On the use of the Senecios in disorders of Menstruation

by W.E. Fothergill, M.A., B.Sc., M.B.
On the use of the Senecio's
in disorders of menstruation

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By William Edward Forthergill
M.A., B.Sc., M.B. Edin. F.R.

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On the use of the Senecios in disorders of menstruation

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On the use of the Senecios in disorders of Menstruation

Several months ago Dr. Leech of Manchester directed my attention to the use, in disorders of menstruation, of certain plants belonging to the genus Senecio. His reading had led him to conclude that those hitherto interested in the subject were better acquainted with drugs than with menstruation, and he expressed a wish that this point in therapeutics should be considered by some one specially interested in the physiology of the menstrual function. I have therefore devoted some attention to the question, and am now in a position to submit, at the least, a reasonable working hypothesis for the emmenagogue action of this drug, and to illustrate it by some clinical observations, which, though small in number, are sufficiently definite in result to justify experiment on a larger scale.

I hope to show that the Senecios provide us with a direct emmenagogue differing
in mode of action and in range of application from drugs to which the name is applied.

In doing this I shall not enlarge upon the so-called emmenagogues, for what little is definitely known of the action of drugs upon menstruation is already far beyond the need of repetition. Neither shall I detail the pharmacology of the genera nor their therapeutic applications other than the one in question. I shall however give a brief summary of these, followed by a bibliography which may be of use to pharmacologists who are interested in plants of this genus.

From the nature of the case laboratory experiments can throw no light upon our subject, unless, indeed, they were made upon certain monkeys, which, like the human female, are characterised by a periodic concurrent uterine discharge. Such animals were not available; thus in the present investigation I have used the clinical method alone.

W.R.F.

200, Oxford Road. Manchester

June 30th, 1897.
I.
History and Previous Observations.

The genus Senecio is the type genus of the tribe of plants known as the Senecioidae, which belongs to the sub-order Subuliflorae of the order Compositae. Several species of the genus are very common and have a very wide distribution. In Dr. Blanchard's "Physical Dictionary" I read "Senecio—Groundsel; the juice of the herb taken in beer; or a decoction of it with honey Vomits gently; outwardly applied it is good for inflammations of the Paps, and for the King's-evil." In other old books it is described as forming a good wash for sore mouths, and is said to cure the vomiting of young children. Senecio vulgaris—groundsel—seems also to have been used as a vermifuge by English Veterinary Surgeons, and it was recommended for epilepsy by Finazzi in 1831. Senecio Jacobaea, the common ragwort, with some other plants of the genus, has long had some reputation for its enemagogue effects in popular medicine.
In old English herbals the plant is found under the name "Female Regulator." In America, Senecio aureus is known as the "Life Rust" and has long been used in disorders of menstruation. Senecio maritimus is said to be used as an emmenagogue on the French coast.

In 1894, having heard of the use of Senecio by old wives, the and herbalists, Dr. William Murrell determined to try it and published the results of some interesting experiments. In June 1896, Dr. Dalché and Stein communicated the Société de Therapeutics some similar results, their paper being followed by a series of clinical observations by Dr. Bardet and Bolognini, contributing little study of the Senecios as emmenagogues. The experiments and conclusions of these authors must be noted.

Murrell made a 1 in 10 tincture of the whole plant of S. Jacobaea and began by taking 3 fl. himself thrice daily. He increased the dose till he was taking 3 fl. four times daily without any injurious effect. One of his students took 3 fl. four times daily for about ...
a month. Murrill next used liquid extracts of S. jacobaea and S. aureus, in doses of 20, four times daily. He also employed senecio, “a dark brown resinous dusting substance obtained from the Senecio” whose minimum dose was 2-3 grains, three or four times daily. He does not say in how many cases he used the drug, but refers to the seven cases named below.

**Cases.**

**Case i.** A girl menstruated on January 17th, and on March 5th began taking senecio, which she continued, with one short break, till June 24th. She was then found to be five months pregnant.

**Case ii.** A girl, aged 18, who had always been regular, had nine months amenorrhoea, on becoming a hard worked chambermaid. She was not pregnant, and the menses reappeared after taking Senecio for 121/2 days.

**Case iii.** A patient, who was not pregnant, and menstruated regularly previously, missed two periods. The menses reappeared after she
had taken sixty-three doses of tincture of senecio.

Case iv. A patient delivered of twins in December, weaned them in two weeks, but did not menstruate till March 15th, after she had taken liquid extract of senecio in 300 doses thrice daily for four days.

Case v. A patient, who was suckling a child five months old, took senecio for a few days, and then menstruated for four days.

Case vi. A patient who had never menstruated, suffered every month from bleeding from the mouth and gums. Senecio caused ordinary menstruation to replace this so-called atavistic haemorrhage. A second administration caused a repetition of the menstrual flow, within two weeks of the first.

