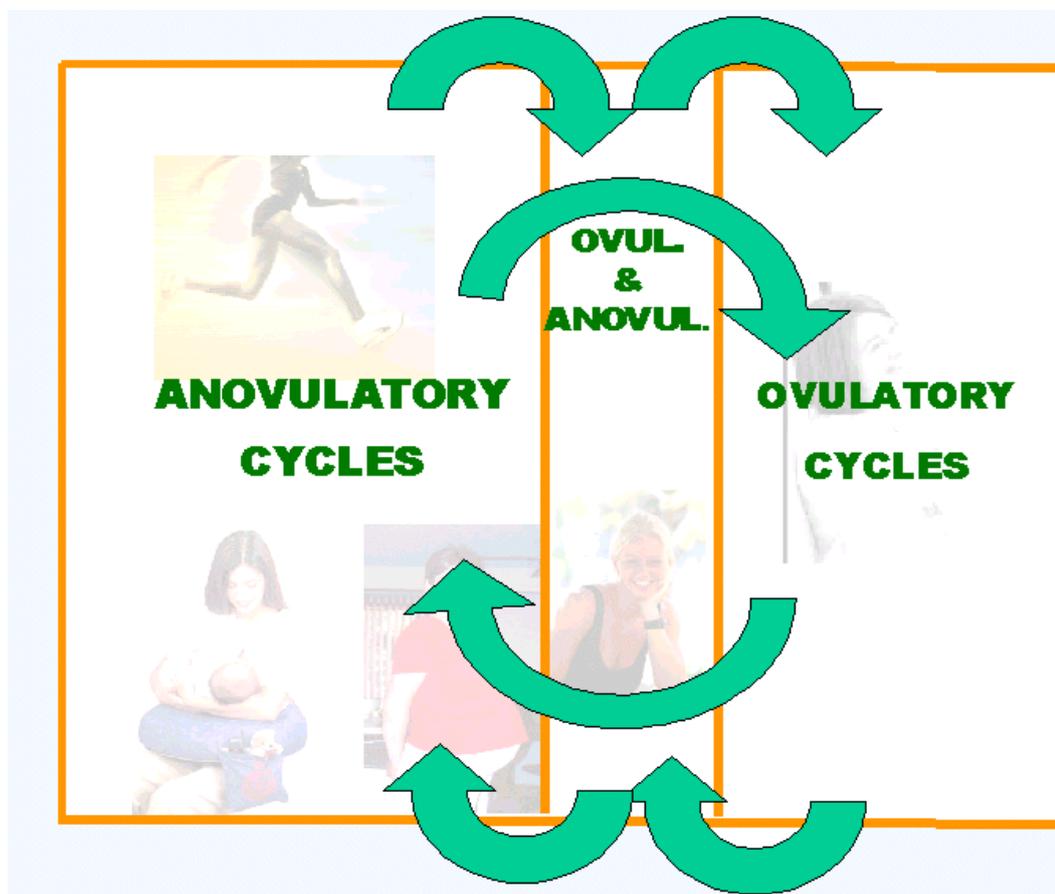


## Introduction

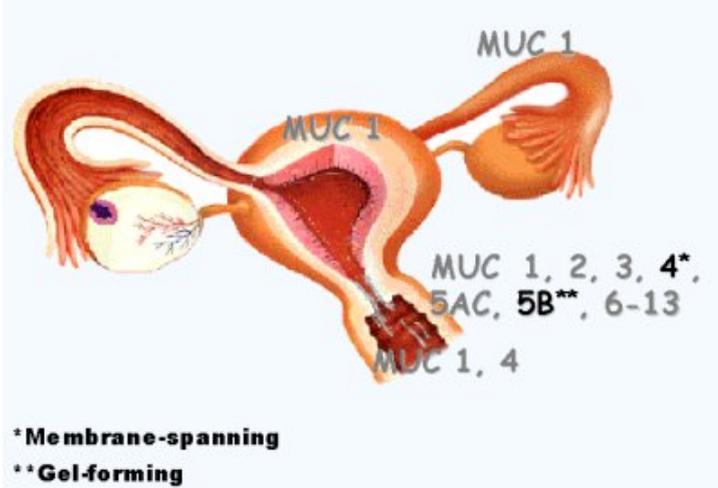
Fertility is a transient biological state that depends on the fertility potential of the couple. During a woman's lifetime, the ovary will go through different states of hormonal secretion and ovulation. The concept of the ovarian cycle as a continuum considers that all types of ovarian activity encountered during the reproductive life are normal responses to different environmental conditions in order to ensure the health of the mother and child.

