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IMPOTENTIA VIRILIS

Its Significance and its Treatment with Yohimbin-Spiegel, a new Aphrodisiac of great efficacy

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CONSTITUTING one of those troubles the consequences of which affect not only the individual sufferer, but, directly or indirectly, the family and State as well, impotence in the male is a malady possessed, to a certain extent, with distinct social significance.

The fact that it is so cautiously approached in public discussion, nay, that the time has but lately arrived when even physicians would concern themselves at all with the matter, is strikingly at variance with the substantial increase of its growth and prevalence,—the situation being an anomaly explicable only by the false notions still unfortunately existent with reference to diseases of the sexual apparatus. False shame, prejudice, and ignorance, all play important parts in this sphere, while the medical point of view, which alone should govern its consideration and treatment, is confused with a cloud of ethical, æsthetic, and even more remote notions, to the consequent dismay and injury of the patient.

Assuredly, impotence is not as fruitful a field for the quack and impostor as formerly. Specialists, urologists and neurologists are familiar with it, and know how greatly underestimated is its frequency. They know, also, the deplorable influence exerted by the malady upon the patient himself, how it discourages and depresses him, while reducing to a minimum his working capacity and interest in life; and especially keen is their knowledge of the pernicious influence exerted by the malady against a wholesome family-life.

But even those not practically concerned with this affection need only be reminded how powerful is the impulse toward reproduction and multiplication, the most imperious of natural instincts, to appreciate that impotence is a disease demanding close attention, and that its treatment has a higher value and importance than that of many other maladies now commanding professional consideration.

It is to be noted, too, that many of these unfortunates owe their trouble not so much to their own transgression as to certain conditions in our present-day civilization, which, in the struggle for existence, tend chiefly to undermine and debilitate the nervous system, one manifestation of which, "sexual neurasthenia," expressing itself in impotence.

Considering the prevalence and seriousness of impotence, it is certain that an effective medicament in its treatment will hold a conspicuous and honored place in materia medica. That such a remedy has long been sought is best evidenced by the large number of aphrodisiacs enumerated therein since the beginnings of medical science.

Unfortunately, however, the majority of these drugs have been either entirely ineffective in the direction sought, or were merely general nerve tonics, without specific effect upon the sexual apparatus, *e. g.*, phosphoric acid, quinine, iron, and spermin. Or, again, they did stimulate sexual activity, but were accompanied, however, with serious by-effects, *e. g.*, strychnine, morphine, cocaine, and cantharides. The latter are the most certain in their effect, but, owing to the irritation frequently produced in the kidneys and urinary passages by their use, they are also the most dangerous.

By a large number of physicians, the recently discovered Yohimbin-Spiegel, a new alkaloid, first elaborated by Dr. L. Spiegel,[1 2 3 4] private lecturer at the Pharmacological Institute of the Berlin University, has been demonstrated beyond question to be the most reliable and harmless of all aphrodisiacs.

Yohimbin-Spiegel occurs in the bark of the Yohimbehe tree, indigenous to German West Africa. This bark, first brought to Europe by the African traveler, Ludwig Scholz, was delivered to the Chemical Laboratory Güstrow, in Germany, with the remark that the natives of the Cameroon Territory had long used decoctions of it for increasing their sexual power.

According to Spiegel's statement, the free base, crystallized from a dilute alcoholic solution, represents well-formed prismatic needles with silky lustre, fusing at about 234° C. In various alcohols, in ether, acetic ether, and acetone, it dissolves readily; in benzol, with difficulty; and in water, hardly at all. Yohimbin-Spiegel turns the plane of polarized light to the right. Nessler's reagent gives a white, amorphous precipitate, as does phosphotungstic acid; with phosphomolybdic acid its precipitate is yellowish-white; and with picric acid, yellow and crystalline.

The reaction following is characteristic for Yohimbin. It forms a colorless solution in concentrated sulphuric acid. On dropping therein a small crystal of potassium bichromate, a streak with a beautiful bluish-violet margin appears that gradually changes to a dirty green.

The reactions of Yohimbin-Spiegel, as compared with those of cocaine have been thoroughly examined by Prof. Dr. C. Arnold and Dr. M. Behrens at the chemical laboratory of the Veterinary High School in Hanover. The results of these investigations are reported in the *Chemiker-Zeitung*, No. 97, 1901, as follows:

The two substances prove to be totally different in chemical properties, though similar in taste and in some physiological qualities. Reference has been made above to the slight aphrodisiac action of cocaine; this, however, is of no practical importance, owing to the toxicity of this alkaloid. Some publications, later mentioned herein, describe a certain analogy between cocaine and Yohimbin, based on their anæsthetic effect upon motor and sensory nerves, as well as upon mucous membranes. Recent investigations by Drs. Wingheimer and Spiegel have shown that the methoxyl group, demonstrated by the latter, is changed to a carboxyl group ester in Yohimbin, as well as in cocaine.

The formula of Yohimbin is not quite determined. The first analyses left it doubtful whether the formula $C_{21}H_{24}N_2O_4$, or the homologous one of $C_{22}H_{26}N_2O_4$, was correct. But later studies by Dr. Spiegel, still unpublished, show the latter ($C_{22}H_{26}N_2O_4$) to be correct; in harmony with that of its anhydride, $C_{22}H_{24}N_2O_3$.

Free Yohimbin-Spiegel changes under the influence of light and air, assuming gradually a slightly yellowish color. In contra-distinction to the free alkaloid, its hydrochlorate, in a dry state, possesses an unlimited stability. Therefore, the manufacturers of the new remedy place on the market not the free alkaloid, but its hydrochlorate, under the name of "Hydrochlorate of Yohimflin-Spiegel." This salt contains one molecule of water less than the composition of the base would warrant us in expecting. Its formula is: $C_{22}H_{28}N_2O_3HCl$. It dissolves with difficulty even in boiling water and crystallizes from an alcoholic solution in small bunches of branching needles. Its fusing point is at 300° C.

A number of other salts, besides the hydrochlorate, have been formed with Yohimbin, *viz.*, the nitrate, sulphate, phosphate, and hydriodate.

