

tendency to occur most frequently in farmers and those in allied occupations. I have a feeling that we shall learn in time that the course of pemphigus foliaceus is somewhat influenced by the age of the patient, and that the disease in younger persons offers a better prognosis than it does in the elderly. I think that in estimating the value of any method of treatment we must not fail to take into consideration the possibilities of spontaneous cure or improvement in these cases.

DR. HOWARD FOX, New York: There are just one or two points that I should like to comment on. Last summer, together with my father, Dr. George H. Fox, I saw an absolutely typical text-book case of pemphigus foliaceus, and the interesting point of this case was that the patient, a woman had previously suffered from lupus erythematosus, for which she had been treated with iodine locally and quinin internally. Several months later she developed pemphigus foliaceus, which ultimately proved fatal.

DR. H. H. HAZEN, Washington, D. C.: I have had the opportunity of seeing four cases of pemphigus foliaceus during the past two years, and I have come to the conclusion that we have not yet reached an absolute classification of this disease. For example, there are cases of dermatitis exfoliativa, the so-called Ritter's disease, which are objectively the same as pemphigus foliaceus. As regards the causation of pemphigus foliaceus, Lipschitz has reported the presence of a distinctive organism in the lesions, a finding that I have not confirmed. As to treatment in one of our cases we gave two injections of salvarsan without any effect. One patient was apparently benefited by continuous tubbing. In another case, treated by keeping the patient covered with a dry powder, as suggested by Drs. Martin F. Engman and Charles J. White, no beneficial effect was observed. The Roentgen ray treatment was also unsatisfactory. I should particularly like to make the point that the lesions are autoinoculable. Serum from a vesicle rubbed into or injected into the skin of the same patient will cause a new lesion, whereas salt solution will not do this.

DR. A. RAVOGLI, Cincinnati: I have at present a patient under my observation, a woman who has been under treatment for the past three or four years for pemphigus foliaceus. She has had numerous outbreaks of bullae. The bullae contain little serum, and soon break. The skin was in such a condition that on merely touching her to give hypodermic injections in the parts not affected with bullae, some of the epidermis would detach and come out on the finger. In the treatment of this patient, in addition to quinin—which was not, however, given in the large and repeated doses suggested by Dr. Kessler—I have used the cacodylate of soda and an injection of staphylococci vaccine. Nothing has done her much good. At present I am using an ointment of resorcin and salicylic acid (15 grains to the ounce) together with a little arsenic internally (Fowler's solution), and she is getting on fairly well.

DR. J. B. KESSLER, Iowa City: The treatment of pemphigus foliaceus outlined in my paper is not entirely new. Several years ago a writer, whose name I do not recall, recommended the use of large doses of quinin in pemphigus vulgaris. That gave me my cue, and I tried the drug in these two cases of pemphigus foliaceus with the happiest results. In order to secure these results, the quinin must be given in large, repeated doses. In one of my cases, that of the boy, I gave 4 grains every four hours, and later increased the dose to 7½ grains every four hours. These patients apparently tolerate the drug in large doses.

**The Tendency to Revert to the Normal.**—Speaking generally, there is undoubtedly a tendency in the individual who has some morbid variation from the normal to reproduce that variation in his offspring, although Nature is forever trying to revert to the normal, and in favorable environment she succeeds in the generality of cases in restoring the normal condition. Hence you see, even in families in which a morbid tendency is strongest, most of the members usually escape.—F. M. Sandwith in *Clin. Jour.*

## THE ACTION OF SO-CALLED EMMENAGOGUE OILS ON THE ISOLATED UTERUS WITH A REPORT OF A CASE OF PENNYROYAL POISONING\*

DAVID I. MACHT, M.D.