Case vii. A girl, aged 17, menstruated regularly, but the flow was scanty, and accompanied by spitting of blood. On senecio, the menstrual discharge became profuse and the blood spitting ceased.
Murrell says, "I found that it succeeded admirably in those cases in which the menstrual function, having been established and performed regularly for some months or even years, was delayed or suspended as the result of exposure to cold or some similar cause. In cases in which the amenorrhoea was associated with or dependent on anaemia, senecio uniformly failed to do any good until the anaemic condition had been removed by iron. In cases in which the menstrual flow has never been established, senecio is frequently most useful, and in four cases of sicarious menstruation——the blood coming from the mouth or gums——nothing could have been more satisfactory. I am satisfied that senecio not only anticipates the period, but that it also increases the quantity. In many cases of dysmenorrhoea it promptly relieves the pain and not unfrequently the headache from which many women suffer at those times. Senecio is apparently not an abortifacient."

2. Dalché and Heim (15) used for some of their
experiments American liquid extract

of Senecea Jakoidea. They employed mainly
the aqueous and alcoholic extracts of
Senecea vulgaris. (1 m l.) brought to a
solid consistency and mixed. This
solidified extract was made into pills
weighing 0.2 to 0.4 grammes.

During six weeks, a young bitch of
small size took 14.4 grammes of the
consolidated extract. She lost weight
during the first few days, but soon re-
gained it. She presented no gastro-intestinal
symptoms, and gave no sign of pelvic
congestion

The American liquid extract, given to
guinea pigs by intra-muscular and intra-
peritoneal injection, was harmless in small
doses, but fatal in large doses. Further
experiments showed that fatal doses con-
tained enough alcohol to kill the
guinea pigs apart from the action of any
other substance.

Considerable quantities of the extract were
given to pregnant guinea pigs, without causing
abortion or in any way affecting the course
of pregnancy, though the alcohol in the extract again manifested itself in the demeanour of the animals. Though doubtless interesting these experiments are of no great importance from our point of view, and it is unfortunate that I have not as yet been able to obtain details as to fifteen patients to whom Balké and Aerni administered Senecio—in three cases without result, in three with doubtful result, and in nine cases they say, with positive result. They mention in detail only the two cases noted below.

Case 1. A neurotic patient with dysmenorrhoea who had previously been amenorrhoeic for six months together, had a second period of amenorrhoea of three months' duration. She was not pregnant, and suffered at the epochs corresponding to menstruation from pain and leucorrhoea. Under the influence of senecio the pain at the dysmenorrheic epochs was relieved, an hysterical attack occurred on the third day of administration, and the menses reappeared four days later.
(Dalché and Heim)

Case II. — A woman, aged 27, with mitral disease, had haemoptysis at her menstrual periods subsequent to an accoasion on which the film was checked by an accidental immersion in cold water. At the next menstrual epoch after consultation Bencelli was administered. She menstruated abundantly and without haemoptysis, the previous menses having been very scanty.

Dalché and Heim conclude that the drug relieves painful menstruation if the organs of reproduction are healthy but not otherwise. They remain doubtful whether or not it provokes the menstrual flow, and they offer no hypothesis as to its mode of action.

3. Bardel and Bolognesi made, during 1895-96, twenty observations in cases of amenorrhoea and dysmenorrhoea. The solidified extract made by Dalché and Heim was employed, in quantities up to 2-5 grammes daily. The cases I have tabulated below, arranging them in three groups.
Table of observations by Bandel and Balducci.
<table>
<thead>
<tr>
<th>No</th>
<th>Cause</th>
<th>Age</th>
<th>Periods missed</th>
<th>Total Opiates given (grams)</th>
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<tbody>
<tr>
<td>1</td>
<td>Epilepsy</td>
<td>17</td>
<td>4</td>
<td>3.5</td>
</tr>
<tr>
<td>2</td>
<td>Chlorosis</td>
<td>21</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>Hysteria</td>
<td>20</td>
<td>2</td>
<td>3.75</td>
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<td>Cerebral</td>
<td>-</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>Tuberculosis</td>
<td>28</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>Puerperal Fever</td>
<td>25</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>Rheumatism (Spondylitis)</td>
<td>23</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>8</td>
<td>Tuberculosis</td>
<td>20</td>
<td>2</td>
<td>1.5</td>
</tr>
<tr>
<td>9</td>
<td>Ophthalmic Suture</td>
<td>23</td>
<td>3</td>
<td>3.75</td>
</tr>
<tr>
<td>10</td>
<td>Indefinite</td>
<td>36</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>11</td>
<td>Fatigue Anemia</td>
<td>24</td>
<td>1</td>
<td>3.75</td>
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<tr>
<td>12</td>
<td>Syne R</td>
<td>25</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>13</td>
<td>Pregnancy</td>
<td>30</td>
<td>1</td>
<td>Small quantity</td>
</tr>
</tbody>
</table>

Seven cases of irregularity:

14. Girl aged 14, menstruation irregular, on surre.
15. ... 25....
16. Hysterical patient, aged 16; dysmenorrhoea. Seen as
17. Patient with metritis aged 30.
18. Patient aged 27; irregular and dysmenorrhoea.
19. Patient aged 20, ...
20. Patient aged 30, Dysmenorrhoea.
<table>
<thead>
<tr>
<th>Quantity</th>
<th>Amenorrhoea</th>
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</thead>
</table>

<table>
<thead>
<tr>
<th>Dosage</th>
<th>Days of Treatment</th>
<th>Result</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>3</td>
<td>5</td>
<td>Cured</td>
<td>2 1/2 grammes needed next month</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>Cured</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>Cured</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>Cured</td>
<td>Treatment for three months later</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>Menstruated</td>
<td>Treatment not repeated</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>Cured</td>
<td></td>
</tr>
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<td>Cured</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>Nothing</td>
<td></td>
</tr>
</tbody>
</table>

Regularity and dysmenorrhoea

On Senecio the function became regular. | Senecio gr 2 1/2 in five days—temporary relief. No success in relieving pain. |

Menstrual period became regular, but pain not relieved. | Pain increased and nausea caused. |

Senecio | Senecio
Bardet and Bolognai conclude that senecio has the constant property of provoking menstruation, though administered in small and harmless doses. They hold that it always tends to regularize menstruation; but that it does not increase the quantity of the discharge. They also hold that it does not relieve pain connected with menstruation. They suggest that it both produces pelvic congestion, and excites contraction of the uterine muscles.

These concluding statements are open to criticism; for though it may be that seldom that senecio is useful in dysmenorrhea, there are doubtless some cases in which the drug has relieved pain accompanying the menstrual discharge. The paper in question conveys to the reader the impression that senecio causes menstruation, according to the authors, by producing pelvic congestion and contraction of the uterus. This is not fortunate, as neither of these phenomena can be considered as causes of dysmenorrhea menstruation. It would indeed be safer to say that menstruation causes pelvic congestion, while such uterine contraction menstruation has no connection at all.
for the supposition that senecio causes pelvic congestion... evidence and is proved by menstruation, no evidence is brought forward in discussion at the Société de Therapeutique. However, Dr. Bardet mentioned the cases on which he bases the statement that the drug causes contraction of the uterus. A woman aged 38, took senecio on three occasions, and each time she said that she suffered from nausea and from hypergastric sensations recalling to her mind those of pregnancy. Such subjective phenomena are slight grounds on which to base, like Dr. Bardet, a statement to the effect that the woman's uterus contracted. The other case is equally slight. A woman missed a menstrual period, and thereafter took some senecio which she obtained from a friend who was under the care of Dr. Bardet for amenorrhea. The menses reappeared in two days. Dr. Bardet found on the patient's diaphragm some "membranes organised," and drew two conclusions: (1) that the woman had been pregnant, and (2) that the senecio
had caused contractions of the uterus followed by abortion. There are various kinds of "membranes organisms" to be found in menstrual discharges, and if Bordet had assured himself that those in question were of patent origin he would doubtless have made this point clear to the reader. Even if we grant that the woman was pregnant, there is no proof that abortion was caused by the seneceis taken, or that uterine contractions can be caused by the drug.

In the course of the same discussion Mr. Blondel's objections to the study of Seneceis. He remarked that the reports on its physiological action are vague and contradictory, and urged that until the action of a drug is definitely known, its indications and contraindications cannot be established. Amenorrhoea, he said, is not a disease but a symptom, and its causes must be discovered before they can be attacked. In half the cases seen, the cause of amenorrhoea he thought to be pregnancy, whose diagnosis, during the early months, was beset with difficulties. He therefore
thought that the treatment of amenorrhoea should always be indirect, both from risk of causing abortion, and in order to preserve a true clinical spirit. The drugs he considered, which act directly in causing menstruation, were unreliable, dangerous and of merely temporary effect.

Now the casuistry of M. Blondel, though it may have caught the ear of the casual hearer, does not bear careful examination. But once it has appeared in print it may be well to briefly consider it. Thus if no drug is to be used until its action is definitely known and its indications and contra-indications clearly defined, there would be an end of the introduction of new therapeutical agents. Again, in certain cases, amenorrhoea is not a symptom of any pre-existent disease, but is due to the action on the nervous system of various external and temporary causes. Secondary effects both mental and physical follow an accidental suppression of the menses, and thus in some instances amenorrhoea may assume the rank of a primary disorder and one eminently suitable for direct treatment.
Thus Edelheit mentions four cases in which amenorrhoea inaugurated a primary and serious affection which was fatal in two cases; recovery, in the other two, following the re-establishment of menstruation.

Thirdly, the difficulties of diagnosis in early pregnancy are not insuperable; and there is no need for anyone to administer a possible embolic while the diagnosis remains in doubt. Lastly, even if we grant that the so-called amenorrhoea in use are unsatisfactory, there is no reason a priori why safe and good agents of this kind should not be discovered.
II.

