

Course: Master of Health Science (Herbal Medicine)

University: University of New England

Unit: Herbal Therapeutics III

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A) Patient 1

- 42 year old woman.
- 1 child born, difficulty conceiving since.
- History of miscarriages; lost triplets at 14 weeks 4 years prior to seeking herbal treatment, lost a single pregnancy at 14 weeks 4 years later.
- Treated with Clomid, which caused her to develop ovarian cysts and amenorrhoea.
- 38 day cycle, suffers PMS, bloating, bursts of anger.
- Suffers headaches due to poor sleep, lies awake worrying
- Takes paracetamol for headaches
- She is depressed due to her inability to conceive, very stressed, not coping well with daily life.
- Blood tests conducted a year ago show elevated prolactin level, all other hormones are at normal levels

Introduction:

Difficulty with conception, often termed infertility, becomes increasingly common in women over the age of 35 years (Brzakowski 2009:F3-7). According to the American Society for Reproductive Medicine three out of four people overestimate by five years the rapid decline in female fecundity, with prime childbearing age occurring up to the age of 32 years for females and a rapid decline at 35, instead of 40 as is commonly believed. By the mid thirties almost 25% of women are infertile and by age 43 it is unusual to still be fertile (Brzakowski 2009:F3-7). It is, however wise to ensure that both the man and woman trying to conceive have been examined and medically tested (by a specialist gynaecologist) to ensure therapeutic focus on the correct patient (Brzakowski 2009:F3-7). If this is not determinable, therapy would be most effectively directed at both the man and the woman (Brzakowski 2009:F3-7).

In the case of the patient detailed above the reality of age must be considered. At 42 years of age conception occurs at a significantly lower rate (Brzakowski 2009:F3-7).

Phytotherapy, however, should be considered along with lifestyle and dietary factors for patients experiencing difficulty with conception related to anovulatory cycles, defective luteal function, viscous cervical mucous and immunological rejection of sperm (Mills and Bone 2000:238-246). Still yet 20-30% of patients suffer idiopathic infertility of no known cause (Brzakowski 2009:F3-7).

Although the patient has been treated previously with clomiphene (Clomid), a selective oestrogen receptor modulator (SERM) used mainly in female infertility due to anovulation, she evidently experienced a common adverse effect of this drug in the form of ovarian cysts (Bates 2009: 586-7). Most ovarian cysts are functional in nature and benign (Brisholt 2009:165-69). There are three types; Graafian, Luteal and Haemorrhagic, the second type being the most likely in this patient (Brisholt 2009 :165-69). They are frequently found in women of childbearing age and up to 14.8% of postmenopausal women (Brisholt 2009:165-69). It is not clear as to whether the ovarian cysts still persist in the patient as they usually resolve after 2-3 menstrual cycles (Brisholt 2009:165-69).

Hyperprolactinaemia is the presence of higher than normal prolactin levels in the blood. Normal levels are less than 580 mIU/L for women and less than 450 mIU/L for men (Patel 2007:455-9). Prolactin is a peptide hormone produced by the anterior pituitary gland, which is normally associated with lactation and breast development during pregnancy (Warrell 2003:550-555). Higher than normal levels of prolactin can cause disruptions in the normal menstrual period and infertility (Patel 2007:455-9).

Hyperprolactinaemia can occur as a normal body change during pregnancy and lactation (Warrell 2003:550- 555). Abnormal function or stimulation of the prolactin-secreting cells in the pituitary gland can cause prolactin levels to rise (Mancini 2008: 67-99). Pituitary tumours are the most common cause of this (Mancini 2008: 67-99), often treated in conventional medicine with Cabergoline and Bromocriptine (Coleo 2006:200-10). Hyperprolactinamia can also be caused by prescription drugs and less commonly heavy metals. The hyperprolactinaemia from which the patient is suffering may be due to the emotional stress she is experiencing (Warrell 2003:550- 555), in direct relationship to her difficulty conceiving. The hyperprolactinaemia could also be the source of the patient's difficulty to conceive (Warrell 2003:550-555) and contributing to the premenstrual syndrome (Warrell 2003:550-555).

Although a common condition; up to 1.5 million women in the United Kingdom experience significant, disruptive symptoms (Wyatt 2001), the cause of PMS is not fully understood. PMS is defined as physical, behavioural or psychological symptoms that recur on a cyclical basis during the luteal phase of the menstrual cycle. The symptoms should resolve completely by the end of menstruation and women should be free of symptoms for at least one week between menstruation and ovulation (O'Brien 1997). Over 150 symptoms have been attributed to PMS, however, the most common are; headache, tension, anxiety, irritability, depression and bloating, among others (O'Brien 1997). An abnormality of the hypothalamic-pituitary axis has been proposed as women suffering from PMS have significantly higher levels of prolactin, especially in the second and third week of their cycles (Tesch 2003:1-3) (Sugino 2006:440-6). Abrahams

(1983:446-464) suggests five distinct subgroups of PMS. The patient in this case displays symptoms corresponding with types A, C and D, as well as the bloating listed in PMS type H (Abrahams 1983:446-464). The herb *Vitex agnus castus* showed good results in a clinical trial for PMS types A, D and H, (Shaw 2009) detailed further in the rationale below. Treatment options are varied and include surgery, antidepressants, non-steroidal anti-inflammatory drugs (NSAID's), hormone preparations, dietary supplements, cognitive therapy and exercise. Surveys show that women are increasingly finding phytotherapy more helpful than conventional medicine in the case of PMS (Corney 1991).