Therapeutic use has thus far been made only of the hydrochlorate, and all the physiological and clinical experiments described further in these pages were made with that salt.

Physiological Effects of Yohimbin-Spiegel.

Dr. Oberwarth,[4] at the Pharmacological Institute in Berlin, first studied the effect of Yohimbin upon frogs, mice, rabbits, and dogs. Using relatively large doses, he found the effect to be first stimulating and then paralyzing upon the central nervous system, especially upon the vital centers for cardiac and respiratory action.

Smaller doses, which alone bring out the specific effect upon the genital organs, were employed by Professor Dr. Loew in experiments made at the veterinary physiologicaly laboratory of the Agricultural High School in Berlin. He injected subcutaneously into rabbits, cats, and dogs from 5 to 15 mgm. of the hydrochlorate in one-per-cent. solution and, several minutes after, observed a dilatation of the vessels of the skin and of the visible mucous membranes. The ocular conjunctiva, the muzzle, the nose, and the ears became red and warm. Coincidently, the animals became more lively, owing probably to vascular dilatation in the central nervous organs.

The phenomena presented by the sexual apparatus were most conspicuous. The testicles and epididymes began to

swell. On being exposed, it appeared that this swelling was due to an enormous dilatation of the vessels of these organs, an enlargement that was most marked in the case of the rabbits. In cats and dogs, a swelling and hardening of the penis was more in evidence, varying with the filling or overfilling with blood. Later, dogs exhibited regular, powerful erections of occasionally an hour's duration or more. Similar results were also observed in the case of mice and guinea pigs, as shown by Professor Dr. Roberts Bartholow, of Philadelphia,[17] who, like Dr. Duhot, of Brussels,[18] and Dr. Poltawzeff,[19] fully confirmed the findings of Oberwarth and Loewy in pursuing the physiological effect of Yohimbin.

As later investigations by Professor Loewy [16] showed, the erections are probably caused by a direct stimulation of the erection center in the lumbar cord. At all events, they are not caused in a reflex way by the testicles, since Yohimbin produces erections even after the removal of both testicles.

Yohimbin-Spiegel, therefore, is a vaso-dilating drug, which, when employed in suitable doses, limits its effect substantially to the vessels of the sexual apparatus, and is thus able to cause erections. Withal it is absolutely innocuous. When its effect has passed off, the animals are again normal. Even subcutaneous injections kept up daily for four weeks caused no injury. In particular, the kidneys proved, even after that prolonged treatment, to be perfectly healthy.

As far as the investigation had gone, it could not be positively asserted that the formation of semen had been stimulated; nor could an increase of the *libido sexualis* in animals be observed by most investigators. Krawkow[20] alone reports an observation in which a dog treated with Yohimbin manifested strong sexual excitement and made violent efforts at intercourse.*

Indications for the Employment of Yohimbin-Spiegel.

From the physiological effects discussed above, we may deduce a number of indications for the exhibition of Yohimbin for curative purposes. It is, first of all, a remedy for male impotence. But, of course, every variety of impotence cannot be relieved with Yohimbin.

* Cited by Lewitt, cf. 50.

The name, impotence, comprises two totally different forms of disease: *impotentia generandi* and *impotentia coeundi*. In the former the performance of the sexual act in a normal manner is possible, but the getting of offspring is out of the question, because the formation of semen is disordered. It seems doubtful whether this form of impotence, in the presence of which we are at present absolutely powerless, can be cured or even improved by Yohimbin-Spiegel, it being still an open question, as intimated before, whether the preparation has any influence upon the secretion of semen.

Its rightful field is the second form of impotence, *impotentia coeundi*, in which performance of the sexual act is impaired. *Impotentia coeundi*, however, occurs in several different forms, in which Yohimbin exhibits different therapeutical values.

Organic impotence is due either to congenital and acquired defects, or to malformations of the sexual organs, rendering coition impossible. In this sphere, we have to deal with diseases affecting the penis and the surrounding parts, or with a lesion or loss of the testicles. Upon the affections first-named, Yohimbin has no influence, but upon impotence due to loss of the testicles, some effect may be noted, in view of the results of the experiments by Loewy, mentioned previously, upon castrated animals.

Organic impotence is closely related to that form based upon diseases of the central nervous system and involving the erection center in the lumbar cord. Conspicuous among such ailments are tabes, myelitis, and others. In such cases the efficiency or the reverse of Yohimbin is conditional upon the fact whether there is present a remnant of the center, which, while no longer responsive to the normal stimuli, will react to the stronger influence of Yohimbin.

The step to the next important variety, termed functional impotence, is formed by that kind of impotence occurring in constitutional disease or in intoxications induced by medicines or articles of diet. It is a form observed in diabetes, obesity, and renal diseases, as well as in cases of excessive use of morphine, opium, potassium bromide, alcohol, tobacco, and tea.

In this sphere Yohimbin-Spiegel is also indicated, where its energy of action will produce a result not obtainable from weaker stimuli. In the early stages particularly, when the trouble is as yet only a functional weakness, without any development of an anatomical lesion of the nervous system, the remedy should be given a trial.

We come, finally, to a consideration of that purely functional impotence dependent on a neurasthenic-psychical basis. It is the most prevalent form of all and most amenable to the curative influence of Yohimbin-Spiegel. It manifests itself in several ways: Normally strong erections pass away too rapidly; they are too weak, occurring under certain conditions only, or—its most severe form—the erections are absent altogether. This last form is designated as paralytic impotence, and is often accompanied by morbid disturbances of the seminal discharge.

The specific effect of the remedy upon the erection center eliminates the reliance of the erection on the psychical or nervous state of the individual. In this manner Yohimbin effects a separation of somatic and temporal conditions, causing, as it were, an erection without the intervention of the patient.

Though the employment of Yohimbin in the treatment of impotence is obviously justified by the experiments on animals described above, we further cite some additional indications derived from the clinical experiences gained.

Physicians' Experience with Yohimbin-Spiegel.

