this character are not proper papers to be read

before the association. These papers are to be slowly and carefully digested. Physicians come to this meeting, he said, to learn something of practical value in their practice, and he doubts if any one got one grain of value from all the statements about veratrum. Apparently nothing is settled about this subject. About every statement Dr. Wood made he said, "seems," "seems to be the chief alkaloids," "seems to be the chief principle," and so on. Dr. Robinson believes it is better that such papers be not read. They may be printed in the transactions, but not read. If they are printed and distributed beforehand, intelligent discussion can be had.

As to Cloetta, before passing censure on him, he said it would be well to be sure of our ground. So far as his recollection goes, Cloetta did not publish a paper on soluble digitoxin. He knows that it is used with remarkable results in many of the hospitals, and it seems generally to act within five minutes; in fact, in one minute its effects can be seen on the pulse. He has not used it himself, but he follows carefully the literature on new preparations, and so far all the reports on digalen are very favorable.

DR. REID HUNT, Washington, D. C., remarked that at least one member must have paid close attention to both papers, else he could not have discussed them so fully.

MR. M. I. WILBERT, Philadelphia, requested Dr. Robinson to refer him to the literature which describes this process. Dr. Waugh made a suggestion, he said, which he thinks has occurred to many others, that is, that digalen, this soluble digitoxin, has an action similar to German digitalin. If that be true, and it probably is true, it would suggest that digalen is not pure digitoxin, but a mixture of principles, similar to the German digitalin, and, therefore, is ordinary digitoxin made soluble by the addition of some of the other proximate principles of digitalis. This is also suggested by a sample of digalen, that he had in his possession, which contained insoluble material. Exactly what this insoluble material is he is not prepared to say, because the vial is still sealed, and he is looking for several others to have them tested subsequently. It is possible, however, that the addition of other materials to the digitoxin is made in small quantities, that the digitoxin may precipitate, and, being precipitated, be given in one dose with very fatal results. He simply suggested this as a possibility. He did not say that the insoluble material in this vial is digitoxin, but, if the mixture is digitoxin, soluble only under certain conditions, and precipitation occurs, that may prove dangerous.

DR. C. S. N. HALLBERG, Chicago, considered the papers appropriate and said that the papers demonstrated that there has been no scientific work done on the veratrums since the famous controversy of thirty years ago by Mitchell and Bullock in Philadelphia. It is a fact, as Dr. Wood stated, that veratrin is used promiscuously instead of veratrum. Dr. Waugh, he said, claimed that there is a decided difference between the action of veratrum and veratrin. That is another question. The point is this: The new Pharmacopeia has placed under the generic title *Veratrum* the two veratrums, *viride* and *album*. The question is, are physicians who have been using Norwood's tincture willing to let the pharmacist give a preparation of *Veratrum album*. Dr. Wood's paper announced to the physician that when he prescribes veratrum he gets the tincture of *Veratrum viride*. It has demonstrated that there has been no work done on veratrum of recent years. Nothing is known about the active principles of veratrum, and very little of the difference between the tincture of digitalis and the infusion. When the diuretic effect is wanted they are to-day the best representatives of this drug. *Digitalinum germanicum*, on account of the name, was all the rage four or five years ago. So he thinks Dr. Hatcher was perfectly justified in calling attention to Cloetta's preparation, telling what it is or what it is not. That is the kind of work that ought to be done in this Section.

DR. R. A. HATCHER, New York City, said he was better aware of the incompleteness of his paper than any of the audience, knowing what he had to leave out, but he thinks it is very important to call attention to the fact that we are prone, like sheep, to follow the German-made advice regardless of its application. It is astonishing to look over the literature

and find how highly this Cloetta stuff is lauded by men who quoted verbatim from the announcement of the manufacturers. Cloetta suggested some years ago that he believed that digitoxin would be rendered soluble by digitonin. By going back a few years and looking over the literature it will be found that digitalin was lauded just as Cloetta's product is to-day. After all, they go back to digitalis leaves. What probably happens is, the digitoxin is held in suspension by digitonin. Mr. Wilbert's suggestion that digalen is not pure digitoxin, but a mixture of principles, or else that decomposition products have been formed, suggests that here is something more dangerous than was supposed before, since it is possible to give a very large dose unwittingly by the use of digitoxin in a soluble form.

Dr. H. C. Wood, Jr., Philadelphia, said that there is a plant known as *Theobroma cacao* from which is produced a popular beverage, cocoa. The similarity of names leads many students to believe that the chocolate plant is the origin of cocain. This ridiculous conclusion is no more absurd than that veratrin and veratrum viride are identical. Veratrum viride and veratrin have no connection, properly speaking, with each other.

FIBROID TUMORS OF THE UTERUS.

A STUDY OF THE DEGENERATIONS AND COMPLICATIONS
IN TWENTY-TWO HUNDRED AND SEVENTY-FOUR
CASES.

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PHILADELPHIA.

(Concluded from page 2003.)