The modern phytotherapeutic approach to treatment of endocrine disorders, with reference to this case aims to: for PMS; to correct any hormonal imbalance, specifically normalise prolactin levels using *Vitex* (White Peony and Licorice were also considered, but decided against, in this case, to avoid over-prescribing and assist compliance) (Mills 2000: 240-2246). The normalization of prolactin levels in itself may be the key with this patient as the inability to conceive may be caused by the hyperprolactinaemia and leading to her subsequent stress and depression, which can in turn aggravate PMS (Tesch 2003:1-3) (Sugino 2006:440-6). The *Vitex* will also assist normalisation of her menstrual cycle and establish regular ovulation as the current 38 day cycle is longer than the normal 28 days, suggesting there may be a possible corpus luteum defect, which is again associated with hyperprolactinaemia (Schellenberg's 2001:134-7). Correct essential fatty acid status with Evening primrose oil, which is especially indicated in prostaglandin deficiency (PMS type C) and connected with the headache symptom (Mills 2000: 240-2246). The

EPO will be dispensed at a subsequent visit, if required, to avoid overloading the patient. Treat the main physical symptoms as they occur (Wuttke 2003:348-57). In this case the headaches could also be treated with a herbal analgesic such as Willow bark or Yellow jasmine, in place of the Paracetamol. However, in light of the number of herbs used and keeping in mind patient compliance and practicality, these herbs could be introduced at a later stage if still required. A hepatic tonic, namely Milk thistle is included to aid phase I/II detoxification and subsequently hormone clearance to assist normalisation of prolactin levels. A key component of the phytotherapeutic approach to treatment of PMS is to treat the emotional disturbances (Wuttke 2003:348-57). St John's Wort is used to treat the depression, Valerian, as a mild sedative to treat the insomnia. The patient is also very stressed, so Tribulus is used as a tonic that will be supportive, but not overly stimulating (Samy 2008: 302-12). The treatment approach is comprehensive in the case of this patient as she is not coping with daily life, suffering insomnia and is very stressed, all whilst trying to conceive at an age where conception will be more of a challenge (Brzakowski 2009:F3-7).

Schisandra has been considered in this case, as it would be most appropriate to provide a number of necessary actions as indicated above however, decided against as a precautionary measure, as it is contraindicated in pregnancy (Mills 2000:46). Tribulus is also contraindicated in pregnancy (Mills 2000:46), however has been selected in light of its fertility promoting action and ease of discontinuation upon conception, as it is dispensed as a tablet. It is also recommended that Chaste tree be used cautiously in pregnancy (Schellenberg's 2001:134-7). That noted, the patient will be advised to

monitor her conception status closely as the treatment outlined here is to promote conception, treat PMS and the additional symptoms and will be discontinued once conception occurs. Treatment will be re-evaluated, based upon patient feedback. As the patient is not coping with daily life a follow up appointment is recommended in one week to assess progress with the insomnia and stress. Referral to a counselling psychologist, experienced in fertility counseling to discuss the anger, stress and ‘lying awake at night worrying’ is recommended in conjunction with phytotherapy, along with offering the patient concurrent treatment with a medical fertility specialist (Zarkova 1982: 223-234).

Treatment Goals and Herbs Considered

Action	Herb: Common Name	Herb: Botanical Name
Prolactin inhibitor	Chaste tree White peony Licorice	<i>Vitex agnus-castus</i> <i>Paeonia lactiflora</i> <i>Glycyrrhiza glabra</i>
Nervine tonic	Korean ginseng St John’s Wort Schisandra Skullcap	<i>Panax ginseng</i> <i>Hypericum perforatum</i> <i>Schisandra chinensis</i> <i>Scutellaria lateriflora</i>
Adaptogen	Schisandra Siberian ginseng Withania (Ashwaganda) Korean ginseng	<i>Schisandra chinensis</i> <i>Eleutherococcus senticosus</i> <i>Withania somnifera</i> <i>Panax ginseng</i>
Tonic (for the general body)	Siberian ginseng Withania (Ashwaganda) Tribulus	<i>Eleutherococcus senticosus</i> <i>Withania somnifera</i> <i>Tribulus terrestris</i>
Hepatic tonic	Schisandra Dandelion root Milk Thistle	<i>Schisandra chinensis</i> <i>Taraxacum officinale</i> <i>Silybum marianum</i>
Ovulation normaliser	White peony Licorice Dong quai	<i>Paeonia lactiflora</i> <i>Glycyrrhiza glabra</i> <i>Angelica sinensis</i>
Oestrogen modulator	Tribulus White peony Licorice	<i>Tribulus terrestris</i> <i>Paeonia lactiflora</i> <i>Glycyrrhiza glabra</i>
Fertility agent	Tribulus	<i>Tribulus terrestris</i>

Action	Herb: Common Name	Herb: Botanical Name
Female tonic	Chaste tree	<i>Vitex agnus-castus</i>
	Dong quai	<i>Angelica sinensis</i>
Antidepressant	St John's Wort	<i>Hypericum perforatum</i>
	Schisandra	<i>Schisandra chinensis</i>
Mild Sedative	Valerian	<i>Valeriana officinalis</i>
	Withania (Ashwaganda)	<i>Withania somnifera</i>
	Skullcap	<i>Scutellaria lateriflora</i>
Essential Fatty Acid provider	Evening Primrose Oil	<i>Oenothera biennis</i>
Analgesic	Willow bark	<i>Salix</i> spp.
	Yellow jasmine	<i>Gelsemium sempervirens</i>

Reference for 'Treatment goals and herbs Considered' section:

Bone, K. 2003, *A Clinical Guide to Blending Liquid Herbs*, Elsevier, London.

Mills, S., Bone, K. 2000, *Principles and Practice of Phytotherapy*, Churchill Livingstone, London.

Final Prescription and Treatment Recommendation

Herbal Liquid Formulation 1

<i>Vitex agnus-castus</i>	1:2	20 mL
<i>Hypericum perforatum</i>	1:2	25 mL
<i>Valeriana officinalis</i>	1:2	25 mL
<i>Silybum marianum</i>	1:1	30 mL
Total		100mL

Dose 5mL with water 3 times daily, for 3 menstrual cycles (Wuttke 2003:348-57).