During the first two years after menarche, occasional anovulatory cycles may occur. However, subsequently, a healthy ovary will exhibit regular monthly ovulations, characterized by a 25 to 36 day cycle (32, 33, and 35). The ovulatory cycles are normally only interrupted by pregnancies and breastfeeding. Normal ovulatory activity and fertility are restored following pregnancy and breast feeding, however, stress or excessive exercise may result in a chronic ovulatory dysfunction that requires therapy. Anovulatory cycles frequently occur as menopause approaches. This is an expected part of woman's reproductive life cycle.



The use of the ovarian monitor has made it possible to identify hormonal variations during different periods of a woman's life and to correlate these changes with the mucus patterns (5, 6, 7). Thousands of measurements have been recorded for this purpose around the world, including Chile. These investigations have raised an enormous amount of information (24, 24). The amount and type of mucus secreted by the cervix changes through the ovarian cycle in response to fluctuating hormonal levels (26, 30 and 31). Mucins are the main components of mucus (18). To date a total of 13 distinct mucin genes have been identified (11,18). Mucins are categorized into 3 groups on the basis of their structural properties: membrane spanning (MUCs 1, 3, 4, 12 and 13, gel forming (MUCs 2, 5AC, 5B and 6) and small soluble (MUC 7). The four large gel-forming mucin genes are located on chromosome 11.p15.5 (12,18). Mucin 5B is the major gel forming mucin expressed by the endocervical epithelium and its expression peaks at midcycle (10). Message levels for mucin 4 also peak at midcycle. Two main types of cervical mucus have been described: oestrogenic and progestative. According to O'deblad's model, the oestrogenic type can be subdivided in L, S and P subtypes (4). The L subtype is the most abundant type of mucus during the periovulatory period and the P subtype appears

close to ovulation (8). Message for all mucins diminishes as progesterone levels increase in blood. (11) During the luteal phase the progestative type of mucus is present.



Estrogenic types of mucus: EP, ES, EL



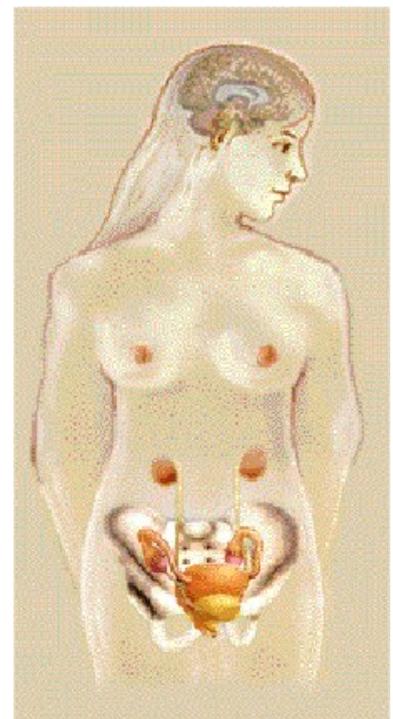
G mucus, stimulated by Progesterone

The usefulness of the BOM in helping women to identify the different stages of her reproductive life cycle has been clearly demonstrated (3 , 4). The BOM is an invaluable tool in helping women to identify these conditions through fertility awareness. As Drs. Billings have stated “self awareness of fertility and infertility is an important knowledge which should be available to every woman. The woman who knows her own mucus patterns will be able to detect a number of gynecological disorders”.

Questions arise as to when irregularities within the mucus patterns and the menstrual cycle should be considered abnormal and when is the point when a woman should be sufficiently concerned to consult a physician.

The persistence of such factors may increase a woman's risk of other reproductive system disorders and may be due to serious metabolic or endocrine abnormalities or to other diseases all of which need to be recognized.

Menstrual disorders and alteration in the mucus pattern can be caused by obstetrical, endocrine, gynecologic or iatrogenic disorders. Early pregnancy complications such as metrorrhagia and vaginal spotting should be identified by recognizing a previous fertile phase with a peak day and can be ruled out with the use of ultra sensitive pregnancy tests and pelvic ultrasound.