Personal Observations

With the intention of making some clinical observations on the action of Senecio I obtained from Munro of London some 1 m 10 Tincture of Senecio Jacobaea. I also procured through the kindness of Mr. Bardsley of Manchester some liquid extract of the same plant, aqueous and alcoholic, the strength being 1 m 1. Messrs. Burroughs and Wellcome also made for me some Tablets each containing one grain of Senecio. The brown resinous looking substance is Murrell.

My experiments have been directed towards determining four questions, namely, (1) Does Senecio cause abortion? (2) Does Senecio produce menstruation in those cases which are sometimes called "functional amenorrhoea," and whose nature shall we define more clearly later? 3. Does Senecio alter the date of appearance of the menses or the quantity or duration of the flow when administered to healthy women? 4. Does Senecio relieve the
Pain in cases of dysmenorrhea? If so in what class of cases?

In making the observations mentioned below there was one fallacy which I had to guard against, namely, the possibility of provoking menstruation by suggestion. I therefore never told the patient what form the medicine was administered, taking in every case some means of disguising my intention until the drug had had some time in which to produce its effect. It may be said that in many cases menstruation accidentally coincided with the administration of medicines. Against this criticism there is little to be said, but there are limits to the probability of coincidence and the observations must be taken for what they are worth.

(1) In Cases of Pregnancy.

Case 1. A. H., aged 23. Menstruation began at the age of 15 and was regular. Last 28 days. Duration 4 days, no pain. No previous pregnancy. Patient was four months pregnant. She took 811 of Jinek, Len. Jusc.
three times daily for two weeks with no effect whatever.

Case iii. D.B. aged 26. Menstruation began
at 13 years of age, regular. Intercourse 21 days. Duration
5 days. No pain. One previous pregnancy.
Missed one period, 10 days later began taking
Seneecin 31653 thrice daily, and continued
dosing so for 10 days, with no effect. When
the administration of seneecin ceased she was
approaching the end of the third month of pregnancy.
This patient previously had amenorrhea apart
from pregnancy which was cured by seneecin. (see
page 25, Case ix)

Case iii. N.D. aged 19. Menstruation began aged
14, regular. Intercourse 28 days. Duration 3 days.
Seven weeks after her last menstruation
patient took 2 31653 of liquid extract of seneecin
four times daily for two weeks, with no effect.
She was, at the end of the administration nearly
four months pregnant. Pregnancy dating from
a single coitus of known date, after which
she menstruated once.
Case VII. Since this was written I hear from Dr. Reginald Jones that a patient named H., whose menstruation began at 14, regular quantity small, has not menstruated since November 14th, 1896. He saw her on March 16th, 1897, and gave her extract of senecio in 3 X 4 doses. She consumed no less than six ounces of the 1 in 1 liquid extract during the next three weeks without any effect whatever. She was then examined, and found to be pregnant.
Case IV. M. D. aged 33. Menstruation regular, light, 30 days duration, 5 days, no pain. Three previous pregnancies. Patient missed two periods, and then took Emerine 3/4 gr. four times daily for fifteen days. She had some nausea which was probably ordinary "morning sickness." She was about 3 1/2 months pregnant at the end of administration.

Case V. A patient aged 28, with irregular menses painful, and lasting 3-6 days, missed one period, and then took Tablads of Emerine 3/4 gr. four times daily for 10 days without effect, and was then found to be about two months pregnant.

BY

Case VI. A patient aged 26. Menstruation began at 15, regular, slight pain. Type 28 days. Duration 2½ days, missed two periods and took my XX of Emerine 3/4 gr. twice daily for nearly three weeks without any effect, after which she was found to be pregnant.

(Case VII. See opposite page)

These cases together with Murrell's case 1 and case 13 by D'Andrea, Bauder, and Bologna.
appears to favour Munnell's statement that Senecio is not an "ecstatic." Indeed it is certainly safe to administer to pregnant women doses of Senecio similar in quantity to those which it is necessary to prescribe for the cure of functional amenorrhoea. In which case, amenorrhoea is complained of, when it is not desirable to make a physical examination for pregnancy, Senecio may safely be used without waiting to complete a diagnosis. To use the drug in this way would undoubtedly be a more scientific cause, but is most useful to the general practitioner in cases of a certain delicacy. A girl is brought for advice by her mother, amenorrhoea being one of the only symptoms. Complete examination is out of the question, and a series of interrogations may be the cause of great and needless trouble and mental suffering. Functional amenorrhoea may be present, or pregnancy. A drug which will cure the former and which will not interfere with the latter has an obvious utility, and Senecio appears to fulfill the requirements of the case.
2. In Cases of Functional Amenorrhoea.