Instructor in Medicine, Johns Hopkins University, and Coroner  
BALTIMORE

*History.*—In August, 1912, I was called as a coroner to the Maryland General Hospital to inquire into the death of a young white girl, aged 16, who was brought to the obstetric ward of the institution in a comatose condition and died there two hours after admission. On investigation and after a necropsy I found that the deceased died as a result of a criminal abortion and under rather peculiar circumstances. Four days previously, the girl, who was some three or four months pregnant, sought relief from her condition by swallowing about thirty-six pennyroyal pills of a well-known brand, recommended as an efficient and harmless emmenagogue. Twenty-four hours later she had an incomplete abortion and at the same time began to develop signs of serious poisoning. The symptoms were partly of gastro-intestinal origin but were chiefly referable to the nervous system. Beginning with a severe headache and pains in the back, they were followed by delirium and convulsions, and finally coma on the third day, and death on the following day.

*Necropsy.*—At my direction, Dr. N. G. Keirle made a post-mortem examination, which pointed to the fact that the abortion was incomplete and had evidently been completed by mechanical means. There were, however, no marked signs of a severe infection, either local or general, and the chief anatomic lesions were of a nature not referable to a septicemia or pyemia. There were noted a patchy congestion of the ileum, an edematous condition of the brain, and most striking of all, an extremely marked fatty degeneration of the liver and kidneys. The spleen was not enlarged or swollen. The lungs showed no special abnormalities, but the heart showed some fatty change.

These findings led to the conclusion that the cause of death was, primarily, poisoning by pennyroyal and, secondarily, a terminal infection; and such was in substance the verdict of the coroner's jury.

Pennyroyal as a household remedy has been known from ancient times, and as far back as Dioscorides<sup>1</sup> we find a description of its many virtues. At present, however, its popularity is confined chiefly to England, America, and parts of Russia, in which countries it enjoys the reputation of being an efficient emmenagogue and abortifacient. As to its efficacy in that respect opinions of writers on the subject differ, some, like Taylor,<sup>2</sup> declaring that it has no action at all, others, as for instance Kobert,<sup>3</sup> holding the opposite view. There is, however, a pretty general consensus of opinion that the drug, oil of pennyroyal, may cause toxic and sometimes even fatal symptoms, and there are three or four cases of poisoning reported in literature which sustain this view.

Thus, Wingate<sup>4</sup> reports a case of a pregnant woman who took a large dose of pennyroyal oil and suffered from severe nervous symptoms, but did not abort. J. G. Marshall<sup>5</sup> describes a case of abortion induced by pennyroyal, with very alarming toxic symptoms and collapse. Flynn<sup>6</sup> describes a case in which a woman two months pregnant took three drams of oil of pennyroyal to produce abortion, without success, but with severe nervous

\* From the Pharmacologic Laboratory of the Johns Hopkins University.

1. Dioscorides: *De Materia Medica*, Ed. C. Sprengel, 1829, Lib. III, Cap. XXXIII.

2. Taylor: *Manual of Medical Jurisprudence*.

3. Kobert: *Lehrbuch der Intoxikationen*, 1893, p. 432.

4. Wingate: *Boston Med. Jour.*, 1889.

5. Marshall: *Brit. Med. Jour.*, 1890, i, 542.

6. Flynn: *Brit. Med. Jour.*, 1893, ii, 1270.

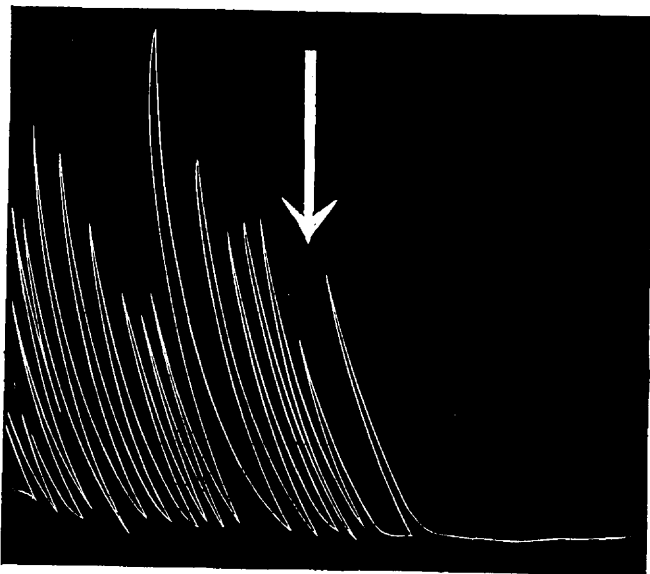
depression and alarming circulatory signs. W. T. Allen<sup>7</sup> reports the following case more fully:

