Cannabis Treatments in Obstetrics and Gynecology: A Historical Review

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SUMMARY. Cannabis has an ancient tradition of usage as a medicine in obstetrics and gynecology. This study presents that history in the literature to the present era, compares it to current ethnobotanical, clinical and epidemiological reports, and examines it in light of modern developments in cannabinoid research.

The author believes that cannabis extracts may represent an efficacious and safe alternative for treatment of a wide range of conditions in women including dysmenorrhea, dysuria, hyperemesis gravidarum, and menopausal symptoms.

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The author would like to thank the dedicated women of the Interlibrary Loan office at the Mansfield Library of the University of Montana, whose continued assistance has helped to revitalize lost medical knowledge. Dr. John Riddle provided valuable guidance, while Drs. Indalecio Lozano, David Deakle and Daniel Westberg translated key passages.

[Haworth co-indexing entry note]: "Cannabis Treatments in Obstetrics and Gynecology: A Historical Review." Russo, Ethan. Co-published simultaneously in *Journal of Cannabis Therapeutics* (The Haworth Integrative Healing Press, an imprint of The Haworth Press, Inc.) Vol. 2, No. 3/4, 2002, pp. 5-35; and: *Women and Cannabis: Medicine, Science, and Sociology* (ed: Ethan Russo, Melanie Dreher, and Mary Lynn Mathre) The Haworth Integrative Healing Press, an imprint of The Haworth Press, Inc., 2002, pp. 5-35. Single or multiple copies of this article are available for a fee from The Haworth Document Delivery Service [1-800-HAWORTH, 9:00 a.m. - 5:00 p.m. (EST). E-mail address: getinfo@haworthpressinc.com].

KEYWORDS. Cannabis, cannabinoids, medical marijuana, THC, obstetrics, gynecology, dysmenorrhea, miscarriage, childbirth, fertility, history of medicine

INTRODUCTION

For much of history the herbal lore of women has been secret. As pointed out in John Riddle's book, *Eve's Herbs* (Riddle 1997), botanical agents for control of reproduction have been known for millennia, but have often been forgotten over time or lost utterly, as in the case of the Greek contraceptive, *sylphion*. The same is true for other agents instrumental in women's health, frequently due to religious constraints. One botanical agent that exemplifies this lost knowledge is cannabis. As will be discussed, its role as an herbal remedy in obstetric and gynecological conditions is ancient, but will surprise most by its breadth and prevalence. Cannabis appears in this role across many cultures, Old World and New, classical and modern, among young and old, in a sort of herbal vanishing act. This study will attempt to bring some of that history to light, and place it in a modern scientific context.

THE ANCIENT WORLD AND MEDIEVAL MIDDLE AND FAR EAST

The earliest references to cannabis in female medical conditions probably originate in Ancient Mesopotamia. In the 7th century BCE, the Assyrian King Ashurbanipal assembled a library of manuscripts of vast scale, including Sumerian and Akkadian medical stone tablets dating to 2000 BCE. Specifically according to Thompson, *azallû*, as hemp seeds were mixed with other agents in beer for an unspecified female ailment (Thompson 1924). *Azallû* was also employed for difficult childbirth, and staying the menses when mixed with saffron and mint in beer (Thompson 1949). Usage of cannabis rectally and by fumigation was described for other indications.

Cannabis has remained in the Egyptian pharmacopoeia since pharaonic times (Mannische 1989), administered orally, rectally, vaginally, on the skin, in the eyes, and by fumigation. The Ebers Papyrus has been dated to the reign of Amenhotep I, circa 1534 BCE, while some hints suggest an origin closer to the 1st Dynasty in 3000 BCE (Ghalioungui 1987). One passage (Ebers Papyrus 821) describes use of cannabis as an aid to childbirth (p. 209): "Another: *smsm-t* [shemshemet]; ground in honey; introduced into her vagina (*iwf*). This is a contraction."

The *Zend-Avesta*, the holy book of Zoroastrianism, survives only in fragments dating from around 600 BCE in Persia. Some passages clearly point to psychoac-

tive effects of *Banga,* which is identified as hempseed by the translator (Darmesteter 1895). Its possible role as an abortifacient is noted as follows (Fargard XV, IIb., 14 (43), p. 179):

> And the damsel goes to the old woman and applies to her for one of her drugs, that she may procure her miscarriage; and the old woman brings her some Banga, or Shaêta ["another sort of narcotic"], a drug that kills in womb or one that expels out of the womb, or some other of the drugs that produce miscarriage . . .

Physical evidence to support the presence of medicinal cannabis use in Israel/Palestine was found by Zias et al. (1993) in a burial tomb, where the skeleton of a 14 year-old girl was found along with 4th century bronze coins. She apparently had failed to deliver a term fetus due to cephalopelvic disproportion. Gray carbonized material was noted in the abdominal area (Figure 1). Analysis revealed phytocannabinoid metabolites. The authors stated (p. 363), "We assume

FIGURE 1. Carbonized residue from 4th century Judea, containing phytocannabinoid elements, as a presumed obstetrical aid. (Permission Courtesy of the Israel Antiquities Authority.)

that the ashes found in the tomb were cannabis, burned in a vessel and administered to the young girl as an inhalant to facilitate the birth process."

Budge (1913) noted Syriac use of cannabis to treat anal fissures, as might occur postpartum.

Dwarakanath (1965) described a series of Ayurvedic and Arabic tradition preparations containing cannabis indicated as aphrodisiacs and treatments for pain. It was noted that cannabis was employed in Indian folk medicine onwards from the 4th-3rd centuries BCE.

In the 9th century, Sabur ibn Sahl in Persia cited use of cannabis in the *Al-Aqrabadhin Al-Saghir*, the first *materia medica* in Arabic (Kahl 1994). According to the translation of Indalecio Lozano of the Universidad de Granada, Spain (personal communication, Feb. 4, 2002), an intranasal base preparation of juice from cannabis seeds was mixed with a variety of other herbs to treat migraine, calm uterine pains, prevent miscarriage, and preserve fetuses in their mothers' abdomens.

In the 11th century, the Andalusian physician, Ibn Wafid al-Lajmi indicated that drying qualities of hemp seeds would inhibit maternal milk production. Tabit ibn Qurra claimed that they would reduce female genital lubrication when mixed in a potion with lentils and vinegar (Lozano 1993).

In the 13th century, the famous Persian physician, Avicenna (ibn Sina) recommended seeds and leaves of cannabis to resolve and expel uterine gases (Lozano 1998).