Case I. J.B., aged 25. Menstruation began at 14, regular, no pain. Lute 28 days, duration 4 days. Before consulting a doctor, the patient was confined 6 months ago. She had no milk at all, and the child was brought up on the breast from the first. She consulted about slight indigestion and was very anxious because the menopause had not reappeared. She was not pregnant and was in good health apart from slight dyspepsia. Instructions were given as to slight alterations of diet, and extract of semenex was ordered in doses of 1 drachm for 3 times daily. When this had been taken for 11 days patient menstruated for 3 days without pain and has since been regular.

Case II. M.M., aged 15. Menstruation began at 14, regular. Lute 28 days, duration 2-3 days no pain. After a change of situation and sleeping in a damp bed, patient had a period of five months amenorrhoea. She was well nourished, no anaemia, no heart or lung trouble. The patient was not pregnant but fear of pregnancy may have had a causal connection.
with the amenorrhoea. After taking m x x. 1 extract of senecio four times daily for two days, she menstruated for two days and has since been regular.

Case iii. E. K., aged 39, began menstruating at 15, regular. Type 28 days, duration 5 days, no pain. Has had 4 children, the youngest being 9 years old. Five months ago the menopause before consultation. The menopause disappeared after a change of residence and five periods were missed. The patient was well in every respect and dreaded pregnancy. After taking senecio extract, m x x four times daily for a week she menstruated for four days and has since been regular.

Case iv. J. H., aged 17, never menstruated. Slight dyspepsia and constipation, well nourished and no disease of any system. Well developed sexually, complaint of languor and headache. Patient took m x x. Extract of senecio four times daily for two weeks and then menstruated for three days. She
Case V. H.M. aged 22. Menstruation began at 14, irregular 4-5 days duration, some pain. Patient missed three periods and complained of pain in abdomen. No other symptoms or physical signs of disease were present. She was not pregnant. After taking M.X.X of the extract of Scenecis three times daily for two weeks she menstruated as usual with some pain, and has since continued to do so at intervals ranging from 26 to 30 days.

Case VI. F.O. aged 25. Menstruation began at 15, regular. Type 26 days, duration 7 days, quantity large, slight pain. Patient missed two periods, the cause being apparently the hope of pregnancy, complained of hypogastric weight and uneasiness. After she was not pregnant, and after taking M.X.X 8 x 1 every four times daily for 10 days she menstruated as usual.
Case VII. M. A., aged 32. Menstruation began at 13 or 14, regular, no pain, duration 3-5 days. Last child weaned five months ago. Patient menstruated twice after weaning the child and then missed three periods. Suffers from chronic bronchitis, no phthisis. After taking the tincture of Nux vomica 1/2 gr. four times daily for a week she experienced discomfort as if about to menstruate and a week later the menses appeared, the drug having been taken in smaller doses during the second week.

Case VIII. E. A., aged 24. Menstruation began at 12, regular 28 days type, duration 7 days; pain for five hours at commencement of flow. One pregnancy three years ago ended in abortion at 3rd month. Patient is a stout healthy young woman. Under the hope of pregnancy she missed three periods, then menstruated twice and again missed a period. She was not pregnant, and after taking B. W. and Cod. Taurina of Cenaria gr. 1. four times daily for three days the menses reappeared.

Case IX. D. B., aged 28. Menstruation began
at 13. regular, type 21 days, duration 5 days, no pain. one pregnancy. patient missed two periods after acquireing specific disease from the husband. the amenorrhoea caused her great anxiety. specific treatment was replaced for four days by Amn. senecio Zips. thrice daily, after which the menses reappeared and continued regularly till she became pregnant, after which she took senecio without any effect. (see page 18. case ii)

Case V. A. J. aged 15. had never menstruated consulted about bruised ribs. her mother was most anxious that menstruation should begin and as the patient was tall and well nourished, besides being perfectly well developed sexually, senecio was administered in dose of 3xx the extract thrice daily. the menses appeared harmlessly after the drug had been taken for 11 days, and the girl has since menstruated regularly.

The reader may remark that these cases are very few in number, and that the results obtained are uniformly good. But it must...
be remembered that there are picked cases in which amenorrhoea was the only marked condition present, (with the exception of the specific case). These cases are not, therefore, like those of Bardet and Biedounevi, (see Table,) and were I to put together all the cases of amenorrhoea of various kinds in which I have tried senecio, I could not show a uniformity of results in any way approaching theirs.

Before I began to understand the use of senecio I tried it in the case of a girl of 18 who had never menstruated. There was no result, and on further investigation I found the mammary poorly developed, the pubic hair arranged in the manner usual in the male subject, the labia small, the rectum firm and hardly formed. I could not feel either ovary, and concluded that a case of congenital reproductive deficiency was not a fair one to include in a report on senecio. Another failure occurred in a woman of 35 who never menstruated after a confinement two years before I saw her. When she allowed examination I found the uterus small and shrivelled; in fact, she was the subject of a premature menopause caused by superinfection after her confinement.
I also found, like Marshall, that senecio will not cause menstruation in the presence of marked anaemia, nor in advanced phthisis, but such cases are not examples of functional amenorrhoea. Suitable cases are of comparatively rare occurrence; but the fact remains that in all I have seen since beginning to use senecio the function has been re-established. These suitable and successful cases may be stated again as below.