*History.*—A woman of 23 years was admitted to the infirmary in Liverpool in a collapsed condition, suffering from symptoms of acute gastritis. It was learned that four days previously she swallowed a tablespoonful of pennyroyal in order to bring on menstruation. Excessive vomiting and collapse followed, from which she did not recover, and she died four days after admission.

*Necropsy.*—A post-mortem examination was ordered by the coroner, and the following lesions were found: Stomach congested, also small intestine, especially the ileum; congestion of large intestine down to rectum; also congestion of the brain.

Two varieties of pennyroyal are known, *oleum hedeomae* (U. S. P.) and *oleum pulegii*, the English variety—which act in practically the same way.<sup>8</sup>

The action of *oleum pulegii* was experimentally studied by Falk<sup>9</sup> in 1890. Working on rabbits he found that acute poisoning caused a fatal central paralysis; more chronic poisoning was followed by slowing of the pulse,



Effect of *oleum hedeomae* (pennyroyal) on the pregnant uterus. Arrow indicates point of injection of the oil of pennyroyal.

and fatty degeneration of all the organs, especially the liver and the heart. A more extensive pharmacologic and pathologic study of the drug was undertaken by W. Lindeman,<sup>10</sup> who also noted an inhibition of respiration and heart action, and anatomically marked fatty degeneration of various organs, especially of the liver.

Basing his conclusions on the above-mentioned, together with some other experimental and clinical data, Kunkel<sup>11</sup> sums up the toxicology of pennyroyal as follows: In acute poisoning—paralysis, slow respiration, subnormal temperature, vomiting, and some slowing of the heart; in chronic poisoning—fatty degeneration of the liver, heart, kidneys, thyroid, pancreas and salivary glands. Comparing this description with the clinical and pathologic picture presented by my case, there seems no doubt but that we had to deal with a case of pennyroyal poisoning. The chief difference between the case

of Allen quoted above and my case is in respect to the gastro-intestinal changes. This can be well understood, however, by noting that in the one case the victim ingested the pure oil, while in the other the girl swallowed not oil but pills.

Although the pharmacologic and pathologic action of pennyroyal were pretty carefully studied by Falk, and Lindeman, as mentioned previously, neither they nor other observers directed their attention to the question how, if at all, *oleum pulegii* affects the uterine contractions. The same is true of the other so-called emmenagogue or abortifacient oils. None of them, as pointed out by Meyer and Gottlieb,<sup>12</sup> have been investigated as to their specific action on the uterus. Thus, for instance, the once very popular preparation *apiol*, still much advertised in French journals, was carefully studied by Hefter,<sup>13</sup> who, it is well to note, observed here, too, the most striking pathologic lesion, a fatty degeneration of the liver; but no mention is made of its action on the uterus, though that is the property of the drug which is most emphasized by the drug dealers.

I have undertaken, therefore, to study the effect of the various so-called emmenagogue oils on the *isolated* uterus, for the purpose of solving this problem.

#### METHOD

The horns of a cat's uterus, pregnant and non-pregnant, were used, and the apparatus was very much like the one used by Dale and Laidlaw in their work on standardization of pituitary extracts.<sup>14</sup> The uterine strip is suspended in a small glass chamber, one end being fixed to the bottom of the chamber; the other, or free end, being attached to the short arm of a lever and lightly weighted. The chamber is filled with Locke's solution kept at a very constant temperature, 38° C, through which a constant stream of oxygen is bubbling. The bottom of the chamber is drawn out into a tube to which a piece of rubber tubing is attached and clamped off at will, so as to draw off and change the solution whenever desired. The whole apparatus is immersed in a water-bath or jacket, for the regulation of the temperature. (There are a great many other details and precautions to be followed in the experiments into which we need not enter in this place.)