According to Lozano (2001), Ibn al-Baytar prescribed hemp seed oil for treatment of hardening and contraction of the uterus (al-Baytar 1291).

In the *Makhzan-ul-Adwiya,* a 17th century Persian medical text, it was claimed that cannabis leaf juice (Dymock 1884, p. 606) "checks the discharge in diarrhoea and gonorrhoea, and is diuretic."

Farid Alakbarov has recently brought to light the amazing richness of cannabis therapeutics of medieval Azerbaijan (Alakbarov 2001). Four citations are pertinent. Muhammad Riza Shirwani employed hempseed oil in the 17th century to treat uterine tumors. Contemporaneously, another author advised likewise (Mu'min 1669). Tibbnama recommended a poultice of cannabis stems and leaves to treat hemorrhoids, and the leaves mixed with asafetida for "hysteria" (Tibbnama 1712).

In China, the *Pen T'sao Kang Mu*, or *Bencao Gang Mu* was compiled by Li Shih-Chen in 1596 based on ancient traditions. This was later translated as Chinese *Materia Medica* (Stuart 1928). In it, cannabis flowers were recommended for menstrual disorders. Seed kernels were employed for postpartum difficulties. It was also observed (p. 91), "The juice of the root is . . . thought to have a beneficial action in retained placenta and post-partum hemorrhage."

EUROPEAN AND WESTERN MEDICINE

The earliest European references to the use of cannabis in women's medicine may derive from Anglo-Saxon sources. In the 11th century *Old English Herbarium* (Vriend 1984, CXVI, p.148), *haenep*, or hemp is recommended for sore breasts. This was translated as follows (Crawford 2002, p. 74): "Rub [the herb] with fat, lay it to the breast, it will disperse the swelling; if there is a gathering of diseased matter it will purge it."

The Österreichische Nationalbibliothek in Vienna, Austria displays a manuscript of the *Codex Vindobonensis 93*, said to be a 13th century southern Italian copy of a work produced in previous centuries, or even earlier Roman sources (Zotter 1996). Plate 108 depicts a clearly recognizable cannabis plant above the figure of a bare-breasted woman (Figure 2). According to a translation of Drs. David Deakle and Daniel Westberg (personal communication 2002), the Latin inscription describes the use of cannabis mixed into an ointment and rubbed on the breasts to reduce swelling and pain.

A translation in Old Catalan of Ibn Wafid's work above, interpreted it differently, indicating that hemp seeds, when eaten in great quantity, liberate maternal milk and treat pain of amenorrhea (Lozano 1993; personal communication, 2002).

Citing the *Kräuterbuch* of Tabernaemontanus in 1564, it was noted (Kabelik, Krejei, and Santavy 1960, p. 7), "Women stooping due to a disease of the uterus were said to stand up straight again after having inhaled the smoke of burning cannabis."

In England, in the *Theatrum Botanicum (Parkinson, Bonham, and L'Obel 1640)*, John Parkinson noted (p. 598) "Hempe is cold and dry . . . the Emulsion or decoction of the seede, stayeth laskes and fluxes that are continuall, . . ."

In 1696, Georg Eberhard Rumpf (Rumphius), a German physician in the service of the Dutch crown, reported on the use of cannabis root in Indonesia to treat gonorrhea (Rumpf and Beekman 1981, p. 197): "the green leaves of the female plant, cooked in water with Nutmeg, to drink to folks who felt a great oppression in their breasts, along with stabs, as if they had Pleuritis too."

According to Hamilton (1852), Valentini recommended hemp seed emulsion in the previous century to treat *furor uterinus*, a loosely defined malady of the era, frequently associated with nymphomania, melancholia or other ills, more fully discussed by Dixon (1994).

In his book, *Medicina Britannica*, Short (1751) employed cannabis for treatment of obstruction of the menses, even of chronic duration. In one case, he stated (p. 137-138), "I once ordered only the Hemp alone, where they [menses] had been obstructed not only Months, but some Years, with Success; and, when it could not break the Uterine or Vaginal Vessels, the Woman threw up Blood from the Lungs, but had them naturally the next Time."

FIGURE 2. Plate from the *Codex Vindobonensis 93* from the 13th century or earlier, depicting use of cannabis to allay breast swelling and pain. (From Bildarchiv d., with permission of the Österreichishe Nationalbibliothek, Vienna, Austria.)

Short (1751) also described a combination of hemp in "New-wort" (steeped crushed grain used in brewing beer) with feverfew (*Tanacetum parthenium*) and pennyroyal (*Mentha pulegium*) employed on three successive nights to (p. 137) "bring down the *Menses minime fallax*." Feverfew has anti-inflammatory effects, while pennyroyal is a known abortifacient (Riddle 1997). Thus, this treatment may well have induced miscarriage.

Finally, Short (1751, p. 138) noted this of a complex herbal mixture with hemp: "Some pretend the following a great Secret against Pissing the Bed . . ."

In 1794, the *Edinburgh New Dispensatory* noted use of a hemp seed oil emulsion in milk, useful for "heat of urine," "incontinence of urine," and "restraining venereal appetites" (Lewis 1794, p. 126).

After the reintroduction of cannabis to Western medicine in the form of solid oral extracts and tinctures by O'Shaughnessy (1842), its spectrum of activity quickly extended to many conditions. The first citation of its use for uterine hemorrhage in modern medicine is probably from Churchill (1849), and its discovery for this indication was apparently serendipitous (p. 512):

> We possess two remedies for these excessive discharges, at the time of the menses going off, which were not in use in Dr. Fothergill's time [18th century]. I mean *ergot of rye*, and *tincture of Indian hemp*. . . .
>
> The property of Indian hemp, of restraining uterine hemorrhage, has only been known to the profession a year or two. It was accidentally discovered by my friend, Dr Maguire of Castleknock, and since then it has been extensively tried by different medical men in Dublin, and by myself, with considerable success. The tincture of the resin is the most efficacious preparation, and it may be given in doses of from five to fifteen or twenty drops three times a day, in water. Its effects, in many cases, are very marked, often instantaneous, but generally complete after three or four doses. In some few cases of ulceration in which I have tried it on account of the hemorrhage, it seemed to be equally beneficial.