As Yohimbin-Spiegel has been widely employed on human subjects, we are able to form a clear idea of the mode of its action, its limits of efficiency, its indications or the reverse, and its dosage.

I. Observations Made on Healthy Subjects.

In many cases, the experiments made with healthy males have confirmed the facts observed in the cases of animals. In some instances swelling of the testicles and a sensation of heat in the genital organs have been noted, even in healthy subjects, as resulting from the use of the remedy. A full description of them has been made by Dr. Seitz, of Erlangen."

Identical symptoms frequently occur, however, in the impotent, and have been referred to in the papers by Prof. Dr. Luigi Maramaldi, of Naples,[24] Dr. Schalenkamp, of Crombach,[14] and Dr. Berger, of Berlin.[24]

In many cases of normal subjects, after their use of Yohimbin, there could be noted turgidity of the penis, succeeded by swelling, stiffness, and erections, more or less prolonged. In this respect, the case reported by Seitz, in the person of a healthy physician, is the most interesting. On the fourth day of the administration of Yohimbin-Spiegel hydrochlorate (one tablet of five mgm. three times a day) powerful early-morning erections were noted, occurring during the several days of the ingestion of Yohimbin. The nocturnal erections, as well, were more powerful and noticeably more prolonged than under normal conditions.

Such results, of course, were not obtained in all healthy subjects. Thus, Dr. A. Hess, of Berlin,[31] states that he could produce no erections with the remedy in healthy persons; but the fact that, even in some of his cases, dreams of a voluptuous nature occurred after being administered, shows the relations of Yohimbin to the sexual organization. N. P. Krawkow, of St. Petersburg,[30] also notes negative results in normal subjects.

Upon the insufficient dosage of the remedy,* however, this absence of effect partially depends. But even were no effect whatever produced from the use of Yohimbin in healthy persons, it would prove nothing, one way or the other, as to the efficiency of the remedy in cases of actual impotence. Other drugs as well are known to produce their effects only in disease. The various antipyretics, for instance, promptly reduce high-fever temperatures, but normal temperatures are affected very little or not at all by them. In the relaxed uterus, ergotin, again, causes powerful contractions, but has little or no effect upon the organ when normal.

II. Observations upon Men Suffering from Impotence.

Discussing the experiences reporting the efficacy of Yohimbin-Spiegel, we will adhere to the classification of the different forms of the affection outlined above.

* On this point, note the arguments later adduced.

At this writing, reports are lacking on the effect of Yohimbin in those cases of organic impotence in which the absence of the testicles comes into question; and this is not surprising in view of the rarity of such observations. In cases of long-standing atrophy or absence of the testicles, however, any attempt with Yohimbin-Spiegel to induce erection seems almost hopeless. Because of the lack of normal stimuli arising within the testicles, alterations in the erection center — a kind of atrophy from inactivity — must eventually develop, arresting the excitability of its cells. But in such cases, where the testicles have been absent only a short time, perhaps because of their removal for disease, the remedy under consideration may prove effective. By its frequent stimulation of the center, its oft-repeated administration may guard the latter and continue its functions. According to Professor Lœwy,[18] Yohimbin is indicated in such cases wherein the testicles have been removed from subjects still young and in the flower of their manhood because of tuberculous or other malignant disease. In cases of these unfortunates, Loewy is of the opinion that by the use of Yohimbin they may be saved from *impotentia coeundi*, otherwise almost certain.

In diseases of the central nervous system, especially in tabes, their most serious form, frequent employment of Yohimbin-Spiegel has been made. Prof. Dr. E. Mendel, of Berlin, was unable to note any marked results, omitting, however, to state what stage of the disease he had under observation; it is obvious that only in its initial period can Yohimbin be effective.

Dr. Fritz Euler-Rolle, of Vienna, has reported successful results in tabes, having produced not only erections, but in one case even ejaculations; though permanent results, of course, were impossible, Prof. Dr. L., of B., in a letter to the proprietors, states that in a certain tabetic patient, impotent six months, normal erections with ejaculations recurred after administration of Yohimbin-Spiegel.

We must conclude, consequently, that Yohimbin is well worthy of a trial in diseases of the central nervous system. A decisive judgment as to its curative effect can be only reached, however, after more evidence is accumulated.

In diabetic impotence, Dr. Felix Hirschfeld, of Berlin, was successful with Yohimbin, and in the impotence of intoxication it has also demonstrated its value. Thus, Dr. James Silberstein, of Vienna,[36] reports the cases of two alcoholic patients, in whom, after one and two weeks' trial, respectively, the recurrence of erections was noted. In a third case, failure was observed.

In two cases of impotency arising from lead-poisoning, Dr. Fritz Euler-Rolle[40] observed that sexual potency returned and remained normal as long as Yohimbin was taken.

Silberstein[36] reports a case of bromine intoxication in which potency returned after a week's use of the preparation, the bromine, of course, being discontinued.

Contrasted with the relatively few investigations concerned with the forms of impotence above recited, the literature covering cases under the neurasthenic-psychical form is quite voluminous. The importance attributable to Yohimbin-Spiegel in the treatment of this wide-spread form of the disease is best expressed in the words of Privy Medical Councillor Prof. Dr. Eulenburg, of Berlin,[41] in his paper* on sexual neurasthenia, appearing in the *Deutsche Klinik:* "In the management of the neurasthenic forms of impotence at least, Yohimbin-Spiegel renders every other form of medicinal treatment unnecessary.

The first to employ Yohimbin-Spiegel in sexual neurasthenia—or indeed first on the human subject—was Prof. Dr. E. Mendel, of Berlin.[7] In forty cases he gave it, and observed, either immediately on administration or later, the occurrence of erections permitting coition, in half of the number.