FIBROMYOMATA A CAUSE OF STERILITY.

Olshausen⁴⁴ states that women having fibroid tumors are often sterile. Among 1,731 married women there were 520, or 30 per cent., who were sterile. As the sterile women are those who most frequently come under the physician's observation, the true percentage of sterility is probably lower. Small subserous fibroids frequently prevent conception by distortion and displacement of the adnexa. Interstitial fibroids form a considerable hindrance to conception, through the changes in the endometrium and the deformity of the uterine cavity which they produce. Cervical fibroids and cervical polyps usually prevent conception, although there are exceptions to this rule.

The statements of Olshausen commend themselves to all those who have large experience in dealing with fibroid tumors.

THE INFLUENCE OF FIBROID TUMORS ON PREGNANCY AND LABOR.

Olshausen,⁴⁴ from the statistics of numerous writers, concludes that the position of the child *in utero* is considerably influenced by the presence of myomata in the cervix or in the lower uterine segment. For example:

Presentation.	Normal.	Fibroids.
Vertex	95 per cent.	54 per cent.
Breech	3.1 per cent.	24 per cent.
Transverse	0.6 per cent.	19 per cent.

He quotes numerous authors concerning dystocia in labor, complicated by fibroids. Süsserott collected 147 cases; in 20 the forceps were used; 8 mothers and 13 children died. Nauss had 19 forceps deliveries in 241 cases; there were 5 maternal deaths. The mortality from version in fibroids is startling. Defour states that in 35 cases, 21 mothers and 27 children died. In Süsserott's 20 cases, 12 mothers and 17 children perished. Nauss reports 26 cases with 20 maternal deaths.

44. Olshausen: "Myom und Schwangerschaft," Velt's Handbuch der Gynäk., 1897, vol. II, p. 767.

J. Whitridge Williams⁴⁵ quotes Pinard as reporting 94 cases of fibroid tumor in 13,917 consecutive labors, or 0.6 per cent. Labor was spontaneous in 54, operative aid was required in 30, and the maternal mortality was 3.6 per cent. Williams states that submucous myomata, on account of the associated hemorrhagic changes in the endometrium, predispose to abortion or miscarriage. Pregnancy also influences the tumors, causing them to increase rapidly in size, more as the result of edema than of actual hypertrophy. The softened tumors, owing to the pressure of the growing ovum, undergo changes in shape, the pedicles may become twisted and gangrenous, and peritonitis may ensue.

At labor, the effect of the myoma depends on its size and situation. Generally speaking, subserous tumors have no great significance, except when their size leads to pressure symptoms. On the other hand, a pedunculated tumor may prolapse into the pelvis and give rise to serious dystocia. As a rule, interstitial fibroids of the lower uterine segment or cervix offer serious obstruction to labor. Fibroids in certain cases seem to predispose to placenta prævia and postpartum hemorrhage. In the puerperium, myomata not infrequently undergo degenerative changes—sometimes gangrene—if they have been subjected to prolonged pressure.

The results reported after forceps and version might be and probably would be improved by substituting the Porro operation, which would not only deliver a living child, but at the same time cure the woman of her fibroid tumor.

Lack of space prevents a further study of the relation of fibroid tumors to labor, but it is well recognized that in certain cases they produce death from dystocia, from accidents to the tumor (such as twisted pedicle, necrosis and infection of the tumor), and that one of the more serious risks of labor complicated by fibroid tumors is postpartum hemorrhage, as the presence of the tumor in the uterus interferes with the normal contraction and retraction of the uterus after the expulsion of the placenta. Nevertheless, there is a general consensus of opinion among those best qualified to judge that the relation of fibroid tumors to pregnancy is most marked in the production of sterility, and that unless unfavorably situated (that is, submucous and particularly in the lower segment of the uterus or in the cervix), women with fibroid tumors of moderate size will probably go through pregnancy and labor without serious trouble. I am not familiar with statistics dealing with a sufficiently large series of cases to state the actual risks entailed.

COMPLICATIONS OF FIBROMYOMATA OUTSIDE THE TUMOR AND UTERUS.

In addition to the deaths which would ensue from degenerations in the tumor and complications in the uterus as a result of fibroid tumors, in 252 women there existed the following complications outside of the tumor and uterus which would have proved fatal without operation in the series of 2,274 cases:

Dermoid cyst, suppurating	3
Dermoid cyst with twisted pedicle	1
Dermoid cyst, suppurating: sinus through abdominal wall from previous drainage operation	1
Ovarian cyst, suppurating	4
Ovarian cyst, twisted pedicle	2
Ovarian cyst, bilateral	16
Ovarian cyst, unilateral	115
Carcinoma of ovary	4
Papillary carcinoma of both ovaries	1
Abscess of ovary, bilateral	2
Abscess of ovary, unilateral	9
Tubo-ovarian abscess	2
Abscess of broad ligament	1
Pyosalpinx, bilateral	33

45. Obstetrics, New York, 1903, p. 574.