Alexander Christison extended the work of Churchill and applied Indian hemp to the problem of childbirth (Christison 1851), offering the following (pp. 117-118):

> Indian hemp appears to possess a remarkable power of increasing the force of uterine contraction during labour . . .
>
> One woman, in her first confinement, had forty minims of the tincture of cannabis one hour before the birth of the child. The os uteri was then of the size of a shilling, the parts very tender, with induration around the os uteri. The pains quickly became very strong, so much so as to burst the membranes, and project the liquor amnii to some distance, and soon the head

> was born. The uterus subsequently contracted well.
>
> Another, in her first confinement, had one drachm of the tincture, when the os uteri was rigid, and the size of a half-crown ; from this the labour became very rapid.
>
> Another, in her first confinement, had also one drachm of the tincture, when the os uteri was the size of a half-crown. Labour advanced very rapidly, and the child was born in an hour and a-half. There were severe after-pains.

Subsequently, Christison studied the oxytocic effects of cannabis tincture systematically in seven cases. He made several conclusions (pp. 120-121):

> Shortening of the [pain] interval was in general a more conspicuous phenomenon than prolongation of the pain.–
>
> It is worthy of remark, that in none of these cases were the ordinary physiological effects produced ; there was no excitement or intoxicating action, and there did not seem to be the least tendency to sleep in any of them.
>
> . . . While the effect of ergot does not come on for some considerable time, that of hemp, if it is to appear, is observed within two or three minutes. Secondly,-The action of ergot is of a lasting character, that of hemp is confined to a few pain shortly after its administration. Thirdly,-The action of hemp is more energetic, and perhaps more certainly induced, than that of ergot.
>
> There appears little doubt, then, that the Indian hemp may often prove of essential service in promoting uterine contraction in tedious labours.

Grigor (1852) also examined the role of tincture of *Cannabis indica* in facilitation of childbirth. In 9 cases, little was noticeable, but in 7, including 5 primiparous women (p. 125):

> I have noticed the contractions acquire great increase of strength and frequency immediately on swallowing the drug, and have seen four or five minutes ere the effect ensued ; . . . when effectual it is capable of bringing the labour to a happy conclusion considerably within a half of the time that would other have been required . . .
>
> I have not observed it to possess any anaesthetic effects . . .
>
> I consider the expulsive action of the cannabis to be stronger than that of ergot, but less certain in its effect . . .
>
> . . . nor have unpleasant consequences, so far as I have seen, appeared afterwards.

By 1854, the first uses of therapeutic cannabis were acknowledged in the *Dispensatory of the United States* (Wood and Bache 1854), and these effects of cannabis to hasten childbirth without anesthesia were noted (p. 339).

Willis (1859) reviewed past literature on therapeutic cannabis, and then described his own experience, which was frequently cited subsequently (p. 176):

> I have used the Indian hemp for some time and in many diseases, especially in those connected with the womb, in neuralgic dysmenorrhoea, in menorrhagia, in cessation of menstruation where the red discharge alternates with uterine leucorrhoea of long continuance, in repeated attacks of uterine hemorrhage, in all cases of nervous excitability, and in tedious labor, where there is restlessness of the patient, with ineffectual propulsive action of the uterus.
>
> . . . I was led to the use of hemp in puerperal convulsions, having also seen its beneficial effects in convulsions in general, after all the common remedies had been tried without relief.

Willis opined that based on literature and experience (p. 178), "It is a safe conclusion, from the many facts which have been published, that Indian hemp deserves further trial; in all cases making sure that the preparation used is good."

McMeens (1860) headed an Ohio State Commission that examined medical effects of cannabis. In addition to many references cited above, he reported on a Dr. M.D. Mooney of Georgia, who noted that a mixture of milk sugar and *Cannabis indica* extract (20 mg) taken every 3-4 h to treat gonorrhea was (p. 90) "successful in every case in from five to seven days."

That same year, a popular text (Stillé 1860) cited many contemporary authorities, noted irregular effects, and opined (vol. 2, p. 88), "From some experiments, cannabis would appear to excite contractions of the uterus."

Wright (1862) specifically noted the benefit of cannabis in relieving vomiting of pregnancy. In an initial letter, he discussed the case of a woman where all other available remedies had failed (pp. 246-247): "In a patient of mine, who was suffering to an extent that threatened death, with vomiting, I found the vomiting completely arrested by cannabis indica, given in repeated doses of three grains every four hours, until several doses were taken." He later revisited the issue in a subsequent article (Wright 1863), and explained (p. 75), "*Cannabis indica* does not paralyze the nerves, but strengthens them directly. It does not *constipate* by paralysis–it *cures* by beneficent virtues."

Silver (1870) devoted an entire article to the use of cannabis to treat menorrhagia and dysmenorrhea, reporting 5 cases in detail, all relieved nicely with cannabis within a few doses. He also referred to a colleague, who had never failed in over a hundred cases to control pain and discomfort in these disorders within 3 doses. When flow was not checked after early treatment, Silver felt this

diagnostic of "organic mischief" (p. 60) due to uterine fibroids, cervical carcinoma or other cause.

Grailey Hewitt authored a comprehensive textbook of obstetrics and gynecology. Cannabis was endorsed as a hemostatic treatment for menorrhagia, analgesic in dysmenorrhea and uterine cancer (Hewitt 1872). He compared it to other available remedies for the latter, including belladonna, hyoscyamus, opium and chloroform, remarking (p. 416), "The Indian hemp is, however, better entitled to consideration, and in many cases undoubtedly exercises a marked influence in allaying or preventing pain."

In another contemporary text (Scudder 1875), the author observed (p. 100), "I have employed the Cannabis specially to relieve irritation of the kidneys, bladder and urethra. It will be found especially beneficial in vesical and urethral irritation, and is an excellent remedy in the treatment of gonorrhoea."

Cannabis was also popular in France for Ob-Gyn indications. Racime (1876) described medical usage of hashish and Indian hemp (p. 443, [translation EBR]): "In women, hemp has a most manifest action on the uterus; this action translates itself into a contraction of the uterine muscular fibers."

A selection from a broad French review follows (Michel 1880, pp. 111-112 [translation EBR]):

> Illnesses of the genito-urinary organs.-Indian hemp has been employed in a large number of uterine affections, but principally in the diverse disturbances of menstruation. The tendency of authors is to administer it while the pain element predominates. . . .
>
> We have ourselves administered it often and in diverse cases of uterine hemorrhage: we have always seen success as well in postpartum hemorrhages, cases in which we employ it today in preference to the ergot of rye . . .
>
> . . . The reader would well permit us to affirm that but one first spoonful of the potion against menorrhagia (see the formula) has almost always succeeded in sufficiently diminishing the flow of blood. Rarely, the patient has had to take 4 spoonfuls. What has certainly struck us in its proper action is that its influence seems to have an effect on the following cycles; the Indian hemp acts, according to our observation and the remarks of Churchill himself, like a regulator of the catamenial function. Administered, in effect, during one sole period, sometimes two, rarely three, the menses return henceforth to just proportions and all medication becomes unnecessary. I know not of a similar effect that has been reported with ergotine or ergot of rye.