Plus 1 MediHerb Tribulus Forte tablet 3 times daily, on days 5 to 14 only of the menstrual cycle (with the start of menstruation being day 1), to be ceased upon conception (Zarkova 1982: 223-234). MediHerb Tribulus Forte is a proprietary product which contains 9.0g Tribulus terrestris extract equivalent to dry herb (aerial parts) which is standardised to contain furostanol saponins as protodioscin 110mg.

Nutritional Considerations

To maximize the overall health of the patient and encourage conception, avoidance of tea, coffee, alcohol, smoking and any drugs (recreational or prescription), as well as a diet comprising mainly of unprocessed foods where beer is abstained from is advised. Beer

causes an increase prolactin levels (Wuttke 2003:348-57).

Table of Medicinal Plant Parts and Key Constituents

Name of Herb	Plant part Used	Key Constituents relevant to this case
<i>Vitex agnus-castus</i>	Fruit (berries)	the diterpene rotundifuran found in the essential oil which also contains monoterpenes, sesquiterpenes, flavonoids, iridoids glycosides (including aucubin, agnuside).
<i>Tribulus terrestris</i>	Herb (aerial parts)	furostanol (steroidal) saponins as protodioscin
<i>Hypericum perforatum</i>	aerial parts	Hypericin (H) and pseudohypericin (PH) –naphroanthrones (0.05-0.6%), flavonoids, phenolics including hyperforin, procyanidins and essential oil. H and PH are collectively called total hypericin (TH).
<i>Valeriana officinalis</i>	root, rhizome	Valepotriates –iridoids 0.5 - 2%, essential oil 0.35 to 1%, non-volatile cyclopentane sesquiterpenes (valerenic acid and its derivatives), amino acids, lignans
<i>Silybum marianum</i>	fruit	Silymarin (comprised of silybin, silychristin and silydianin) – flavanolignans

Table Reference: Mills, S., Bone, K. 2000, *Principles and Practice of Phytotherapy*, Churchill Livingstone, London.

Rationale for Herb Selection

The female reproductive system presents to modern medicine, one of its greatest challenges (Low 2009 58-8). Despite the technology available and the advances made, many women are dissatisfied with the current procedures, that are often surgical and lacking in a holistic approach and favourable outcomes (Low 2009 58-8). As a result, increasing numbers of women (up to 45%) are turning to herbal medicine, not only seeking better outcomes, but also to gain more personal input into their reproductive

health (Low 2009 58-8) (Huang 2008:211-5).

There is, however, a particular lack of quality scientific and clinically relevant data, leading phytotherapy practitioners to be guided by some useful clinical trials and case evidence for the remainder when treating women for reproductive concerns (Low 2009:54-8) (Huang 2008:211-5). In terms of pregnancy Mills and Bone state (2000:246) that there is a professional reluctance to prescribe herbs during pregnancy, again, likely due to the limited amount of clinically relevant data at present (Low 2009:54-8), but that nevertheless herbs such as Zingiber (ginger), Vitex (chaste berry) and Rubus idaeus (raspberry leaf) have been used on a traditional basis (Felter: 1905) during the trimesters of pregnancy (Harefuah 2006:738-42).

Phytotherapy seems to be well suited to treatment of the female reproductive system, due to its ability to be applied subtly. Mills and Bone (2000:238-240) suggest the tendency to self - correction of this system, when provided with a light phytotherapeutic nudge. They draw parallels between the concept of self- organization in the female reproductive system and its consistency with other complex biological systems, including its rhythmicity (Mills 2000:238-240).

The approach used towards the female reproductive system here utilizes these concepts in an attempt to prompt the body to return to its original program and normalise ovarian-pituitary communication and rhythmicity.

***Vitex agnus-castus* (Chaste tree or Chaste berry)**

A 2003 Cochrane Review (Shaw 2003:2-3) concerning the use of *Vitex agnus-castus* for premenstrual syndrome highlights the long traditional history of use of Chaste tree for women's reproductive health with a range of applications, including, what is now termed premenstrual symptoms (Felter: 1905). The review also confirms that clerodadienol diterpenes have been identified as the dopaminergic agents in a double-blind placebo-controlled clinical trial involving 180 women (Wuttke 2003:348-57). These diterpenes bind to dopamine receptors, acting as an agonist (ie stimulating the receptor) (Gorkow 2002:364-72). Tesch (2003) suggests that *Vitex agnus castus* causes a decrease in prolactin, which leads to reversal of luteinizing hormone (LH) suppression, enabling full development of the corpus luteum, which in turn increases progesterone levels and reduces symptoms of PMS. Schellenberg's randomised double-blind placebo-controlled, parallel group, multicentre study (2001:134-7) involving 178 women of a mean age of 36 years over three consecutive menstrual cycles concluded that the extract of *Vitex agnus-castus* fruit at a dose of 1ml of 1:2 liquid extract daily improved irritability, mood alteration, anger, headache and bloating, when compared to the placebo group ($P < 0.001$). Schellenberg's study (2001:134-7) also concluded that analysis of the clinical global impression (the severity of the condition, global improvement of the condition and risk versus benefit assessment) showed significant positive results ($P < 0.001$). In addition, Berger's prospective multicentre trial (200:150-3) demonstrated that an improvement in the parameters discussed in Schellenberg's study above persisted up to three menstrual cycles after treatment cessation and that resting levels of blood prolactin remained within the physiological parameters throughout this time.