1. J.B., aged 25: missed 5 periods and last senecio 11 days.
2. M.M., aged 18: missed 5 periods and last senecio 2 days.
3. E.K.: 39: missed 5 periods and last senecio 7 days.
6. F.O.: 25: missed 2 days. After senecio, 10 days.
8. E.R.: 24: missed 1 day. After senecio, 3 days.
Attempts to anticipate menstruation in healthy subjects

There are several minor gynaecological operations which ought to be done soon after the end of a menstrual period, so as to allow as long a time as possible for healing before the parts are disturbed by the reappearance of menstrual discharge. Both patient and operator are often put to inconvenience by having to postpone the date of operation while waiting for menstruation to occur, and I thought myself justified in trying whether, by the use of serenities in such cases, menstruation could be prevented at a date earlier than that on which it was expected. The cases are quite good for experiment; so, being of a plastic nature such as repairs of a torn perineum, the operations in question are needed quite apart from any disease of the reproductive organs or disorder of the menstrual function. Needless to say, only patients whose menstruation is regular could be selected for this purpose. These cases also show whether or not serenities tend to increase the quantity and duration of the menstrual flow. The entries in my diary on these cases
resemble the following in form.

"Mr. W. menstruated Sept. 22nd to Sept. 25th.

Next period expected to begin Oct. 20. As her type is 28 days regular, duration 4 days. Oct. 11th beganamenorrhoea, extract-m.x.x four times daily. Oct. 15th menstruation began and lasted three days." As the reading of each date and figure will not give without much calculation, I prefer to tabulate, for each of the six cases in which I used the drug in this way, a period of 28 days, or one menstrual cycle. As each patient was regular and of the 28 days type, menstruation was expected on the day marked 29 in the table. The days on which menstruation actually occurred are marked with a short line, and the days on which menescio was taken in m.x.x doses four times daily are indicated. The result is clearly visible in each case. It is noticed that menstruation occurred sooner than it was expected by two or more days in each case. And also that the period was generally of shorter duration than usual. As to the next appearance of the menses, the dates are not worth observing; for the following
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Notes:
- 5 days early
- 1 day past
- 3 days early
- 2 days early
- 9 days early
- 9 days past

Table of cases in which menstruation in healthy subjects occurred earlier than expected after use of Senecio.
following reason. When a patient is operated on soon after menstruation, and kept in bed for some weeks, it is not at all unusual to find that the next appearance of the menses is more or less delayed. I am therefore unable to say whether the menstural period following one provoked prematurely by senecio will occur after 28 days or after a longer period. It is noticeable that the earlier after menstruation that senecio is taken, the greater is the quantity necessary to provide the menstural flow. It is probable that during the first few days after the termination of the period no dose of senecio would produce a repetition of the discharge.

I cannot help but confirm Murrell's statement that senecio anticipates the discharge. But I do not agree with him that it increases the quantity. My experience being that a period provoked by senecio is of shorter duration than one occurring naturally. The conclusions of Bardet and Balogneri are identical with my own on both these points. Though I differ from their views as to the mode of action of the drug.
In Cases of Dysmenorrhoea.

The following cases are too few and too indefinite to be of any great value. They are all cases in which there is no discoverable disease of the reproductive organs, and in which numerous remedies have been tried with but small success. Murrell as also Delchev and Reini found the drug useful in certain cases, contrary to the experience of Bardet and Bolognesi. My experience up to the present time does not afford any new information.

Case 1. E.S. aged 23. single. Menstruation began at 14. and has always been irregular and painful. the patient is somewhat anaemic and suffers much from headache. Menstruation lasts 14 to 5 days. and pain is severe during the first two days of the flow, and for a few hours before its commencement. She has now taken for several months Trichinum di Sanecio in 3i doses every two or three hours. While the pain lasts and states that it gives her more relief than any remedy she had previously tried.
Case II. A.G., aged 28, married. Menstruation began at 13 and was always painful and irregular. The flow lasting 3 to 4 days. There is no marked condition of the uterine appendages, no pregnancy. Pain is usually severe for four to five hours after the commencement of the flow. 3i of tincture Juncus was taken and a similar dose was given an hour later. Some nausea was complained of and the pain was worse rather than better than usual.

Case III. Mrs. A., aged 32. Menstruation began at 14. Type 31 days regular. Duration 2 days. Considerable pain during flow. Patient took 3i in 3i doses during the two days, and expressed relief. She repeated the treatment at the next period but has not since thought it worth while to do so.