Michel also endorsed cannabis treatment for blennorrhagia, or bloody uterine mucous discharge.

In 1883, two consecutive letters to the *British Medical Journal* attested to the benefits of extract of *Cannabis indica* in menorrhagia, treating both pain and bleeding successfully with a few doses. In the first, cannabis was termed "a valuable remedy" (Brown 1883, p. 1002):

> Indian hemp has such specific use in menorrhagia–there is no medicine which has given such good results . . . A few doses {commencing with 5 minims of tincture} are sufficient . . . The failures are so few, that I venture to call it a specific in menorrhagia. The drug deserves a trial.

The second letter also extolled the benefits of cannabis (Batho 1883, p. 1002):

> . . . considerable experience of its employment in menorrhagia, more especially in India, has convinced me that it is, in that country at all events, one of the most reliable means at our disposal. I feel inclined to go further, and state that it is par excellence the remedy for that condition, which, unfortunately, is very frequent in India.
>
> I have ordered it, not once, but repeatedly, in such cases and always with satisfactory results. The form used has been the tincture, and the dose ten to twenty minims, repeated once or twice in the twenty-four hours. It is so certain in its power of controlling menorrhagia, that it is a valuable aid to diagnosis in cases where it is uncertain whether an early abortion may or may not have occurred. Over the hemorrhage attending the latter condition, it appears to exercise but little force. I can recall one case in my practice in India, where my patient had lost profusely at each period for years, until the tincture was ordered; subsequently, by commencing its use, as a matter of routine, at the commencement of each flow, the amount was reduced to the ordinary limits, with corresponding benefit to the general health. Neither I this, nor in any other instance in which I prescribed the drug, were any disagreeable physiological effects observed.

One dissenting voice of the era was that of Oliver (1883) who felt that cannabis was not useful in dysmenorrhea since (p. 905) "its action seems so variable and the preparation itself so unreliable, as to be hardly worthy of a place on our list of remedial agents at all." Quality control problems with cannabis were a frequent concern throughout its reign in Western medicine.

Sydney Ringer, the British pioneer of intravenous fluid therapy, observed the following of *Cannabis indica* extract (Ringer 1886, p. 563):

> It is said to relieve dysuria, and strangury, and to be useful in retention of urine, dependent on paralysis from spinal disease. It is used occasionally in gonorrhoea. It is very useful in menorrhagia, or dysmenorrhoea. Half a grain to a grain thrice daily, though a grain every two hours, or hourly, is

> sometime required in those who can tolerate so large a dose, often relieve the pain of dysmenorrhoea. It is said to increase the energy of the internal contractions.

In India, it was reported of *Cannabis indica* (McConnell 1888, p. 95), "its powerful effect in controlling uterine hemorrhage (menorrhagia, &c.) has been repeatedly recorded by competent observers, and its employment for the relief of such affections is well understood and more or less extensively resorted to."

Farlow (1889) penned a treatise on the use of rectal preparations of cannabis describing its use in young women before marriage to alleviate premenstrual symptoms and subsequent dysmenorrhea (p. 508):

> If the excitement can be moderated, if the pelvic organs can be made less irritable, there will be less pain, less hemorrhage, less weakness, and consequently a much longer period of health between the catamenia. This, I feel sure, can often be very successfully done by the rectal use of belladonna and cannabis indica, beginning a few days before the menstrual symptoms or prodromes appear.

Farlow continued by describing another setting in sexually active, but nulliparous women (p. 508):

> After marriage and before childbirth, the uterus and pelvis, especially the left ovary, are very liable to be tender and irritable, even when there is no evident organic disease. The backache, bearing down, pain in the side, groin and legs, the frequent micturition, painful coitus, constipation and headache are often much relieved by the suppositories.

Finally, Farlow mentioned another cannabis indication (p. 580): "At the menopause the well-known symptoms, the various reflexes, the excitement, the irritability, and pain in the neck of the bladder, flashes of heat, and cold, according to my experience, can frequently be much mitigated, by the suppositories."

Farlow employed low doses of these agents, 1/4 grain each (15 mg) or extracts of belladonna and *Cannabis indica*, administered by rectal suppository at night, or bid. Apparently no intoxication was necessary for therapeutic benefit (p. 509): "I do not think there is anything to be gained by pushing the drugs to their physiological action."

Aulde (1890) recommended cannabis extract for dysmenorrhea, sometimes combined with gelsemium (pp. 525-526):

> The majority of these cases uncomplicated by displacements, such as seen in young girls and married women, will be promptly benefited, and the menstrual flow appears, when there is no further trouble until the next pe-

riod.

. . . Cannabis has been highly recommended for the relief of *menorrhagia*, but is not curative in the true sense of the term.

Sir John Russell Reynolds was personal physician to Queen Victoria, and it has been widely acknowledged that she received monthly doses of *Cannabis indica* for menstrual discomfort throughout her adult life. In 1890, after more than thirty years' experience with the agent, Reynolds reported (Reynolds 1890, p. 38), "Indian hemp . . . is of great service in cases of simple spasmodic dysmenorrhoea."

Another textbook of the era noted the following therapeutic indications for *Cannabis indica* (Cowperthwaite 1891, p. 188): "Said to be especially useful in gonorrhoea when the chordee is well marked. Uterine colic."

J.B. Mattison wrote extensively on therapeutic cannabis. He noted the following among several gynecological conditions reviewed (Mattison 1891, p. 268): "In genito-urinary disorders it often acts kindly-the renal pain of Bright's disease ; and it calms the pain of clap equal to sandal or copaiva, and is less unpleasant."

The Indian Hemp Drugs Commission of 1893-1894 exhaustively examined the uses and abuses of cannabis, noting its indication for prolonged labor and dysmenorrhea (Kaplan 1969; Commission 1894).

In this era, patent medicines containing cannabis were very common. One preparation, named "Dysmenine," contained cannabis with a variety of other herbal tinctures, "Indicated for Dysmenorrhea, Menstrual Colic, and Cramps" (Figure 3). Interestingly, one component was capsicum, raising the possibility of synergistic action on cannabinoid and vanilloid receptors.