***Tribulus terrestris* (Tribulus)**

Tribulus is used, in this case, as a tonic that will be supportive, but not overly stimulating and to promote fertility. In a study involving infertile women, patients were administered 750-1500mg of *Tribulus terrestris* extract per day on days 5 to 14 of the menstrual cycle (Zarkova 1982: 223-234). The trial was conducted over a 3 month period and concluded that combined treatment with epimestrol (an ovulatory stimulant drug used in infertility) and *Tribulus terrestris* was better than with either agent alone. Patients treated with the *Tribulus* alone experienced no adverse effects, where as those treated with epimestrol exhibited side effects from treatment with an ovulatory stimulant (Zarkova 1982: 223-234). Pharmacological studies conducted using *Tribulus terrestris* demonstrated tonic activity (Toshkov 1998: 24-30) (Taskov1998: 35-42), supported by the traditional use of *Tribulus* in Ayurvedic medicine as a male and female reproductive tonic (Samy 2008: 302-12).

***Valeriana officinalis* (Valerian)**

Valerian is employed as a mild sedative to treat insomnia in this case. It is used to assist the patient in achieving restful night time sleep towards the aim of improving overall health, especially advantageous when trying to conceive (Lindahl 1989:1065-6). In a multicentre, randomised, placebo-controlled, parallel group clinical trial involving 184 adults, 110 being women, *Valeriana officinalis* standardised extract (standardised to contain not less than 5ml/ kg of essential oil) was administered three times a day for 28 days (Morin 2005:1465-71). Morin and colleagues (2005:1465-71) concluded that patients in the 'valerian group' rated their insomnia severity lower when assessed at 14 days treatment. Patients also reported an increase in quality of life based on clinical

outcome ratings from patients and physicians. No adverse event were reported and no rebound insomnia followed their discontinuation of treatment (Morin 2005:1465-71). These finding are supported by Donath and colleagues and also Schmitz and Jaeckel's (1998:291-8) randomised, double-blind, placebo-controlled, crossover trial using *Valeriana officinalis* standardised extract (standardised to contain not less than 5ml/ kg of essential oil) (2000: 47-53).

***Hypericum perforatum* (St John's Wort)**

A key component of the phytotherapeutic approach to treatment of PMS is to treat the emotional disturbances (Doell 2009:186-91). The phytotherapeutic use of St John's Wort in mild depression is well established (Brattstrom 2009:277-83) (Kasper 2008:803-13) (Sarris 2009) (Baruch 2009:183-5). The randomised, double-blind, placebo-controlled clinical trial conducted by Hicks and colleagues (2004:925-32) supports the use of *Hypericum perforatum* in the treatment of premenstrual symptoms. The trial was conducted with 169 women experiencing premenstrual symptoms and used 4mL of 1:2 liquid extract per day standardised to 0.2mg/mL hypericins. A menstrual diary was used to assess changes in symptoms and particular improvement was measured in depression – related symptoms. In addition, the results of a pilot study using *Hypericum perforatum* (Stevinson 2000:870-6) reported that the degree of improvement in overall premenstrual syndrome scores between the baseline and the end of the trial was 51%, with over two-thirds of the sample demonstrating at least 50% decrease in symptom severity and that tolerance and compliance were high. Symptoms were rated daily and the Hospital Anxiety and Depression Scale, Hamilton Depression Rating Scale (HAMD) and Beck Depression Inventory were used in conjunction with the Clinical Global Impression scale

(CGI).

***Silybum marianum* (Milk Thistle)**

Milk thistle has been prescribed to support liver function, specifically, to aid phase I/II detoxification and subsequently hormone clearance to assist normalisation of prolactin levels (Mills 2000:241). Greenlee (2007:1601-9) concludes in a placebo-controlled, parallel study conducted on 180 premenopausal women that *Silybum marianum* at a dose of 5mL of 1:1 liquid extract per day, standardised to contain 25mg/mL of silymarin, decreased early follicular phase androgens, when urine and blood samples were compared from the first menstrual cycle during the study to the fifth cycle at the end. Specifically dehydroepiandrosterone, dehydroepiandrosterone-sulfate and androstenedione and estrone-sulfate decreased (P=0.02). In addition a randomised, double-blind, placebo-controlled trial conducted by El-Kamary and colleagues (2009:391-400) found statistically significant p values of 0.012 for improved clinical markers of biliary excretion and that the patients who received a dose of 140mg of silymarin for four weeks with an additional four week follow-up, demonstrated faster resolution of symptoms related to biliary retention, including normalization of hormone levels.

Conclusion

Phytotherapy seems to be well suited to treatment of the female reproductive system, due to its ability to be applied subtly, despite the fact that there is a lack of quality clinically relevant data, leading phytotherapy practitioners to be guided by some useful clinical trials and case evidence for the remainder when treating women for reproductive concerns (Low 2009:54-8) (Huang 2008:211-5). Mills and Bone (2000:238-240) suggest the tendency to self - correction of this system, when provided with a light

phytotherapeutic nudge. As a result, increasing numbers of women (up to 45%) are turning to herbal medicine, not only seeking better outcomes, but also to gain more personal input into their reproductive health (Low 2009 58-8) (Huang 2008:211-5).