Case IV. Mrs. H., aged 25. Menstruation began at 13, regular. Type 28 days duration 3 days. Considerable pain during first day. One ovary is tender. Patient took several 3i doses of the tincture on one occasion and derived some benefit from it, but has not repeated the treatment.

In a definite conclusion.
III.

Action of the Drug, and Indications.

A consideration of the physiology of the menstrual function is necessary in order to understand the mode of action of Senecio, and define its indications.

A man, while his weight remains constant, elaborates from his food an amount of highly organized material exactly equivalent to the amount of similar material broken down by his activity and removed from his body by lungs, kidneys and skin. Income and expenditure of protoplasm are equal — the anabolic changes balance the catabolic, the two making the sum of the metabolism of the body. Before puberty and after the menopause, though female in structure, woman is not reproductive in function, and the balance between the anabolic and catabolic changes that constitute her metabolism is disturbed, just as in man, only when she is gaining or losing weight.*

* A woman, on the other hand, during the whole of her reproductive life, manu-
factsures more highly organized material than is necessary for her individual use.

The protoplasmic income is greater, from puberty to the menopause, than the protoplasmic expenditure; the anabolic changes preponderate over the catabolic, and the surplus of highly organized material is expressed as follows:—While pregnant it goes to form the foetus and provide for its growth; during lactation it supplies the milk; at other times it is represented merely at monthly intervals by haemorrhage from the uterine mucosa.

Thus we see the significance of a periodic sanguineous discharge from the uterus. With the evolution of the function we are not here concerned, and I will not repeat the explanation if it has been given elsewhere.

It is necessary, however, to know what agency determines the particular time at which the periodic haemorrhage shall occur.

Congestion of the reproductive organs

accompanying the rupture of an ovum has, until recently been thought to be the immediate cause of each menstrual flow. But we now have abundant proof that ovulation can occur at any part of the menstrual cycle, quite apart from menstruation, and that menstruation can occur without ovulation. We may omit the now familiar proofs of these two statements.* Two cases however recently described by Bassi† are worthy of mention as they contradict very clearly the ovulation theory of menstruation. The first was a patient who had a periodic monthly discharge of blood from the anus. It was found that she had no vagina and that her uterus and ovaries were infantile. The second was a woman aged 34 who had always menstruated regularly, and, at last, too profusely. Vaginal hysterectomy revealed the fact that she had no trace either of ovaries or of uterine tubes.

The fact that the operative removal of both

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ovaries and tubes does not always cause cessation
of the menstrual function has driven us to believe that when Battey's or Tait's operation
does cause a premature menopause, it is not through the removal of organs but by the
division of certain nerves in the broad ligaments.
This view has led to the formulation of the
"nervous theory" of menstruation, and there
is now a strong tendency in obstetric circles
to agree with Christophe Martin, whose
view may be stated as follows. The function
of menstruation is preserved over by a special
centre situated in the lumbar part of the cord,
from which impulses to menstruate reach
the uteri through the pelvic splanchnics
or the ovarian plexus or by both routes.
Thus we may say that menstruation
expresses an endocrine surplus produced by
the healthy human female from puberty
to the menopause and interrupted only by
pregnancy and lactations and further, that
the time of occurrence of the discharge is
determined by the activity of a special
centre in the lumbar part of the cord.
This view of menstruation allows the formation
Of a reasonable working hypothesis for the action of Senecio, it is clear that substances like iron, which affect the quality or quantity of the blood, are only indirectly enmenagogue, indeed they are no more enmenagouges than are food and drink. Similarly, substances which, by causing renal or gastro-intestinal irritation, promote pelvic congestion and as favour uterine haemorrhage have no true claim to the term. It is also necessary to distinguish between an enmenagogue and an ecliptic, the latter being a substance which causes contraction of the uterine muscles either by acting on the fibres themselves or on their motor nerves. To be a direct enmenagogue a substance must have a stimulating action on the nervous mechanism which initiates the menstrual discharge, namely upon the hypothetic centre for menstruation. Now if we assume that Senecio is such a direct enmenagogue, and acts by stimulating the nervous mechanism of menstruation, our theory will account for all the facts in connection with the drug which are now before us.
For it is clear that senecio will terminate a period of amenorrhoea only when the sole cause of that amenorrhoea is a temporary inhibition of the activity of the nervous mechanism which habitually initiates menstruation.

The other factor necessary for menstruation, namely the presence of an anaesthetic surplus of blood, must be present in order that senecio may act. We have at present no drug which has been proved to inhibit the nervous mechanism of menstruation, though the possession of one would be both interesting and useful.

The centre for menstruation is, however, often inhibited by external physical impressions such as immersion in cold water, and also by the cerebral nervous centres; as, for instance, in cases where fear of pregnancy or hope of pregnancy cause the menstrual function to be arrested for months together.