An 1898 text opined of the fluidextract of cannabis (Lilly 1898, p. 32), "Its anodyne power is marked in chronic metritis and dysmenorrhea."

Shoemaker (1899) reported a case of endometritis with metrorrhagia, that required surgery, but in which (p. 481) "Marked relief of symptom was afforded, however, by the administration of Indian hemp. It relieved pain and diminished hemorrhage, and was highly valued by the patient."

Lewis (1900) observed the following (p. 251):

> Dysmenorrhea, not due to anatomical of inflammatory causes, is, in my opinion, one of the principal indications for indian hemp. No other drug acts so promptly and with fewer after effects.
>
> From my own personal observation, I am convinced that cannabis indica does exert a powerful influence on muscular contraction, particularly of the uterus. It may not, as Bartholow says, have the power of initiating uterine contraction, but I have demonstrated time and time again to my own satisfaction that the presence of the merest contractile effort is enough to permit its fullest effects. It is therefore of some service in uterine hemor-

> rhage, but since its action is much slower than that of ergot, it is not as useful in those sudden hemorrhages great enough to require immediate check. I have noticed, however, that ergot is considerably quicker and more prolonged in its action when combined with cannabis indica.
>
> The drug is very useful in profuse menstruation, decreasing the flow nicely without completely arresting it, as ergot very frequently and improperly does.

Felter and Lloyd (1900) described numerous Ob-Gyn indications for cannabis (pp. 426-427):

> The pains of *chronic rheumatism, sciatica, spinal meningitis, dysmenorrhea, endometritis, subinvolution*, and the vague pains of *amenorrhoea*, with depression, call for cannabis. Owing to a special action upon the reproductive apparatus, it is accredited with averting *threatened abortion*. . . .
>
> Cannabis is said in many cases to increase the strength of the uterine contractions during parturition, in atonic conditions, without the unpleasant consequences of ergot, and for which purpose it should be used in the form of tincture (see below), 30 drops, or specific cannabis, 10 drops, in sweetened water or mucilage, as often as required. In *menorrhagia*, the tincture in doses of 5 or 10 drops, 3 or 4 times a day, has checked the discharge in 24 or 48 hours.
>
> The greatest reputation of cannabis has been acquired from its prompt results in certain disorders of the genito-urinary tract. In fact, its second great keynote or indication is irritation of the genito-urinary tract, and the indication is even of more value when associated with general nervous depression.
>
> It is therefore useful in *gonorrhoeas, chronic irritation of the bladder, in chronic cystitis*, with painful micturition, and in *painful urinary affections generally*. It makes no difference whether a urethritis be specific or not, or whether it is acute or chronic, the irritation is a sufficient guide to the selection of cannabis. Use it in *gonorrhoea* to relieve the *ardor urinae*, and to prevent urethral spasm and avert chordee, and in *gleet*, to relive the irritation and discharge; employ it also in *spasm of the vesical sphincter*, in *dysuria* and in *strangury*, when spasmodic. Burning and scalding in passing urine, with frequent desire to micturate, are always relieved by cannabis.

The authors clearly understood that the potency of the preparation directly affected clinical results. While both Indian hemp and American hemp were said to be effective, much higher doses of the latter were said to be required.

In a popular American text of the era, Bartholow (1903) noted (p. 557):

FIGURE 3. Photo of “Dysmenine” a late 19th century patent medicine for menstrual cramps, containing cannabis. (Photo by Ethan Russo, with permission of Michael Krawitz, the Cannabis Museum.)

> It is well established that hemp has the power to promote uterine contractions. It can not initiate them, but increased their energy when action has begun. It may be given with ergot. In consequence of this power which it possesses to affect the muscular tissue of organic life, hemp is used successfully in the treatment of *menorrhagia*. It is said to be especially useful in that form of *menorrhagia* which occurs in the climacteric period (Churchill). It has, more recently, been show to possess the power to arrest *hemorrhage* from any point, but it is chiefly in menorrhagia that much good is accomplished. . . .
>
> This agent has also been used with success in the treatment of *gonorrhoea*. It diminishes the local inflammation, allays chordee, and lessens the pain and irritation, with accompanying restlessness.

In Ceylon, Ratnam (1916) defended use of therapeutic cannabis against legislative challenges (p. 37): "I and other medical practitioners have used it extensively in the treatment of tetanus, asthma and uterine disorders, especially dysmenorrhea and menorrhagia."

In a text of the era, cannabis was deemed useful in menopausal headaches (Hare 1922), as well as the following (p. 182):

> In cases of *uterine subinvolution*, *chronic inflammation*, and *irritation* cannabis is of great value, and it has been found of service in *metrorrhagia* and *nervous and spasmodic dysmenorrhea*. Not only does it relieve pain, but it also seems to act favorably upon the muscular fibers of the uterus.

Another popular text (Sajous and Sajous 1924) cited cannabis as an analgesic for menopause, uterine disturbances, dysmenorrhea, menorrhagia and impending abortion, and postpartum hemorrhage.

In 1928, in *Pharmacotherapeutics, materia medica and drug action*, the authors remarked on the ability of cannabis to counteract "painful cramps" and its "particular influence over visceral pain" (Solis-Cohen and Githens 1928, p. 1702). More specifically, they noted (p. 1705):

> Cannabis acts favorably upon the uterine musculature and may be used as a synergist to ergot in sluggish labor. It is useful also in relieving the pain of chronic *metritis* and *dysmenorrhea* and reduces the flow in *menorrhagia*. It is employed as a symptomatic remedy in *gonorrhea* in doses of 1/4 grain (0.015 Gm.) of the extract four times a day, relieving the pain, dysuria, and chordee.

An anonymous editor (probably Morris Fishbein) noted the ability of cannabis to achieve a labor with pain burden substantially reduced or eliminated, followed by a tranquil sleep (Anonymous 1930, p. 1165):

> Hence a woman in labor may have a more or less painless labor. If a sufficient amount of the drug is taken, the patient may fall into a tranquil sleep form which she will awaken refreshed. . . . As far as is known, a baby born of a mother intoxicated with cannabis will not be abnormal in any way.

The *British Pharmaceutical Codex* retained an indication for cannabis in treatment of dysmenorrhea in 1934 (Pharmaceutical Society of Great Britain 1934).