The manipulation and exposure of the uterus, followed by immersion in the warm bath almost invariably produce a high degree of tonus in the suspended preparation. When it is left to itself, however, the tonus slowly gives way, with small rhythmic interruptions, until a condition of almost complete relaxation is produced. This condition of uniformly low tonus is usually attained after suspension from fifteen to thirty minutes, when the uterus is ready for testing. In this condition the uterus is either quiescent, or, in ideal preparations for our purpose, it shows small rhythmic contractions. These contractions are recorded on the kymograph, and after a normal tracing is taken, the drug to be tested is introduced into the chamber and its effect observed.

#### RESULTS

I have tested out in the above manner the actions of the following oils: *oleum hedeomae* (pennyroyal), *oleum sabinæ* (savin), *oleum tanacetii* (tansy), *oleum rutæ* (rue), *oleum thymi* (thyme), *oleum terebinthinæ* (turpentine) and *apiol*. The results obtained were as fol-

7. Allen: *Lancet*, London, 1897, 1, 1022.

8. Peterson and Haines: *Text-Book of Medicine and Toxicology*, 1904, II, 636.

9. Falk: *Therap. Monatsh.*, IV, 448.

10. Lindeman: *Arch. f. Exper. Path. u. Pharmacol.*, XIII, 356.

11. Kunkel: *Toxikologie*, 1901, II, 962.

12. Meyer and Gottlieb: *Experimentelle Pharmakologie*, Ed. 2, p. 202.

13. Hefter: *Arch. f. Exper. Path. u. Pharmacol.*, XXXV, 365.

14. Dale and Laidlaw: *Jour. pharmacol. and exper. therap.*, IV, 75.

lows: All of these substances, even in small quantities, have absolutely no stimulating action on the uterus. On the contrary, they cause its relaxation and even paralysis. Thus the illustration shows the powerful normal contractions of a pregnant uterus, immediately inhibited, and paralyzed by the addition of a small amount (0.05 per cent. solution) of pennyroyal. The same effect is produced by tansy and apiol. These three drugs, pennyroyal, tansy, and apiol, seem to be the most toxic of the group examined. All of the drugs mentioned, however, acted in a similar way. The difference was only in degree. The least deleterious of the group, as might be expected, was turpentine. It required a much greater quantity relatively of that drug to paralyze the contractions. In no case, however, was there any stimulating or tonic effect.

#### CONCLUSIONS<sup>15</sup>

My observations lead me to the following conclusions:

1. The so-called emmenagogue oils are by no means innocuous substances.
2. They have absolutely no direct stimulating action on the uterine contractions or tonicity.
3. On the contrary, they inhibit such contractions, and even paralyze the uterus.
4. Their action as abortifacients, if they act as such, is no different from that of any other powerful systemic poison, such as phosphorus or arsenic.
5. They have very little if any therapeutic value, and do not deserve the place among the official pharmacologic preparations which many of them hold.

1511 Madison Avenue.

## RECENT IMPROVEMENTS IN THE QUININ TREATMENT OF LOBAR AND LOBULAR PNEUMONIA

THE AUXILIARY USE OF COCAIN, POSTERIOR-PITUITARY EXTRACT, AND BACTERIAL PRODUCTS

SOLOMON SOLIS COHEN, M.D.

Professor of Clinical Medicine, Jefferson Medical College; Physician to Jefferson Medical College Hospital and the Philadelphia General Hospital

PHILADELPHIA

That acute pneumonia, and especially acute lobar pneumonia, has for many years occupied first place in the dangerous infections of the temperate zone is so well known that it has become unnecessary to cite statistics. Twenty-five or thirty years ago it was usually stated that the mortality of acute lobar pneumonia was about 25 per cent. under all circumstances, and the tendency of systematic writers was to teach that treatment, apart from good nursing and the meeting of certain symptomatic indications, exerted but little influence. On the other hand, many medical men not occupying official positions, and especially those who practiced in country districts, expressed great faith in the influence of certain special methods of treatment, and looked on a mortality of over 10 per cent. as excessive.