B) Patient 2

- 40 year old woman.
- Pritikin (low fat) diet for last 2 years
- Benign breast lumps (cystic)
- PMS
- Very light menstrual periods
- Slightly underweight

Introduction:

Breast disorders may be malignant or in this case benign (Herrerros-Villaraviz 2008: 599-600). The majority (approximately 90%) are benign and not life threatening, however for many women breast cancer is a fear (Herrerros-Villaraviz 2008: 599-600). Fine needle tissue biopsy is the only means currently by which malignancy or non-malignancy can be confirmed. Due to monthly hormonal cycles changes may also occur in the breast including swelling and tenderness (Herrerros-Villaraviz 2008: 599-600). Women are advised to conduct a monthly breast self examination and to consult a general practitioner or specialist gynaecologist should a lump, change or irregularity in the breast appear suddenly or persist (Herrerros-Villaraviz 2008: 599-600). Regular monitoring is especially recommended for women who have a family history of breast cancer, as early detection is essential to successful treatment (Herrerros-Villaraviz 2008: 599-600). Benign breast lumps may be fibrous masses (Fibroadenomas) or cysts (termed cystic disease of the breast) (Herrerros-Villaraviz 2008: 599-600). A clearer understanding of the aetiology of benign breast disorders has led to their being described as aberrations of normal breast development and involution (ANDI) (Dixon 1991) (Shpontak 2008: 61-2). Hughes (1992: 1316-9) proposed that benign breast disorders often occur due to the normal stages of reproductive life, through which changes in the breast lobules occur and that they

should not be considered benign neoplasms. Benign breast cysts may be single, multifocal and or bilateral in distribution (Hughes 1992: 1316-9). Cyclic mastalgia associated with breast nodularity can occur in women of reproductive age (25 to 40) and aetiologically may be related to latent hyperprolactinaemia (Hughes 1992: 1316-9). Women between the ages of 40 and 50 are more likely to suffer from palpable, discrete breast cysts, which are likely to be an abnormality in lobule involution, which occurs normally as reproductive functions decline (Mills 2000: 244-5). The hypothalamic-pituitary-ovarian axis and its response to stress should be considered in the treatment approach (Hughes 1992: 1316-9). In addition, elevated oestrogen activity, hyperprolactinaemia and luteal insufficiency are possible processes involved in benign breast disease (Shpontak 2008: 61-2).

Hypomenorrhoea, or very light menstrual blood flow may be due to a small uterine bleeding surface or hormonal causes (Philippi 2009:63). Nervous emotional states or stress, excessive exercise and dieting can also be a cause or contributing factor (Can 2008: 310-4). Light menstrual blood flow is sometimes normal among members of the same family, suggesting a possible hereditary component (Philippi 2009:63). Women who are approaching menopausal age (menopause usually begins between 45 and 55 years) may notice their menstrual blood flow begin to reduce as ovulation becomes irregular and the endometrial lining may not develop normally (Philippi 2009:63). Low thyroid hormone, high prolactin, insulin or androgen levels can also cause light menstrual flow, along with long term use of the oral contraceptive pill (Can 2008: 310-4). Hypoprolactinaemia, specifically, can cause ovulation and menstruation to cease. It must

also be remembered that hormonal control of menstruation begins at the hypothalamus and is mediated by ovarian - pituitary communication and the production of oestrogen and progesterone (Can 2008: 310-4).

Fats are complex molecules composed of fatty acids and glycerol, which the body utilizes to synthesise hormones and hormone-like substances including prostaglandins (Wertz 2009:279-83). Prostaglandins are local chemical mediators derived from arachidonic acid (a component of the plasma membrane). Prostaglandins reduce the blood supply to the uterus and cause the uterine myometrium to rhythmically contract to help expel blood and endometrial debris from the uterine cavity out through the vagina as menstrual flow (Wuttke 2003:348-57). Prostaglandins are synthesized from essential fatty acids (EFA's), which cannot be synthesized by the body and must be consumed in the diet (Wertz 2009:279-83). A low fat diet consumed over a considerable time period, that does not take EFA's into consideration, may lead to deficiency, which may in turn affect prostaglandin production and thus menstrual flow (Wuttke 2003:348-57).

For the phytotherapeutic treatment of this case, *Vitex agnus-castus* is a major herb in its application as a normaliser of ovarian function. *Vitex* also has the added benefit of acting as a tonic for the female reproductive system and acting to normalize oestrogen levels (Wuttke 2003:348-57). *Hypericum perforatum* is employed for its action as a nervine tonic to alleviate the negative physiological effects of stress. *Echinacea angustifolia* is selected for immune modulation to normalize benign growths. *Silybum marianum* is selected as a hepatic tonic to support hormone clearance at the liver and assist in the

normalization of oestrogen levels. Oestrogen promoting herbs have been avoided in this case due to their association with growth of breast tissue anomalies (Hughes 1992: 1316-9). Herbs used for the treatment of premenstrual syndrome (PMS) are covered in detail in Patient Case A and have been used to effect the same actions.

Treatment Goals and Herbs Considered

Action	Herb: Common Name	Herb: Botanical Name
Ovarian function (oestrogen) normaliser	Vitex	<i>Vitex agnus castus</i>
Nervine tonic	St John's Wort	<i>Hypericum perforatum</i>
Immune modulator	Echinacea	<i>Echinacea angustifolia</i>
Hepatic tonic	Milk Thistle	<i>Silybum marianum</i>

Reference for 'Treatment goals and herbs Considered' section:

Bone, K. 2003, *A Clinical Guide to Blending Liquid Herbs*, Elsevier, London.
Mills, S., Bone, K. 2000, *Principles and Practice of Phytotherapy*, Churchill Livingstone, London.

Final Prescription and Treatment Recommendation

Herbal Liquid Formulation

<i>Vitex agnus- castus</i>	1:2	30ml
<i>Hypericum perforatum</i>	1:2	25ml
<i>Echinacea angustifolia</i>	1:2	25ml
<i>Silybum marianum</i>	1:1	20ml
Total		100ml

Dose 5mL with water 3 times daily for 3 months (ie 3 menstrual cycles).