Despite the fact that cannabis had been dropped from the *National Formulary* the previous year, Morris Fishbein, the editor of the *Journal of the American Medical Association*, continued to recommend cannabis in migraine associated with menstruation (Fishbein 1942, p. 326):

> In this instance the patient may be given either sodium bromide or fluidextract of cannabis three days before the onset of the menstrual period, continued daily until three days after the menstrual period. . . . The dose of fluidextract of cannabis is five drops three times daily, increased daily by one drop until eleven drops, three times daily, are taken. Then the dosage is reduced by one drop daily until 5 drops are taken three times daily and so on.

Medical investigation of cannabis persisted in Czechoslovakia. One group noted success in use of a cannabis extract in alcohol and glycerine to treat rhagades, or fissures, on the nipples of nursing women to prevent staphylococcal mastitis (Kabelik, Krejei, and Santavy 1960).

MODERN ETHNOBOTANY OF CANNABIS IN OBSTETRICS AND GYNECOLOGY

In the folk medicine of Germany, in the late 19th century (Rätsch 1998, p. 122), a cannabis preparation was "laid on the painful breasts of women who have given birth; hemp oil is also rubbed onto these areas; hempseed milk is used to treat bladder pains and dropsy."

Although the carminative properties of cannabis seeds had been noted since the time of Galen, Lozano (2001) notes that al-Mayusi (1877) claimed similar properties for the leaves, and to treat uterine gases.

In 19th century Persia, Schlimmer (1874) reported his observations on usage of *Cannabis indica* leaves as a treatment for urethritis associated with the practice of prostitution. In modern Iran, Zargari (1990) notes continued use of *Cannabis sativa* seed oil rubbed on the breasts to diminish or even completely prevent lactation.

Cannabis or *nasha* was employed medicinally despite Soviet prohibition in Tashkent in the 1930s (Benet 1975, pp. 46-47): "A mixture of lamb's fat with *nasha* is recommended for brides to use on their wedding night to reduce the pain of defloration." In the same culture (p. 47), "An ointment made by mixing hashish with tobacco is used by some women to shrink the vagina and prevent fluor alvus [leukorrhea]." More fancifully, Benet noted that in German folk medicine (p. 46), "sprigs of hemp were placed over the stomach and ankles to prevent convulsions and difficult childbirth."

Nadkarni (1976) reported the use in India of a poultice of cannabis for hemorrhoids, and (p. 263) "The concentrated resin exudate (resinous matters) extracted from the leaves and flowering tops or agglutinated spikes of C. sativa, and known as *nasha* or *charas* . . . is valuable in preventing and curing . . . dysuria and in relieving pain in dysmenorrhea and menorrhagia . . ."

In a book about medicinal plants of India (Dastur 1962), we see the following (p. 67): "Charas [hashish] . . . is of great value in-dysuria . . . it is also used as an anaesthetic in dysmenorrhea . . . . Charas is usually given in one-sixth to one-fourth grain doses." A seed infusion was also employed to treat gonorrhea.

Aldrich (1977) has extensively documented the Tantric use of cannabis in India from the 7th century onward as an aid to sexual pleasure and enlightenment (p. 229):

> The Kama Sutra and Ananga Ranga eloquently detail Hindu sexual techniques, and the Tantras transform such sexual practices into a means of meditational yoga.
>
> . . . In Hindu Tantrism, the female energy (shakti) is dynamic and paramount: the male is passive and takes all his vitality from the shakti. . . . In Buddhist Tantra it is just the opposite: the male is active and assumes the dynamic role of compassion, while the female is the passive embodiment of wisdom.

We have little modern research to document a biochemical basis to these claims, which persist, nonetheless. In his inimitable prose, Ott (2002, p. 29) has stated of cannabis, "many women I have known are effusively enthusiastic about its aphrodisiacal amatory tributes."

A treatise on cannabis usage in India includes the following citation (Chopra and Chopra 1957, p. 12): "It [cannabis resin] is considered a sovereign remedy for relieving pain in dysmenorrhea and menorrhagia, and against dysurea."

In Cambodia, mothers reportedly use hemp products extensively after birth (Martin 1975), making an infusion of ten flowering tops to a liter of water to provide a sense of well-being. When insufficient milk is present for nursing, female hemp flowers are combined with other herbs for ingestion. An alcoholic extract of cannabis and various barks is said to alleviate postpartum stiffness. Another hemp extract mixture is employed to cure hemorrhoids and polyps of the sex organs.

In Vietnam (Martin 1975), cannabis seed kernels in a preparation called sac thuoc are said to cure dysmenorrhea, or provide a feeling of wellness after childbirth. Citing Martin's work, Rubin noted the following usage in Vietnam (Rubin 1976, p. 3): "21 kernels boiled in water may be given to the expectant mother to reset the neonate in normal position at birth."

Hemp is of ancient use in China, but it was noted (Shou-zhong 1997, p. 148): "In modern clinical practice, Hemp Seeds are still in wide use. They are able to . . . promote lactation, hasten delivery, and disinhibit urination and defecation."

Perry and Metzger (1980) noted continued folk use of cannabis in China and Southeast Asia, where the seeds were specially prepared for treatment of uterine prolapse and as a birthing aid.

In South Africa, a Sotho herbalist used cannabis to facilitate childbirth (Hewat 1906, p. 98), and was "in the habit of getting his patient stupified by much smoking of dagga."

In modern times, urban Africans have also employed cannabis medicinally for a number of purposes (Du Toit 1980), as one informant related (p. 209):

> ". . . pregnant women should always have some burnt for her so as to have a completely healthy child." But is particularly during childbirth that "pregnant women were given dagga to make them brave," and "so that they wouldn't feel pain."

In Brazil, it was observed (Hutchinson 1975, p. 180), "Such an infusion [of marijuana leaves] is taken to relieve rheumatism, 'female troubles,' colic and other common complaints."

In a 20th century English herbal, Grieve (1971) noted the following uses of hemp (p. 397): "The tincture helps parturition, and is used in senile catarrh, gonorrhoea, menorrhagia, chronic cystitis and all painful urinary affections. An infusion of the seed is useful in after pains and prolapsus uteri." Dosages were provided (p. 397): "Of tincture for menorrhagia, 5 to 10 minims. Three to four times a day (i.e., 24 grains of resinous extract in a fluid ounce of rectified spirit)."