The next reports of successful results from Yohimbin were made in five cases by Dr. Berger, of Berlin,[11] in ten cases by Dr. Duhot, of Brussels,[13] in three cases each by Dr. Schalenkamp, of Crombach,[14] and Dr. Franz Weisz, of Budapest,[15] in several by Prof. Giacomo di Lorenzo, of Naples,[37] and in twenty-four cases by Dr. Vincenzo D'Amato, of Rome.[38] Experiences with Yohimbin-Spiegel are reported as well by the following, some of whom are enthusiastic over its results in neurasthenic impotence: Prof. N. Barrucco, of Bologna,[39] Privy Med. Councillor, Prof. Dr. A. Eulenburg, of Berlin,[41]

Dr. H. Kühn, of Hoya a/W.,[23] Dr. L. Löwenfeld, of Munich,[40] Prof. Dr. Luigi Maramaldi, of Naples,[24] Dr. J. Munoz, of Madrid,[19] Prof. Dr. C. Posner, of Berlin,[22] Dr. Victor G. Vecki, of San Francisco,[46] Prof. W. F. Waugh, of Chicago,[27], [28] Prof. Reynold W. Wilcox, of New York,[29] J. Rutter Williamson, of Lahore, India,[17] and others.

A complete list of these papers with their titles is comprised in the bibliography appended.

Naturally the percentages of cures or improvements vary with these different authors, but, with most, it is gratifyingly large. Cures in all cases were noted by some. Eulenburg, for example, writes that in all the twelve cases of neurasthenic impotency persistently treated with the remedy positive results were achieved in spite of the fact that the disease was severe.

In all of his twenty-four cases of the same form of the malady, Dr. Vincenzo D'Amato, of Rome,[38] reports that the patients were cured after three to six weeks' treatment.

Maramaldi[24] again reports the cure of five patients; Munoz was successful with it in five out of six cases; Duhot[13] in eight out of ten, etc., etc.

The gravity and duration of the disease, as well as the skill and experience of the physician, are, of course, important factors in its treatment. In cases of feeble and short erections, treatment with Yohimbin-Spiegel is more promising than in those cases wherein no erection at all responds to normal stimuli. This is especially true when the latter condition is of several years' standing. But that relief is possible, even in this sphere, is shown in the experience of Berger,[34] who succeeded with Yohimbin in grave cases of paralytic impotence of several years' standing; it is further shown by the experience of Dr. George J., of B., who succeeded in a case of impotence of ten years' standing, as well, finally, by an additional case of Eulenburg, who successfully cured a case of impotence of twenty years' standing with Yohimbin-Spiegel.

Rather than cite additional figures, we will here submit certain statements of opinion formed by various authors as a result of their study of Yohimbin-Spiegel as a remedy for impotence.

Prof. N. Barucco, of Bologna,[38] writes: "The medicament has triumphed even in very graves cases in which hydrotherapy, electrotherapy, and the administration of strychnine had failed."

The statement of Prof. Dr. Eulenburg, that Yohimbin-Spiegel renders all other medicinal treatment in neurasthenic forms of impotence unnecessary, has been previously cited, and will probably recur to our readers.

Dr. Duhot, of Brussels,[13] concludes that in Yohimbin-Spiegel physicians will find a powerful weapon in the fight against neurasthenic impotence, and one that may be employed without the slightest danger.

Prof. Giacomo Di Lorenzo, of Naples,[37] states that with electricity, hydrotherapy, and the strychnine and iron treatment introduced by him, he had been fairly successful formerly, but he unreservedly acknowledges the great therapeutic superiority of Yohimbin-Spiegel over these methods.

The preparation, according to Prof. Maramaldi, of Naples[40], has furnished to the treatment of impotence one of the most valuable contributions in the solution of the difficult problem.

In view of the innocuousness of the remedy, it is the opinion of Dr. E. Kraus, of Vienna, that the practitioner will readily avail himself of it, especially as it will insure him the gratitude of his patients.

While the preponderance of evidence is thus in accord on the great value of Yohimbin as an acquisition to materia medica and its singularity as the only useful aphrodisiac, some physicians express opinions less favorable. Thus, after experiments upon healthy subjects, Dr. A. Hess, of Berlin,[41] and Prof. N. P. Krawkow, of St. Petersburg,[10] express an unfavorable view of the preparation.

We have indicated before that the results in healthy subjects are dissimilar from those with the sick, an assertion demonstrable by the fact that in the one case of impotence treated by him, Hess could note a successful issue with the remedy.

Furthermore, Professor Fürbringer, of Berlin,[42] the only author who claimed until recently not to have seen a single successful use of Yohimbin-Spiegel in impotence, now reports a case in which the preparation had a surprising effect.

If it does not prove effective in every instance, Yohimbin, in this respect, is like all other remedies, even the most powerful. Nevertheless, we are quite justified, from the observations already noted, in concluding that at present Yohimbin-Spiegel is the only remedy for impotence that has been tested scientifically and demonstrated to be both effective and innocuous.

Mode of Action of Yohimbin-Spiegel.

The assertion that the effect of the remedy under notice upon the sexual apparatus depends on the idea of suggestion is negatived by many circumstances. In the section on physiology, for instance, it is shown that in animals like mice, Guinea-pigs and dogs, Yohimbin-Spiegel also causes erections; and of course in such cases, any theory of suggestion is excluded. Further evidence against such a hypothesis is furnished hy Dr. L. Dejace, of Brussels,[15] who reports that Yohimbin-Spiegel proved effective after treatment by suggestion had failed. Again, Dr. Duhot, of Brussels,[15] reports success in nearly all of his cases, although the fact that the medicine was likely to have an aphrodisiac effect was imparted to none of the patients.

The action of the alkaloid, therefore, is a real one, though opinion is at variance regarding the objective point of the remedy. The authors of one group, especially Maramaldi, maintain that it acts directly upon the testicles, and that with each dose fresh blood is carried to them, thus producing improved nutrition and more active function. The invigoration, in this manner, of the testicles is said to be followed by more vigorous erections.

As opposed to this view, other physicians seem disposed to regard Yohimbin-Spiegel as a direct stimulation of the erection center. Confirmatory of this theory is the experiment, described before, of Professor Dr. Loewy, who was even able to produce erections in animals deprived of their testicles.