Nutritional Considerations

Increased consumption of phytoestrogens and oestrogenic lignans will assist in the modification of the effects of oestrogen and may reduce the risk of breast cancer (Wong 2009:166-77).The minimization of emotional and physical stress can be assisted by the

dietary elimination of stimulants (Wong 2009:166-77). Caffeine and methyl-xanthines increase levels of adrenaline and nor adrenaline. This includes elimination of tea, coffee, chocolate and cola (Wong 2009:166-77). Elimination of tyramine-containing foods such as aged and processed meats, aged cheese, wine, mushrooms and bananas may assist some women as well as cessation of smoking (Wong 2009:166-77). Nicotine contributes to breast anomalies (Wong 2009:166-77). In terms of the low fat diet the patient has been following for 2 years, it would be advisable to ensure adequate dietary levels of fatty acids, especially essential fatty acids (EFA's), as the body is unable to synthesise these, thus they need to be consumed in the diet as discussed previously (Wertz 2009:279-83). Omega-6 fatty acids; linoleic acid and arachidonic acid are present in vegetable oils such as sunflower, safflower, cottonseed, soya bean oils and also egg yolks (Wertz 2009:279-83). Omega-3 fatty acids; eicosapentanoic acid (EPA) and docosahexanoic acid (DHA), which are essential for brain development can be synthesized from linoleic acid (Wertz 2009:279-83). EPA and DHA are also found in marine fish oils such as lake trout and deep-sea fish including mackerel, salmon, herring and tuna, which are a more efficient source (Wertz 2009:279-83). Omega-3 fatty acids (including linolenic acid) are also found in walnuts and green leafy vegetables (Wertz 2009:279-83). Alternately, an EFA supplement can be added at the follow up appointment in 1 month.

Table of Medicinal Plant Parts and Key Constituents

Name of Herb	Plant part Used	Key Constituents relevant to this case
<i>Echinacea angustifolia</i>	root	Caffeic acid derivatives: echinacoside chicoric acid cynarin (in <i>E. angustifolia</i>)

Name of Herb	Plant part Used	Key Constituents relevant to this case
		lipophilic alkylamides polysaccharides

Please refer to the Table of Medicinal Plant Parts and Key Constituents in Patient Case A for *Vitex agnus castus*, *Hypericum perforatum* and *Silybum marianum*.

Table Reference: Mills, S., Bone, K. 2000, *Principles and Practice of Phytotherapy*, Churchill Livingstone, London.

Rationale for Herb Selection

Please refer to Patient Case A for the rationale for selection of *Vitex agnus castus*, *Hypericum perforatum* and *Silybum marianum*.

***Echinacea angustifolia* and *E. purpurea* (Echinacea blend)**

Echinacea modulates the immune system by improving immune surveillance, thus the immune response to pathogens is accelerated (Bone 1997:19). Another phagocytic mechanism, enhanced by Echinacea includes improved clearance and inactivation of pathogens (Bone 1997:19). Extrapolation of this concept is applied to the use of Echinacea to normalise the changes that occur in aberrations of normal breast development and involution (ANDI) such as breast cysts, which are likely to be an abnormality in lobule involution. Echinacea is employed in this context to encourage normal tissue development, through enhanced immune surveillance and as a preventative measure for breast cancer as 2 out of 4 women who have ANDI develop breast cancer (Herrerros-Villaraviz 2008: 599-600).

C) Patient 3

- 25 year old woman.
- Presents with acute cystitis.
- History of chronic urinary tract infections.
- Suffers from tiredness, poor appetite, loose bowels and frequently experiences nausea after eating.

Introduction:

Fifty percent of women have a history of at least one episode of urinary tract infection (UTI) (Nicolle 2008: S40-5). UTIs are responsible for over twenty five percent of all community - acquired bacteraemias and account for over forty percent of hospital-acquired infections, often as a result of bladder catheterization (Nicolle 2008: S40-5). Cystitis, also known as recurrent lower urinary tract infection, is common among women, often first arising after becoming sexually active (Tomson 2003:420-423). Cystitis refers to infections, most commonly of *Escherichia coli*, that are localized to the urinary bladder (Tomson 2003:420-423). Other possible organisms include *Staphylococcus saprophyticus*, *Klebsiella* and *Proteus* (Nicolle 2008: S40-5). Cystitis can be due to fungal infection and occasionally viral infection, but is usually due to Gram- negative bacteria, in 80% of adult cases (Nicolle 2008: S40-5). This highlights the fact that most cystitis infections originate from the perineum and are transferred to the urinary tract via the urethra. Persistent, or chronic infections, are due to the infectious organism remaining and often being suppressed by antibiotic treatment, without full resolution of the infection (Tomson 2003:420-423). Recurrent and chronic infections can suggest poor immune defences in the patient, vesicoureteric reflux, incomplete bladder emptying and poor flow or volume of urine, among other causes (Tomson 2003:420-423).

Ascent of the infecting organism up the urethra, is the mode of acquisition of the majority

of urinary tract infections (Tomson 2003:420-423). A reduction of transepithelial resistance and loss of tight junctions between the umbrella cells of the bladder wall enables components of urine to penetrate and an inflammatory response to begin through the release of cytokines (Nicolle 2008: S40-5). Adherence by the bacterium to the uroepithelium is a significant determinant in colonization and subsequent clinical infection (Nicolle 2008: S40-5). According to Mills (2000:224-225) lower urinary tract infections are one of the most appropriate indications for phytotherapy.

Tiredness, non-specific malaise and nausea are symptoms associated with urinary tract infection (Tomson 2003:420-423) and also with bile deficiency and inadequate digestive liver function (Mills and Bone 2000:183-187). The patient's poor appetite and nausea after eating, specifically suggest bile deficiency. *Andrographis* (*Andrographis paniculata*) is employed in this context to improve immunity and thus, reduce the recurrence of urinary tract infections, to act as a bitter tonic to stimulate digestion and as a choleric, to increase the production of bile by the liver. *Andrographis paniculata* has the added benefit of providing anti-inflammatory and hepatoprotective actions, the latter being of benefit following prolonged treatment with prescription drugs. It is likely that the patient has been prescribed antibiotic treatment for the UTI in the past and the loose bowels may be a result of gut dysbiosis. This could be addressed with the use of an acidophilous and bifidus supplement at a subsequent visit, if the loose bowels have not normalized.