Finally, this passage was offered (p. 397): "The following is stated to be a certain cure for gonorrhoea. Take equal parts of tops of male and female hemp in blossom. Bruise in a mortar, express the juice, and add an equal portion of alcohol. Take 1 to 3 drops every two to three hours."

Merzouki et al. (Merzouki, Ed-derfoufi, and Molero Mesa 2000) have examined the usage of cannabis as part of herbal mixtures employed by Moroccan herbalists to induce therapeutic abortion, concluding that the cannabis component did not produce this effect, but rather other clearly toxic components were responsible. The herbal mixture is applied per vaginam, or alternatively, its smoke is fumigated in close proximity to the genitals (Merzouki 2001).

By the late 1960s, cannabis cures entered the scene in modern America. A popular treatise on marijuana noted medicinal effects (Margolis and Clorfene 1969, p. 26):

> You'll also discover that grass is an analgesic, and will reduce pain considerably. As a matter of fact, many women use it for dysmenorrhea or menorrhagia when they're out of Pamprin or Midol. So if you have an upset stomach, or suffer from pain of neuritis or neuralgia, smoke grass. If pains persist, smoke more grass.

Popular cannabis folklore, thus, did not escape American consciousness. Another example was noted by Thompson (1972, p. 3): "In the Jack's Creek area of Fayette County, Kentucky, poultices with hemp leaves are supposed to relieve hemorrhoidal pains and bleeding when applied in the appropriate area of the human body."

RECENT THEORY AND CLINICAL DATA

Solomon Snyder, the discoverer of opiate receptors, examined cannabis' pros and cons as an analgesic (Snyder 1971, p. 14):

> For there are many conditions, such as migraine headaches or menstrual cramps, where something as mild as aspirin gives insufficient relief and opiates are too powerful, not to mention their potential for addiction. Cannabis might conceivably fulfill a useful role in such conditions.

In the mid-1970s, Noyes et al. wrote several articles on analgesic effects of cannabis. In case reports (Noyes and Baram 1974), one young woman successfully employed cannabis to treat the pain and anxiety after a tubal ligation, and another in dysmenorrhea (p. 533): "The relief she got from smoking was prompt, complete, and consistently superior to that from aspirin."

In 1993, Grinspoon and Bakalar published *Marihuana, the forbidden medicine*, and subsequently revised it (Grinspoon and Bakalar 1997). The book contains numerous "anecdotal" testimonials from patients and doctors documenting clinical efficacy of cannabis where other drugs were ineffective. An entire section with case studies was included on premenstrual syndrome (PMS), menstrual

cramps, and labor pains, supporting excellent symptomatic relief at low doses without cognitive impairment.

Numerous surveys cite cannabis usage for obstetric and gynecological complaints, but in one Australian example, 51% of the women indicated indications for PMS or dysmenorrhea (Helliwell 1999).

Rätsch (1998) has observed (p. 162), "Several women who delivered their babies at home have told me that they smoked or ate hemp products to ease the painful contractions and the birth process in general."

Beyond direct effects mediated by the cannabinoid receptors, McPartland has proposed that therapeutic effects of cannabis in dysmenorrhea involve anti-inflammatory mechanisms (McPartland 1999, 2001).

It has been observed that women with PMS exhibit a fault in fatty acid metabolism that impedes the conversion of linoleic acid (LA) to gamma-linolenic acid (GLA) and prostaglandins. A daily dose of 150-200 milligrams of GLA over a twelve-week period significantly improved PMS-related symptoms (Horrobin and Manku 1989). As pointed out by Leson and Pless (2002), this amount of GLA can be supplied by only 5 ml of hemp seed oil daily.

Experimentally, Δ^9-THC inhibited herpes virus replication (HSV-1 and HSV-2) *in vitro*, even at low concentrations (Blevins and Dumic 1980), and was suggested for trials of topical usage.

An Italian group recently demonstrated the inhibition of proliferation of human breast cancer cells by anandamide *in vitro* (De Petrocellis et al. 1998); 2-arachidonylglycerol and the synthetic cannabinoid HU-210 acted similarly, while this activity was blocked by the CB_1 antagonist, SR 141716A. It was felt that these effects were mediated through inhibition of endogenous prolactin activity at its receptor. It is likely that THC acts similarly. Palmitylethanolamide has subsequently been demonstrated to inhibit expression of fatty acid amidohydrolase, thereby enhancing the antiproliferative effects of anandamide on human breast cancer cells (Di Marzo et al. 2001).

Recent animal work has elucidated the role of endocannabinoids in mammalian fertility. Recently Das et al. (1995) detected CB_1 receptor mRNA in mouse uterus, thus suggesting that this organ is capable of anandamide production. Anandamide (arachidonylethanolamide, AEA) and Δ^9-THC inhibited forskolin-stimulated cyclic AMP production in mouse uterus, whereas cannabidiol did not, suggesting that the uterine site is active in endocannabinoid production.

Schmid et al. (1997) demonstrated very high levels of anandamide in the peri-implantation mouse uterus. Data suggest that down-regulation of AEA levels promote uterine receptivity, while up-regulation may inhibit implantation. It was surmised that aberrant AEA synthesis or expression may be etiological in early pregnancy failure or infertility. The corresponding role that THC or canna-

bis may have in human females at the time of fertilization and implantation is open to conjecture, but deserves further investigation.

Wenger et al. (1997) claimed similarity in effects of injected THC and AEA in pregnant rats, prolonging length of gestation, and increasing stillbirths, perhaps due to inhibition of prostaglandin synthesis. The same lead author posited cannabinoid influences on hypothalamic and pituitary endocrine functions in a subsequent paper (Wenger et al. 1999).

Paria et al. (2001) suggested the need for tight regulation of endocannabinoid signaling during synchronization of embryonic development and uterine receptivity. They demonstrated inhibition of implantation in wild-type mice with sustained high-level exposure to "natural cannabinoid" while not in CB_1 (−/−)/CB_2 (−/−) double knockout mutant mice.

Issues of cannabis use in human pregnancy remain a great concern. The topic is reviewed in (Fried 2002; Murphy 2001; Zimmer and Morgan 1997). A variety of studies have demonstrated transient effects of cannabis on endocrine hormone levels, but no consistent effects seem to occur in chronic settings (Russo et al. 2002). Certainly subtle changes at critical times of fertilization or implantation may be significant. A valid assessment was provided (Murphy 1999, p. 379): "the hormone milieu at the time of exposure may dictate a woman's hormonal response to marijuana smoking."