This divergence of opinion as to the objective point of the drug seems to have some influence on conceptions as to its mode of action. It is evident, speaking generally, that the use of Yohimbin-Spiegel does not relieve impotence immediately, although such cases are actually reported by Mendel[7], Williamson[17] and Vecki.[18] Its more customary action is a

tendency, rather, to a gradual swelling, stiffening and erection of the member. The necessity for its prescription over a fair period of time is explained by Maramaldi[11] on the theory that by degrees the testicles become normal again and only gradually exert again the physiological stimulus bringing about erections.

The supporters of the theory of direct irritation assume that only by repeated stimuli can the abnormally irresponsive center be sufficiently invigorated to resume its function.

Most physicians agree further that after potency has been restored by means of Yohimbin-Spiegel, it is retained for a variable period after discontinuance of the same. Few only report that the effect of the remedy lasted solely for the period of its administration.

This after-effect of Yohimbin can be explained, whatever may be the theoretical standpoint favored. According to Maramaldi, the testicles, made normal by the stimulus of the alkaloid, continue to act upon the erection center until they are damaged anew.

Those accepting the direct action theory assume, in line with other well-known facts in neuro-pathology, that the repeated exhibition of the drug establishes a "path." Only much beaten paths are easily travelled on. As long as the impotence existed, the path to the penis from the erection center was not in use and thus became obstructed. Under the energetic stimulation of Yohimbin-Spiegel on the erection center, the currents again begin to pass along this channel and continue doing so with repeated ingestion of the drug. Once thus cleared, the path remains pervious for a variable length of time, perhaps permanently, even after the displacement of Yohimbin with weaker normal stimuli.

Mode of Employment and Dosage of Yohimbin-Spiegel.

In most patients, the preparation has had the desired effect when given internally in three daily doses of 5 mgm. of the hydrochlorate. The manufacturers make tablets containing exactly 0.005 gm. of hydrochlorate of Yohimbin-Spiegel. They are put up in glass tubes holding ten tablets each.

As these tablets keep for an unlimited time, while the one-per-cent. solution of the hydrochlorate (Solutio Yohimbini-Spiegel) deteriorates in a few weeks, the solid form is, for internal use, decidedly preferable to the liquid.

In many cases, the use for some weeks of the normal daily dose of three tablets will serve to induce erections; and only in rare cases will it be found necessary to continue the treatment for four to six weeks in order to achieve marked results. The three tablets are best administered at these intervals: The first, in the morning, one hour before rising; the second immediately after the chief meal of the day, and the third in the evening after retiring. It is advisable, after taking the second tablet, to rest at least half an hour. The tablets may either be swallowed entire or chewed; to dissolve them before using is unnecessary.

After a medication of six to eight days and no results or incidental effects are apparent, many physicians think it advisable to hasten the action of the remedy, either, like Berger, by increasing the dose, or, as Eulenburg suggested, by introducing the alkaloid in the form of subcutaneous injection.

Without injury to the patient, Beyer[11] has given, in some cases, as much as nine tablets, equivalent of 0.045 grammes daily before erections warranting intercourse occurred.

Again, in order to obtain prompt results, Prof. W. F. Waugh, of Chicago,[17, 18] administers one tablet at seven, eight and nine o'clock on several successive evenings.

In the calculation of dosage, physicians should be governed, as a rule, by the question, as to whether or not any of the incidental effects later described are manifest in the patient.

In cases of such gravity that ordinarily the tablets would fail, Eulenburg[17, 47] begins by injecting, usually into the inner surface of the thighs, 0.5 gm. of a two-per-cent. solution of the hydrochlorate, the equivalent of 0.01 gm. of the salt; and should the effect of this be nil or insufficient, he rapidly increases the dose to one gm., the equivalent of 0.02 gm. of the hydrochlorate of Yohimbin-Spiegel. At first these injections are made daily; but after the effect is apparent, only every two or three days or at longer intervals; while, after

about twenty injections have been made, they are suspended for even longer periods.

The prescription reads:

℞ Yohimbin-Spiegel ..... 0.2 gm.
Solve in
Aq. dest. sterilisat..... 10.0 gm.
D. ad. vitr. fusc.

S. Two-per cent. Yohimbin solution for subcutaneous injection (0.5 to 1 gm. pro dosi).

The solution must be made in boiling sterilized water; keeps only a few weeks and is most effective when freshly prepared. A drop of chloroform may be added to improve its stability.

In certain patients of Krawkow, there were pronounced incidental effects even after the injection of but 5 mgm. (one tablet). Such cases indicate an idiosyncrasy, or abnormal sensibility, towards the drug. In such and other cases where an increase of dosage to an effective quantity is thus precluded, treatment with the preparation is, naturally, inadmissible.

On the other hand, as with other drugs and conditions, there are cases where no results, even with large doses, are obtainable, owing the abnormally slight or absent irritability of the center. The number thus far of such cases is relatively small, and the percentage will be still less when physicians decline to restrict themselves, as was often done, to small initial doses, but, instead, will gradually increase the quantity and resort, if necessary, to subcutaneous injections.

That the same dose of Yohimbin is not effective in all persons need not surprise us. Excitability, varying individually, is found in all centers of the nervous system, and the fact is also well known that the erection center, in particular, differs greatly in sensibility even toward normal stimuli.

Sensual concepts or perceptions toward which some are indifferent have an extremely stimulant effect upon others. In like manner, the degree of stimulus exerted by Yohimbin-Spiegel necessarily varies with the individual, before it finally becomes effective.

On the assumption of the stimulant effect of Yohimbin-Spiegel on the erection center the necessity accordingly exists

that where small doses of it show insufficient results, the stimulus must be increased to the limit permissible. In other words, larger doses must promptly replace smaller ones.

Should Maramaldi's theory, on the other hand, be accepted, then more prolonged treatment with smaller doses is preferable, as is done by Mendel, and the former, who declares that Yohimbin-Spiegel acts upon the testicles, improves their nutrition and gradually invigorates them. Their functions being improved in this manner, they will accordingly transmit more energetic stimuli to the center, making the latter act more powerfully upon erection. Effects of this kind with Yohimbin are, of course, produced not suddenly, but only slowly. In addition, the results of this method are also very good, as regards duration and permanence.