## Fertility Disorders

Numerous studies have shown that 10 -15% of couples suffer with a fertility disorder. These are mainly due to: a) ovulatory dysfunction (OD) generally caused by hormonal disorders and b) inflammatory processes usually secondary to genital tract infections (GTI), mainly sexually transmitted diseases.

Ovulatory dysfunction is the most common disorder diagnosed in infertile couples (37%) and is predominantly associated with irregular menstrual cycles (IC). Irregular cycles are present in 10% of women, but having an irregular cycle doesn't necessary mean having an ovulatory dysfunction. We have been able to show according to the BOM charting that 43% of women with irregular cycles present an ovulatory dysfunction, which can be characterized by the absence of ovulation or abnormal ovulatory activity, as seen in cycles with short or abnormal luteal phases. On the other hand, young nuliparous women with regular cycles, (i.e., cycle length between 25 and 36 days) may also present an ovulatory dysfunction as identified by BOM charts (32).

## Ovulatory Dysfunctions

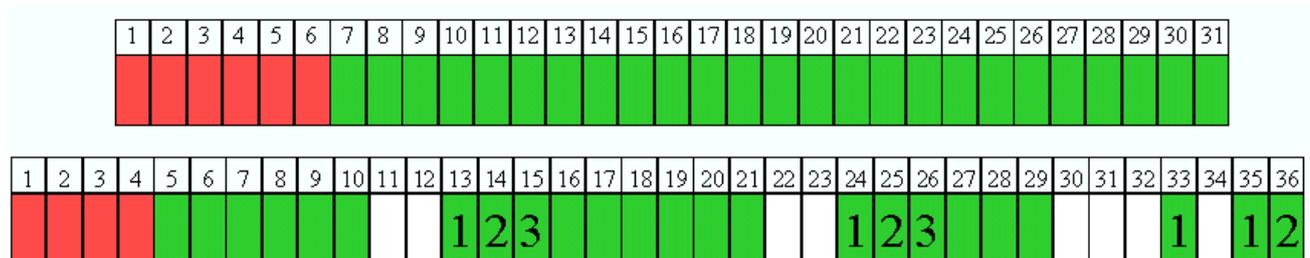
### Endocrinological disorders

Endocrinological disorders are the most common cause of ovulatory dysfunction (27, 28, and 32). They can be divided into hypothalamic disorders, pituitary disorders, general endocrine disorders and adrenal and/or ovarian disorders (1).

### Hypothalamic disorders

Hypothalamic disorders (e.g., anorexia nervosa) are characterized by hypo-estrogenic cycles with the persistence of "dry" days. Amenorrhea may be present. This type of cycle is also seen in athletes, although in this case it should be considered as a normal part of the continuum. In the later case there is a frequent return to regular ovarian cyclic activity as observed within three months of less strenuous physical exercise. However, some of the young women in this category may further develop an anorectic state and despite discontinuation of strenuous physical activity they do not return to normal cycles.

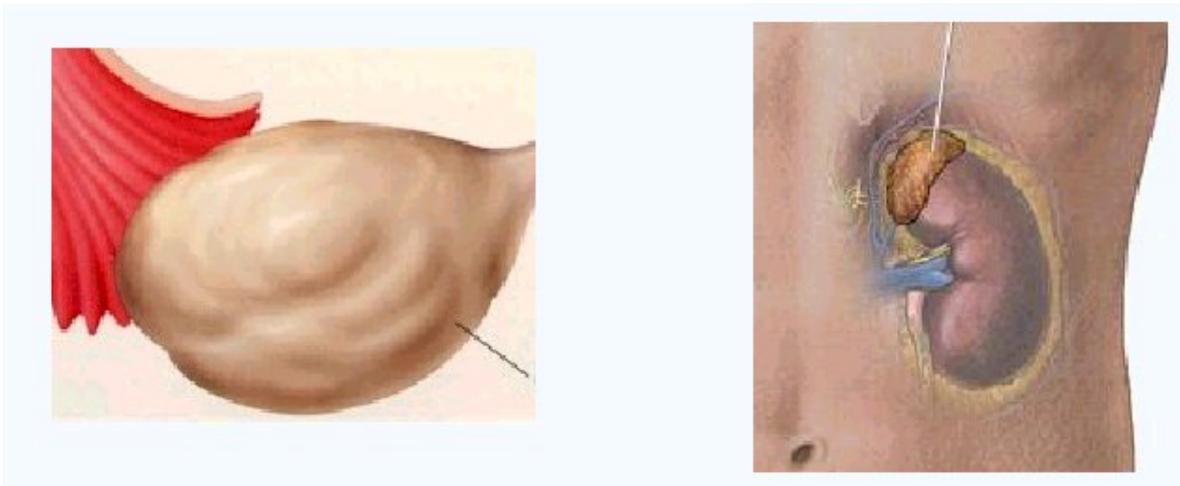
Hypoestrogenic cycles: Anorexia athletes