Studies are hampered by the obvious fact that laboratory animals are not human in their responses. Estrous cycles and behaviors in animals are not always analogous to menstrual cycles and other physiological effects in women. Nevertheless, animal data suggest that in female rats, at least, THC acts on the CB_1 receptor to initiate signal transduction with membrane dopamine and intracellular progesterone receptors to initiate sexual responses (Mani, Mitchell, and O'Malley 2001).

One available approach to the issues is provided by examining factors in spontaneous abortions. In a study of 171 women, 25% of pregnancies ended spontaneously within 6 weeks of the last menses. Cannabis exposure seemed to have no observable effect in these cases (Wilcox, Weinberg, and Baird 1990).

The population of Ottawa, Ontario, Canada has been extensively examined over the last two decades with respect to cannabis effects in pregnancy. In a small study of cannabis using mothers vs. abstainers (O'Connell and Fried 1984), ocular hypertelorism and "severe epicanthus" were only noted in children born to users.

In 1987, the Ottawa group compared effects of cannabis, tobacco, alcohol and caffeine during gestation (Fried et al. 1987). Whereas tobacco negatively affected neonatal birth weight and head circumference, and alcohol was associated with lower birth weight and length, no effects on any growth parameters were ascribable to maternal cannabis usage.

In a subsequent study (Witter and Niebyl 1990), examination of 8350 birth records revealed that 417 mothers (5%) claimed cannabis-only usage in pregnancy, but no association was noted with prematurity or congenital anomalies. The authors suggested that previously ascribed links to cannabis were likely confounded by concomitant alcohol and tobacco abuse.

A group in Boston noted a decrease in birth weight of 79 g in infants born to 331 of 1226 surveyed mothers with positive using drug screen for cannabis ($p = 0.04$) (Parker and Zuckerman 1999), but no changes in gestation, head circumference or congenital abnormalities were noted.

The largest study of the issue to date evaluated 12,424 pregnancies (Linn et al. 1983). Although low birth weight, shortened gestation and malformations seemed to be associated with maternal cannabis usage, when logistic regression analysis was employed to control for other demographic and exposure factors, this association fell out of statistical significance.

Dreher has extensively examined prenatal cannabis usage in Jamaica (Dreher 1997; Dreher, Nugent, and Hudgins 1994), wherein the population observations were not compounded by concomitant alcohol, tobacco, or polydrug abuse. This study is unique in that regard, no less due to the heavy intake of cannabis ("ganja"), often daily, in this cohort of Rastafarian women. No differences were seen between groups of cannabis-using and non-cannabis-using mothers in the weight, length, gestational age or Apgar scores of their infants (Dreher, Nugent, and Hudgins 1994). Deleterious effects on progeny of cannabis smokers were not apparent; in fact, developmental precocity was observed in some measures in infants born to women who smoked ganja daily. The author noted (Dreher 1997, p. 168):

> The findings from Jamaica, however, suggest that prenatal cannabis exposure is considerably more complex than we might first have thought. Loss of appetite, nausea and fatigue compound the "bad feeling" that women in this study commonly reported. For many women, ganja was seen as an option that provided a solution to these problems, i.e., to increase their appetites, control and prevent the nausea of pregnancy, assist them to sleep, and give them the energy they needed to work. . . . The women with several pregnancies, in particular, reported that the feelings of depression and desperation attending motherhood in their impoverished communities were alleviated by both social and private smoking. In this respect, the role of cannabis in providing both physical comfort and a more optimistic outlook may need to be reconceptualized, not as a recreational vehicle of escapism, but as a serious attempt to deal with difficult physical, emotional, and financial circumstances.

DISCUSSION AND CONCLUSIONS

This presentation supports the proposition that cannabis has been employed historically for legion complaints in obstetrics and gynecology. To list briefly, these include treatment of: menstrual irregularity, menorrhagia, dysmenorrhea, threatened abortion, hyperemesis gravidarum, childbirth, postpartum hemorrhage, toxemic seizures, dysuria, urinary frequency, urinary retention, gonorrhea, menopausal symptoms, decreased libido, and as a possible abortifacient.

It is only recently that a physiological basis for these claims has been available with the discovery of the endocannabinoid system. Limited research to date supports these claims in terms of cannabinoid analgesia, antispasmodic and anti-inflammatory activities, but requires additional study to ascertain mechanisms and confounding variables.

Recommendations for cannabis therapeutics have often supported only utilization for terminal, intractable, or chronic disorders (Joy, Watson, and Benson 1999). However, simple logic would indicate that side effects of any medicine would be less evident when the agent is employed sporadically. Generally, that situation prevails for many of the listed Ob-Gyn indications for cannabis. Available historical and epidemiological data supports very low toxicity, even in pregnancy, to mother or child. Professor Philip Robson of Oxford has summarized the situation with cannabis in obstetrics nicely (Lords 1998, p. 123):

> If you could have an agent which both speeded labour up, prevented hemorrhage after labour and reduced pain, this would be very desirable. Cannabis is so disreputable that nobody would begin to think of that and yet that is really an obvious application that we should seriously consider with perhaps some basic research and pursue it.

A few intriguing issues remain. Is cannabis truly an abortifacient? Our four specific references are equivocal, one ancient (Darmesteter 1895), one old (Short 1751), and two modern (Merzouki, Ed-derfoufi, and Molero Mesa 2000; Merzouki 2001), but these and current epidemiological data would seem to indicate that cannabis does not produce this effect *sui generis*. Perhaps its actual role is one to *mitigate side effects* of the active components.

Numerous citations historically support the notion that cannabis is quite potent in its obstetric and gynecological actions, with specific attestation that medical benefits are frequently obtained at doses that are sub-psychoactive. The therapeutic ratio of cannabis with respect to cognitive impairment seems generous.

Another mystery worthy of additional study surrounds the very rapid activity claimed for cannabis extracts in promotion of labor (Grigor 1852; Christison 1851). Certainly modern anecdotal claims of a similar nature are legion when

cannabis is smoked. Pharmacodynamically, oral administration of extracts would be unlikely to provide benefits within minutes. Perhaps these tinctures were demonstrating a sublingual or mucosal absorption akin to those in modern trials of cannabis-based medical extracts (Whittle, Guy, and Robson 2001).

In summary, the long history of cannabis in women's medicine supports further therapeutic investigation and application to a large variety of difficult clinical conditions. Cannabis as a logical medical alternative in obstetrics and gynecology may yet prove to be, in the words of Robson (1998), a phoenix whose time it is to rise once more.

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