The current infection is treated with a urinary tract antiseptic; Buchu (*Agathosma betulina*), which is particularly applicable to this case as it also acts to improve appetite

and provide symptomatic relief of nausea. Due to the above mentioned release of inflammatory cytokines, the local inflammation is treated with a urinary tract demulcent to soothe the acute infection with Corn silk (*Zea mays*). Crataeva (*Crataeva nurvala*) is included to act as a bladder tonic to support bladder tone and thus micturition function, encouraging normal bladder voiding, which reduces the number of residual organisms in the bladder (Tomson 2003:420-423). If the patient is still suffering from tiredness, after initial treatment, as described below, a general tonic could also be included at a subsequent visit.

Treatment Goals and Herbs Considered

Action	Herb: Common Name	Herb: Botanical Name
Urinary tract antiseptic (antibacterial and antifungal)	Buchu Bearberry (or Uva ursi) Juniper Cranberry	<i>Agathosma betulina</i> <i>Arctostaphylos uva-ursi</i> <i>Juniperus communis L.</i> <i>Vaccinium macrocarpon</i>
Urinary tract demulcent	Couch grass Corn silk Marshmallow (root and leaf)	<i>Agropyron repens</i> <i>Zea mays</i> <i>Althaea officinalis</i>
Bacterial adherence minimiser	Licorice (high glycyrrhizin) Cranberry (juice)	<i>Glycyrrhiza glabra</i> <i>Vaccinium macrocarpon</i>
Bladder tonic	Crataeva	<i>Crataeva nurvala</i>
Immune support	Andrographis Echinacea Astragalus	<i>Andrographis paniculata</i> <i>Echinacea angustifolia</i> <i>and Echinacea purpurea</i> <i>Astragalus membranaceus</i>
Bitter tonic	Andrographis Barberry Globe artichoke Golden seal	<i>Andrographis paniculata</i> <i>Berberis vulgaris</i> <i>Cynara scolymus</i> <i>Hydrastis canadensis</i>
Choleretic	Andrographis Barberry Globe artichoke Golden seal	<i>Andrographis paniculata</i> <i>Berberis vulgaris</i> <i>Cynara scolymus</i> <i>Hydrastis canadensis</i>

Reference for ‘Treatment goals and herbs Considered’ section:

Bone, K. 2003, *A Clinical Guide to Blending Liquid Herbs*, Elsevier, London.

Mills, S., Bone, K. 2000, *Principles and Practice of Phytotherapy*, Churchill Livingstone, London.

Final Prescription and Treatment Recommendation**Herbal Liquid Formulation**

<i>Agathosma betulina</i>	1:2	20mL
<i>Crataeva nurvala</i>	1:2	30mL
<i>Andrographis paniculata</i>	1:2	20mL
<i>Zea mays</i>	1:1	30mL
Total		100mL

Dose 5mL with water 4 to 6 times daily during acute outbreaks of cystitis and then 3 times a day for up to 3 months, to prevent recurrent cystitis and urinary tract infections (Mills 2000: 220-224). Phytotherapeutic treatment, to provide immune support is recommended on a continuing basis to prevent acute attacks (Mills 2000: 220-224). Once the patient has been free of infection for 3 to 4 months, phytotherapeutic treatment can be reduced and eventually discontinued if the patient is still free of infection and healthy, as long term use of urinary antiseptics is not advisable (Mills 2000: 223). A liquid formulation was prescribed in preference to capsules (which can be more effective in the case of urinary antiseptics) to enable the bitters to stimulate appetite via taste. Ideally, Buchu (*Agathosma betulina*) is best taken with food as it can occasionally cause gastrointestinal irritation if taken on an empty stomach (Bone 2003:111).

The patient is advised to drink 100mL pure Cranberry (*Vaccinium macrocarpon*) juice daily to reduce bacterial adherence to the urothelium and as a preventative dose (Mills 2000: 223). Care must be taken in the case of patients with renal insufficiency, the potential for developing uric acid or calcium oxalate stones due to the high oxalate

content of cranberry (Mills 2000: 220-224).

Nutritional Considerations

Ensure adequate fluid, especially water intake to assist the hydrokinetic defense, ie frequent voiding flushes the infectious organisms and prevents them reaching critical mass (Nicolle 2008: S40-5). The patient is also encouraged to consume cranberry juice daily and to restrict intake of refined carbohydrates and dairy products (Mills 2000: 220-224).

Table of Medicinal Plant Parts and Key Constituents

Name of Herb	Plant part Used	Key Constituents relevant to this case
<i>Agathosma betulina</i>	Leaf	Essential oil (2%), consisting mainly of the monoterpene diosphenol.
<i>Crataeva nurvala</i>	Bark	Sterols (especially lupeol, a pentacyclic triterpenes), flavonoids, glucosinolates (a characteristic of the Capparidaceae family).
<i>Andrographis paniculata</i>	Aerial parts	Andrographolides (diterpenoid lactones) including aglycones (such as andrographolides itself) and glucosides (such as neoandrographolide and andrographiside)
<i>Zea mays</i>	Style, stigma	Flavonoids, especially 6-C-glycosylflavones (including maysin), rutin, anthocyanidins and flavon-4-ols (including luteoforol and apiforol), chlorogenic acid, essential oil, phytosterols and potassium.
<i>Vaccinium macrocarpon</i>	Berry-like fruit	Procyanidins, anthocyanidins, organic acids

Please refer to the Table of Medicinal Plant Parts and Key Constituents in Patient Case A for *Vitex agnus castus*, *Hypericum perforatum* and *Silybum marianum*.

Table Reference: Mills, S., Bone, K. 2000, *Principles and Practice of Phytotherapy*,

Churchill Livingstone, London.