The Effect of Measures in Support of the Action of Yohimbin.

Impotence can frequently be regarded merely as a symptom of a disease, often indeed the most important one. At times, merely the wish for the removal of this symptom is the motive of the visit to the physician by the patient. But the former, not neglecting the causative disease underlying the symptom, will take his measures accordingly, and with the cure of the fundamental disease the impotence usually disappears. When the latter is due to diabetes, excessive obesity, general debility from defective nutrition or anæmia, the treatment for such indications should, of course, be instituted. When caused by the abuse of drugs, tobacco, alcohol, or the bromides, these poisons naturally must be withheld during treatment.

If the impotence is a neurasthenic manifestation, attention to a proper regulation of the mode of life must be paid, assisted by methods of physical treatment, *e. g.*, massage, hydrotherapy, and electrotherapy, coincident with which the greatest possible curtailment of such nervous stimulants, as strong coffee, tobacco, alcohol andtea should be inaugurated.

When these latter are used simultaneously with Yohimbin, their effects and that of the remedy may become cumulative and perhaps followed by untoward incidental effects. Special

care in the use of alcohol should be observed. Seitz[39] reports the case of a healthy physician who, on taking champagne after the use of Yohimbin, suffered with violent occipital headache, accompanying excessive erections. The ingestion of Yohimbin *per se* apparently requires no special diet.

Incidental Effects.

Yohimbin-Spiegel can be truthfully described as an innocuous remedy for impotence. Upon this point, Mendel, Dejace, Posner, Duhot and the majority of other physicians who have used it lay particular stress.

After the initial dose of 5 mgm. the symptoms, as a rule, observed in the genitals are sensations of heat and tension in the testicles and the scrotum. Occasionally a slight hyperæmia of the ocular conjunctiva can also be noted.

With the increase or frequent repetition of the dose, the first general symptom noted, along with greater fulness of the ocular vessels, is a feeling of vertigo. This disappears, however, very soon and should not, in any sense, be regarded as contra-indicating the treatment. Besides the vertigo, some salivation and a slight degree of weakness can perhaps be observed. In a few cases, a slight chill preceding a perspiration has also been noticed, but even these do not signify that the use of Yohimbin should cease. In many cases, the first doses only produce such violent reactions; while under continued use, all these concomitant symptoms are absent, instances of which are supplied by Eulenburg[38] and Kraus.[41] However, should the by-effects just mentioned set in after the ingestion of Yohimbin with a certain intensity and occur invariably after, the dose must first of all be reduced.

D'Amato has also reported increased frequency of the pulse, palpitation of the heart, præcordial anxiety, and sleeplessness. Should these be observed without erections accompanying, they can also be ascribed to excessive doses. If associated with erections, their cause is found, not in Yohimbin, but in the erections it produces; for young neurasthenics are said to show similar symptoms whenever vigorous erections occur and opportunity for intercourse is lacking.

Mention should be made, finally, of gastric troubles after internal exhibition, noted by a few authors, *e. g.*, loss of

appetite, pain in the stomach, and slight colic. When the Yohimbin is given after meals, such by-effects will disappear.*

In patients suffering from piles, the occurrence was observed of rather profuse hemorrhoidal losses of blood.

Excessively large doses are no longer pharmacological but rather toxic, and produce conditions of excitement resembling those due to alcohol. Talkativeness, a sort of intoxication, and marked liveliness are the signs of such conditions. These, however, have not been reported as following the administration of medicinal doses. They have been observed, though, under the conditions described, and hence were communicated to the manufacturers as instances of the abuse of the drug in the shape of excessively large doses.

Contra-Indications.

A contra-indication to the use of Yohimbin-Spiegel would be first of all furnished by the incidental effects above enumerated, should they occur with the smallest doses, not alone after the first administration, but after each ingestion, and should they be pronounced in character; in other words, when an idiosyncrasy against the drug manifests itself.

In the case of nervous and easily excitable persons caution in the dosage of Yohimbin-Spiegel is advisable, the necessity therefor being apparent in the data furnished at the close of the previous section. According to Berger,[24] another contra-indication, dependent upon the nature of the Yohimbin effect, is formed by chronic inflammations or hyperæmias of the pelvic organs, especially of the male genitals. Schalenkamp[14] likewise takes this view, having particularly in mind chronic prostatitis. On the other hand, Dr. Tretzel, of Rothenburg, states in a letter to the manufacturers, that he noted a beneficial effect upon prostatitis, especially on the drawing pains in the testicles; therefore, he advises the use

* Offsetting this, Privy Sanitary Councillor Dr. Mylius, of Rathenow, writes that he has observed extremely favorable influence of Yohimbin upon digestive activity. In two patients who had long suffered from impotence and severe gastric catarrh, for the cure of which all possible measures had been employed, it was noted that all the stomach troubles disappeared along with the impotence. The tongue, thickly coated before, became perfectly clean, even noticeably red; the appetite improved and digestion became absolutely normal; there was even noted a gain in weight.

of Yohimbin-Spiegel in impotence complicated with that complaint.

Equally happy results in impotence complicated with prostatitis are reported by Dr. Hauptmann, of Reichenau, and Dr. A. Bunge, of Buenos Ayres.

In diseases of the kidneys, too, the plethora occasioned by the drug must have a beneficial influence. Dr. Roberts Bartholow[39] thinks that this hyperæmia may act favorably in albuminuria, but advances merely theoretical reasons, and only further tests in this direction can furnish the certainty desirable.

The Employment of Yohimbin-Spiegel in Women.

The successful use of Yohimbin in sexual diseases of women rests upon its power to produce hyperæmia of the female sexual organs. Accordingly it should prove effectual wherever there is desired an increased afflux of blood to the pelvic organs.

It was for this reason recommended by Dr. E. M. Simons[38] to the Berlin Society of Obstetrics and Gynæcology, in cases of parametritis atrophicans, in aplasia of the female genital organs, and in amenorrhœa, with its manifold nervous sequelæ; while Schalenkamp[14] observed an actual prolongation of menstruation after administering Yohimbin-Spiegel. It is also worthy of trial in climacteric disturbances.