Recent mortality statistics as collated by G. A. Gibson<sup>1</sup> are, however, even more unfavorable than those given by teachers and writers of a generation ago. Gibson's figures are taken from the mortality returns of

Great Britain, and from the papers of Wells, Musser and Norris, Beddard, Rychner, and other American, British and Continental writers, and from many of the leading hospitals of the world. The death-rate over a period of forty years, as given by the various sources and authorities cited, ranges between 20 and 22 per cent., but, if the last decade alone be taken, it is between 30 and 40 per cent. Thus in the Massachusetts General Hospital, according to Wells, it was 18 per cent. in 1822 and 30 per cent. in 1903. In the Boston City Hospital it was 21 per cent. in 1865 and 39 per cent. in 1903; in the Cincinnati Hospital, 31 per cent. in 1866 and 43 per cent. in 1903; in the Wiener allgemeines Krankenhaus, 18 per cent. in 1840 and 27 per cent. in 1899; in the Glasgow Royal Infirmary, 16 per cent. in 1831 and 30 per cent. in 1900. From his own wards Gibson reported a mortality, during the last ten years, of 31.9 per cent.

The classes of cases treated in different hospitals differ so much, and age, sex, race, social status and personal habits of the patient count for so much, that comparison between various series of statistics would teach but little. Moreover, it is well known not only that there are seasonal variations, but also that in certain years the attacks are much more severe and the fatalities correspondingly greater than in other years. Still, the fact is evident that all over the world the percentage mortality of pneumonia is increasing, and reference to any volume of vital statistics will show likewise that the number of cases reported is steadily rising. Improved diagnosis may account for this in part; but it would tend to lower, rather than increase, the reported mortality percentage.

From the experience of any one observer, sweeping conclusions cannot be drawn. Nevertheless, it is worth while to continue to direct professional attention to the comparatively favorable result (that is, a much reduced mortality, ranging from 9 to 20 per cent.)<sup>2</sup> that attends a special method of treatment systematically carried out during the last decade at two hospitals<sup>3</sup> receiving quite different classes of patients, as well as in private and consultation practice; that is, carried out not only during the time of greatest general increase in mortality, but also under a great variety of conditions as regards persons, environments, seasons, years and other factors.

The underlying principle of this method of treatment is not new; and while its systematization, which has been gradually worked out since 1904, in my hospital services, partly at Jefferson Hospital and partly at the Philadelphia General Hospital, contains some original features, the object of this paper is not to claim priority, but to try to gain a wider use for certain life-saving measures.

During the last few years the roof wards at Jefferson and the galleries at Blockley have offered improved facilities for obtaining that constant supply of fresh air which is an integral part of the method, and the more favorable showing for this period may be attributed in part to that factor. The attempt was always made, however, to secure ample ventilation of the wards or special rooms in which the pneumonia patients were placed, so that the difference, after all, is not the great disparity between air and no air, but that moderate but still important difference between well-aired rooms and the open air. There is a difference also between a roof

15. A fuller account of my experiments will be published separately in the Journal of Pharmacology and Experimental Therapeutics.

1. Gibson, G. A.: Acute Pneumonia, Its Prognosis and Treatment, Glasgow Med. Jour., May, 1911.

2. Cohen, S. Solis: Trans. Assn. Am. Phys., 1911, xxvi, 169; Am. Jour. Med. Sc., January, 1912, N. S., cxliii, 40; Internat. Med. Clinics, Series 22, iii, 56.

3. At the Philadelphia General Hospital any mortality under 50 per cent. is quite favorable, owing to the large number of alcoholics and neglected cases, etc., there received.