Rationale for Herb Selection

Buchu (*Agathosma betulina*)

Buchu leaves and essential oil have been used by the indigenous people of South Africa for hundreds of years for stomach complaints, kidney and urinary tract diseases (Simpson 1998:189-91). More recently, the essential oil from *Agathosma betulina* demonstrated antimicrobial action against *Escherichia coli* in a study using animal smooth muscle (Lis-Balchin 2001:579-82). Further quality clinical trials need to be conducted regarding the application of *Agathosma betulina*. As is evident, use of Buchu leaf extract is based mainly on its long-term traditional use (Felter 1983:891-892) in inflammation of the lower urinary system, especially for cystitis and urethritis. Felter (1983:891-892) also recommends the use of Buchu for improving appetite and relieving nausea.

Crataeva (*Crataeva nurvala*)

Crataeva liquid extract, derived from the bark of *Crataeva nurvala* is employed as a bladder tonic on the basis of traditional Ayurvedic use in disorders of the urinary system (Chopra: 1982). Deshpande and colleagues (1982:46-53) found that eighty five percent of patients with proven urinary tract infections were free of symptoms following treatment with *Crataeva nurvala* for 4 weeks. Deshpande and colleagues (1982:46-53) also concluded that the Crataeva relieved urine retention, increased bladder tone and increased force of urination in patients.

Andrographis (*Andrographis paniculata*)

Andrographis, known in Ayurvedic medicine as kalmegh ('king of bitters') (Mills 2000:

262) has been used traditionally for its ability to stimulate appetite, relieve digestive complaints associated with the liver and relieve general debility and tiredness (Samy 2008: 302-12). Andrographolide from *Andrographis paniculata* (aerial parts) produces a significant dose dependent choleric effect (4.8-73%) as evidenced by increase in bile flow, bile salts and bile acids in rats (Shukla 1992: 146-9). Puri and colleagues (1993: 995-9) concluded that the liquid extract of *Andrographis paniculata* (aerial parts) standardised to contain diterpene andrographolides induced significant stimulation of antibodies and nonspecific immune response in mice. This was measured in terms of macrophage migration index (MMI) phagocytosis of *Escherichia coli* and proliferation of splenic lymphocytes. Puri and colleagues (1993: 995-9) also commented that the stimulation of both antigen specific and nonspecific immunity suggested that a substance(s) in the *Andrographis paniculata* standardised extract other than andrographolides may also be contributing toward immunostimulation. In addition, the study using 100 patients conducted by Muangman and colleagues (1995: 310-3) concluded that *Andrographis paniculata* (aerial parts) is beneficial in the treatment of urinary tract infection (in this context of use after Extracorporeal Shock Wave Lithotripsy (ESWL) as treatment for kidney stones). Further quality clinical trials would further confirm the use of *Andrographis* as an immunostimulant and choleric.

Corn silk (*Zea mays*)

Corn silk is used in this case as the liquid extract of the style and stigma of *Zea mays* for its action as a urinary tract demulcent. Its use is drawn primarily from traditional use (Felter 1983) in Western herbal medicine for cystitis, which drew upon the Native American's use of corn products for medicinal purposes as far back as the sixteenth

century (Vogel 1970). Velazquez and colleagues (2005:363-9) have confirmed the diuretic effect of the liquid extract of *Zea mays* in an animal study, which may be related to its demulcent effect on the urinary system. Further quality clinical trials would add support to the traditionally derived use of Corn silk as a urinary tract demulcent.

Cranberry (*Vaccinium macrocarpon*)

The use of *Vaccinium macrocarpon* as a bacterial adherence minimiser in urinary tract infection, specifically cystitis, is confirmed by the double-blind, randomised, placebo-controlled cross over trial conducted by Di Martino and colleagues (2006:21-7). The Di Martino clinical trial (2006:21-7) used 100mL of pure cranberry juice extracted from *Vaccinium macrocarpon* (which was diluted with 500mL water) taken once daily by 20 patients for 3 months. A dose dependent significant decrease in bacterial adherence, especially of *Escherichia coli* uropathogenic strains was confirmed upon urinary analysis when compared with placebo. A subsequent, longer term pilot study was conducted over 2 years by Bailey and colleagues (2007:237-41) using 12 female patients between the ages of 25 and 70 years, with a history of a minimum of 6 UTI's in the preceding year, who were prescribed 100mL of pure cranberry juice extracted from *Vaccinium macrocarpon* (which was diluted with 500mL water) taken once daily for 12 weeks. All the women in the study had urinalysis within 24hrs before commencing the study and the same once a month for 4months. The patients were then followed up after 2 years. Bailey and colleagues (2007:237-41) concluded that during the entirety of the study none of the women had a UTI, no adverse events were reported and 2years after the study all 12 women who continued to take cranberry juice as prescribed, continued to be free of

UTI's. McMurdo and colleagues (2009:389-95) also concluded that cranberry juice extracted from *Vaccinium macrocarpon* was more successful than Trimethoprim (an antibiotic frequently used to treat urinary tract infections) in the treatment of recurrent UTI's. McMurdo and colleagues (2009:389-95) added that cranberry juice provided the significant advantage of no risk of antimicrobial resistance or super-infection and the women who used it in their randomised, controlled trial experienced less adverse effects than using Trimethoprim.

Conclusion

Considering fifty percent of women have a history of at least one episode of urinary tract infection (UTI) (Tomson 2003:420-423) and chronic infections, are often due to the infectious organism remaining and often being suppressed by antibiotic treatment, lower urinary tract infections are one of the most appropriate indications for phytotherapy (Mills 2000:224-225). However, several of the herbs used above to treat urinary tract infections (UTIs) are prescribed on the basis of long-term traditional use and would benefit greatly from further well designed clinical trials. Nevertheless, based on clinical the clinical experience of phytotherapy professionals (Mills 2000:224-230), treatment is still highly effective.

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