Schalenkamp did not observe any stimulation of the *libido sexualis* in women sexually frigid, although, in this respect, Berger[24] is of opinion that an improvement could be noted. This observation of the latter appears not to be an isolated one; for communications to the manufacturers show that it may not seldom be possible—contrary to what has hitherto been possible in the male subject—to excite the absent desire in women.

In the case of a woman whose daily dose had been increased to eight tablets of Yohimbin, which were entirely well borne, Dr. Fritz Euler-Rolle, of Vienna,[40] witnessed an awakening of the sexual impulse, absolutely lacking previously.

While our knowledge of the influence upon the female sex of Yohimbin-Spiegel is still in its infancy, it can hardly be

doubted that here, too, the drug will prove itself a useful remedy applicable to many cases.

The Possibility of Additional Application of Yohimbin-Spiegel.

The vaso-dilating action of Yohimbin Spiegel, as has been shown, is not confined to the sexual organs, but affects other vascular territories as well. The manner in which it acts in larger doses shows that the vessels of the central nervous system are likewise acted upon, and that the increased afflux of blood to these induces several symptoms, described as following the administration of Yohimbin.

There is ground also for the belief that in some forms of mental disease, especially melancholia and stupor, Yohimbin may prove quite serviceable. As these are diseases hardly amenable to other modes of treatment, a trial should be made as having a sound scientific basis; while in the event of failure with it the attempt can do no possible injury.

It is quite possible as well that the effect of the remedy in the direction of the altered blood distribution in the central nervous system would have a beneficial influence upon the general health in neurasthenic states. At any rate, Dr. Fritz Euler-Rolle[40] reports neurasthenic cases showing improvement with the medicament. We quote him: "The effort to collect further data of this kind is worth making, as well as to employ Yohimbin in cases of uncomplicated nervousness and neurasthenia, without any disturbance in the sexual sphere, in order to determine whether the preparation can also be used as a nervine pure and simple."

Writing to the manufacturers, a physician stated that in cases of nervous and irritable women treated with very small doses of Yohimbin-Spiegel he had observed an extremely favorable effect upon the neurasthenic symptoms. Rest of the most complete character is said to be a valuable aid.

Dr. L., Chief Physician of the District of L., claims that, given in small doses for a considerable length of time, Yohimbin is a valuable tonic, free from the dangers associated with the administration of cocaine.

Maramaldi[44] likewise mentions the peculiarly favorable effect of the alkaloid upon the entire organism.

To conclude, Dr. Zu'z, of Eberstadt, near Darmstadt, writes that he regards Yohimbin-Spiegel not only as the best aphrodisiac, but as a good remedy also in general neurasthenia. Treated by him with the remedy, his patients felt invigorated and better able to work after its use. The cutaneous vessels are dilated also by larger Yohimbin doses. Thus, heat dispersion is increased, in consequence of which the bodily temperature must fall, as Krawkow[20] has likewise found in the experiments on animals. In this respect, the action of Yohimbin resembles that of certain antipyretics. Whether this property of the alkaloid can be advantageously used in practice seems doubtful.

In view of what Dr. Mylius, Privy Sanitary Councillor of Rathenow, has noted (see footnote on page 23), it would appear that Yohimbin-Spiegel is worthy of trial in long-standing cases of gastric catarrh, especially of the nervous variety, all of which yield with difficulty to other medication.

Yohimbin-Spiegel as an Anæsthetic.

As shown by recent investigation, Yohimbin-Spiegel, aside from the effects resulting from its internal or subcutaneous administration, produces an additional local action when it is directly applied to a nerve trunk, or when its solutions come in contact with a mucous membrane. We thus have effects which promise to open up an entirely new field to the drug, by virtue of which it will compete with a number of remedies now in extensive use.

The anæsthetic properties of the remedy were first observed in December, 1901, in the course of a comparative examination chemically of Yohimbin-Spiegel and cocaine. C. Arnold and M. Behrens, of Hanover,[21] found that hydrochlorate of Yohimbin-Spiegel "applied to the tongue produces a furry taste and a temporary anæsthesia similar to that of cocaine."

This observation, however, remained entirely unnoticed, and independently of it, in August, 1902, Dr. Camillo Magnani, of Turin,[22] starting from different premises, found that a one-third to one-per-cent. solution of hydrochlorate of Yohimbin-Spiegel dropped into the conjunctival sac rapidly produced insensibility of the conjunctiva and cornea. This

anæsthesia may last as long as half an hour. The paper of Dr. Magnani induced Prof. Dr. Lœwy and Private Lecturer Dr. Müller[14] to make experiments at the Veterinary Physiological Laboratory of the Berlin Agricultural High School upon rabbits and dogs, and in part on human subjects as well.

These showed that Yohimbin-Spiegel produced anæsthesia, not only in the conjunctiva—confirmatory of Magnani's statements—but also in the nasal mucous membrane, and that the sense of taste in the tongue was abolished. When directly applied to a nerve trunk, Yohimbin retards the excitability and conductivity of the motor and sensory nerves. In the effects mentioned above Yohimbin-Spiegel closely resembles cocaine. In the strength in which it is used (one or at most two per cent. of the hydrochlorate) it must be designated as innocuous in comparison with cocaine. It differs from the latter, however, in not producing vaso-constrictor effects; it has either no influence upon the width of the vessels or causes some slight dilatation of them.

In the case of its use in the eye a difference from cocaine is shown. Cocaine dilates the pupil; according to Magnani's observation, Yohimbin leaves it either unchanged or causes a slight contraction.

In consequence of these physiological investigations, the anæsthetic property of Yohimbin-Spiegel has been repeatedly utilized for therapeutic purposes. Thus, in his experiments at the Royal Charité Hospital Clinic, of Berlin, Dr. Haike[15] found a one-per-cent. solution of the hydrochlorate to be without effect, in the human subject, in the middle ear and the nose. There was an anæsthesia effected in the ear, however, by a 1.5-per-cent. solution in 30-per-cent. alcohol, and in the nose by a two-per-cent. solution in boiling distilled water. Absolute anæsthesia of the nasal mucosa was secured on the surface only; in deep cauterizations some pain was felt, but the patients were insensitive to superficial applications of caustics.