A minor point—worthy of notice is that when in a healthy subject, menstruation is initiated earlier than usual by the use of senecio, there is less surplus blood than usual in the body, and accordingly the menstrual flow is of unusually short duration.
The easiest and shortest way of completing this statement is to classify the usual varieties of amenorrhoea in a way which will indicate the treatment.

I. **Physiological amenorrhoea**, that is to say the absence of menstruation before puberty, after the menopause, during pregnancy, and during lactation, of course requires no treatment. Certain pathological conditions such as congenital or operative absence of essential reproductive organs often produce amenorrhoea which calls for no treatment.

II. **Amenorrhoea due to local defects**, such as atresia vaginae; atresia cervicis uteri, congenital or acquired; or to the presence of certain neoplasms demands local treatment of a surgical nature.

III. **In general disease** which so disturbs metabolism that no analytic surplus is produced, amenorrhoea, being merely a symptom, should be treated indirectly.
The various forms of amenorrhea. Disturbances to produce amenorrhea of this kind.

iv. Amenorrhea due to inactivity of the nervous mechanisms initiating menstruation may be caused by nervous disease, shock, mental or physical, fear or hope of pregnancy, and other less definite impressions. There are also numerous cases in which the menstrual function has never been established and where there is no local defect or general disease sufficient to account for its absence. In cases of this class direct treatment by a true emmenagogue is justified. Securus appears to be a drug of this nature. Cases of the nature here indicated have often been named "functional amenorrhea."
IV.

Chemical and Pharmacological Notes

The plants belonging to the genus Senecio which have been specially examined are as follows.

- Senecio vulgaris - These both contain two alkaloids.
- Senecio Jacobaea - Senecic and senecione in small quantity.
- Senecio aureus - This has been used in America.
- Senecio maunichus - Used in France.
- Senecio camicida - Mexico; poisonous; fatty acid.
- Senecio Koempferi - Java; fatty acid of Shimoyana.
- Senecio Piresianthus - United States; resin and essential oil investigated by Sudd & Lloyd.
- Senecio crucifolius - alkaloids with present.
- Senecio paludosus - alkaloids in larger quantity.
- Senecio gracilis - Known to herbalists.

1. Organic Acids

Shimoyana found a new fatty acid in Senecio Koempferi a Japanese species. This was named Senecic acid (C₂₅H₄₇O₃); it is not, however, necessarily identical with the similarly named fatty acid which has been found in Senecio camicida, a poisonous species growing in Mexico. This latter is a colourless volatile liquid.
whose salts are soluble in water. Twenty centigrammes of it killed small dogs in from 1½ to 6 hours. After its administration a phase of excitement occurs, followed by a phase of depression. Then convulsions occur, first clonic, later tonic; finally the reflexes are suppressed, and the heart and respiration are arrested (Guillouër (5) and Saussard (7)). In spite of the convulsive action of its fatty acid, S. anacida has been recommended in epilepsy by some Mexican physicians. (3)

2. Resins and Essential Oils

Senechin is the name which has been given to a brown resinous substance derived from S. jacquemear and other species. It was thought by Murrell to contain the active principle of the plant. It is probably a mixture. A resin and an essential oil have been obtained from S. hieracifolius (Euphr. Echites), a species growing in the United States (Lund and Lloyd) (6). I have not used enough senechin to be able to say whether or not it has the same therapeutic action as an
3. **Alkaloids**

Senecionine \((C^{15}H^{25}\text{Ag}O^{6})\) and Senecline are two alkaloids isolated by Grindalow and Lajkovc.\(^{(11)}\) They are bitter substances whose salts are soluble in water. They are found in very small quantities in Senecio vulgaris and S. Jacobaea, and in slightly larger quantities in S. erucifolius and S. paludosus.

The difficulty of obtaining these alkaloids in any quantity has hitherto prevented their use for clinical experiment. It is probable, however, that the therapeutic value of the senecios in menstruation does not depend upon these alkaloids. My reason for stating this was similar. It has been well shown by Lutjé\(^{(12)}\) that the alkaloids exist only in the subterranean portions of the plants.

Now while the tincture of Murrell\(^{(10)}\) and the liquid extract of Darbishie and Heinri were made from the whole plant, the 1 in 1 liquid extract which Mr. Barley had prepared for me was made from the aerial portions of the plant alone. Now my liquid extract was quite as active
as the preparations used by the observers named. I therefore conclude that the activity the drug is not due to the alkaloids which have been found in the roots of the plant.

Wild (14) found by experiment on frogs and guinea pigs that chlorohydrate of senecionine destroys the excitability of motor nerves, but leaves intact the irritability of muscle itself. In sufficiently large doses it is a curariform poison. Its effect on sensory nerves remains doubtful. It blocks the reflex action, and in fatal doses stops the organ in septicole.

V. Bibliography

N.B. The figures in the text refer to the numbers in this list of papers.

Gazeta medica 1866.


Mexico, 1891. T.IV. p. 5-199.


16. Baudet et Balagnesi.