Haike recommends Yohimbin primarily to avoid the toxicity of cocaine, and, further, for all cases in which the vaso-constricting effects of cocaine are undesirable, particularly in the removal of polyps and granulations from the middle ear

and in operations on the posterior extremities of the turbinated bodies.

In a comprehensive paper, Dr. A. Strubell[51] publishes his investigations relative to Yohimbin-Spiegel as an anæsthetic, the experiments having been conducted in the State Polyclinic for Diseases of the Nose and Larynx in the Kurländer Palace in Dresden.

He summarizes the results covering some twenty cases as follows:

1. An unquestionable hyperæsthesia, sometimes full anæsthesia, of the mucous membranes of the upper air passages follows the local application of a one-per-cent. solution of Yohimbin-Spiegel.

2. This anæsthesia is quite sufficient for operations that do not extend too deeply.

3. The anæsthesia persists without anæmia, rather with moderate hyperæmia, and hence without contractions of the erectile tissues of the nose.

4. Marked primary or secondary hemorrhages have not been observed by me.

5. In the concentration and quantity employed, the drug is absolutely innocuous, as is shown also by the results of internal medication.

Concluding his paper, Strubell points to the public excitement in Vienna caused by a recent death after treatment with cocaine, emphasizing the importance to the practitioner of a perfectly harmless anæsthetic.

With reference to the eye, Dr. H. Salomonsohn, of Berlin,[52] has also subjected Magnani's statements to a test. He confirms the anæsthetic action of Yohimbin-Spiegel upon the conjunctiva and cornea, adding that the latter becomes insensitive one minute after the one-per-cent. solution is directly dropped upon it. As with cocaine, the anæsthesia changes to a burning sensation lasting about a minute, but this is quite tolerable.

Accommodation is not markedly influenced. Contrary to Magnani's observation it is said that in the healthy eye mydriasis occurs but not until from one to two hours after the application of Yohimbin; it is claimed that it lasts twelve

hours. Such dilatation of the pupil does not occur in the irritated eye.

No anæmia being produced, Salomonsohn thinks Yohimbin-Spiegel to be less suitable for operations upon the lids, owing to the profuse hemorrhage. "But in cases of corneal operations, where no value attaches to the cosmetic anæmia that may be obtained with cocaine and adrenalin, Yohimbin is to be regarded as a most valuable acquisition to our materia medica."

Both Magnani and Haike call attention to the fact that even in cases where the vaso-constrictor effect is as important as the anæsthesia, the advantages of Yohimbin may be utilized. In such cases Yohimbin should be used in combination with suprarenal extract (adrenalin). The properties of these two substances show all the advantages of cocaine, with none of its drawbacks.

The experience derived to date with Yohimbin-Spiegel as an anæsthetic is sufficiently profitable and satisfactory to lead to further tests in the same direction. Applied to other mucous membranes than these mentioned, it is extremely probable that it will prove a valuable remedy as well.

In the reports of the sixteenth Congress of the Italian Ophthalmological Society, Dr. Magnani is quoted as stating that in experiments upon human subjects Yohimbin-Spiegel has shown its value as an anæsthetic in every respect.

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METHOD OF EMPLOYMENT AND DOSAGE OF YOHIMBIN-SPIEGEL.

(See also page 19)

Yohimbin-Spiegel is preferably administered *per os* in the form of tablets, each tablet containing 0.005 gramme ($^1/_{12}$ grain) of Yohimbin hydrochlorate. The usual dose is from one to three tablets per day. They are supplied in vials containing ten tablets each.

For subcutaneous injections use is made of a one-per-cent. solution (Solutio Yohimbini-Spiegel), prepared by dissolving 1 part of Yohimbin hydrochlorate-Spiegel in 100 parts of *boiling* distilled water. Of this solution one-quarter to one-half syringeful is injected three times a day; *i. e.*, 0.0025 to 0.005 gm. of the salt *t. i. d.* The solution keeps only a few weeks and is most effective when freshly prepared. The stability of the solution will be improved by the addition of a drop of chloroform.

For the convenience of physicians in the United States the manufacturers offer hypodermic tablets of Yohimbin, each containing 0.005 gm. of Yohimbin hydrochlorate.

This mode of administration is most advisable on account of the unlimited stability of the tablets as compared with the solution. The tablets are supplied in small glass tubes containing 10 tablets each. The minimal dose 0.0025 gm. for injections and 0.005 gm. internally three times a day will frequently suffice; but in cases in which this dose produces no result after a number of days the amount can be unhesitatingly doubled.

Even much larger doses have been given in isolated cases without causing untoward symptoms, so that the admissible maximum dose may be said to exceed 1 cgm.

The occurrence of salivation is to be looked upon as an incidental effect that demands caution with reference to a further increase of the dose.

The exhibition of the minimal dose of Yohimbin-Spiegel has in some cases been kept up for six weeks before the effect became manifest.

YOHIMBIN

is supplied in the original vials put up by the manufacturers, containing one gramme and one-half gramme; also in tablets, 0.005 gramme each ($^1/_{12}$ grain), in bottles of ten, in which form they are preferably prescribed by physicians.

Several complaints about unequal weight, inaccurate dosage, fragility, etc., in Yohimbin tablets lead us to state that we can guarantee the correct composition and stability of the preparation only when dispensed in our original packages, glass tubes containing 10 tablets each, bearing on the label the inscription "Dr. SPIEGEL'S YOHIMBIN TABLETS."

Yohimbin-Spiegel, in fact all our medicinal specialties, are to be had of retail and wholesale druggists and are generally carried in stock by them. If not readily obtainable we will place supplies within easy reach if you will kindly notify us.

LEHN & FINK,

120 WILLIAM STREET, - NEW YORK.