### Ovarian-Adrenal dysfunctions

Adrenal and ovarian abnormalities are the most frequent cause of ovarian dysfunctions. The most common is the polycystic ovarian syndrome: an ovulatory dysfunction caused by hyperandrogenemia. In these women, irregular cycles are usually present, early after menarche (21, 22, 28).

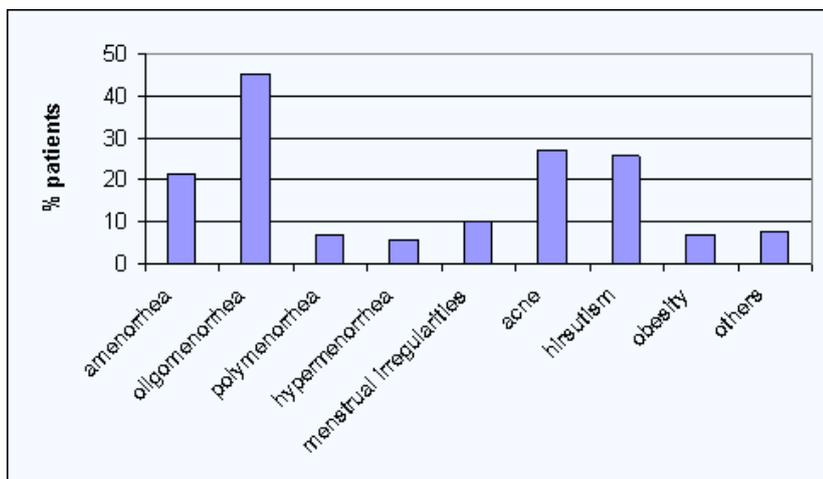
## Polycystic Ovarian Syndrome(PCO)



They can also complain because of acne and/or hirsutism as well as increased body weight and mood changes.



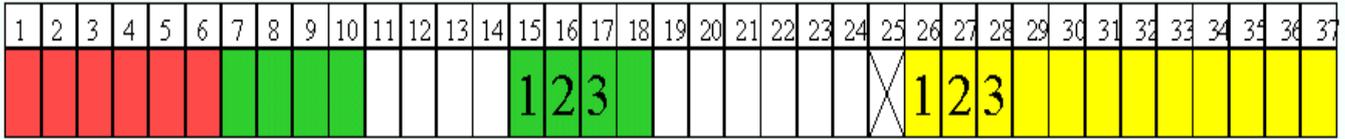
Reasons for consulting a physician in women with PCO (number of patients = 229, more than one reason for some patients)



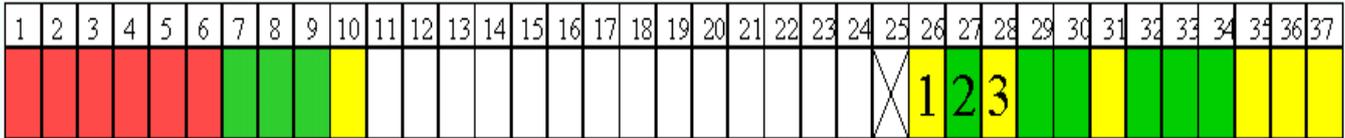
Cycles are characterized by a hyper estrogenic state where a continuous fertile type of mucus pattern is identified or mucus patches are present. Cycles can be ovulatory, with a long follicular phase or anovulatory.

## Hyperestrogenic cycles

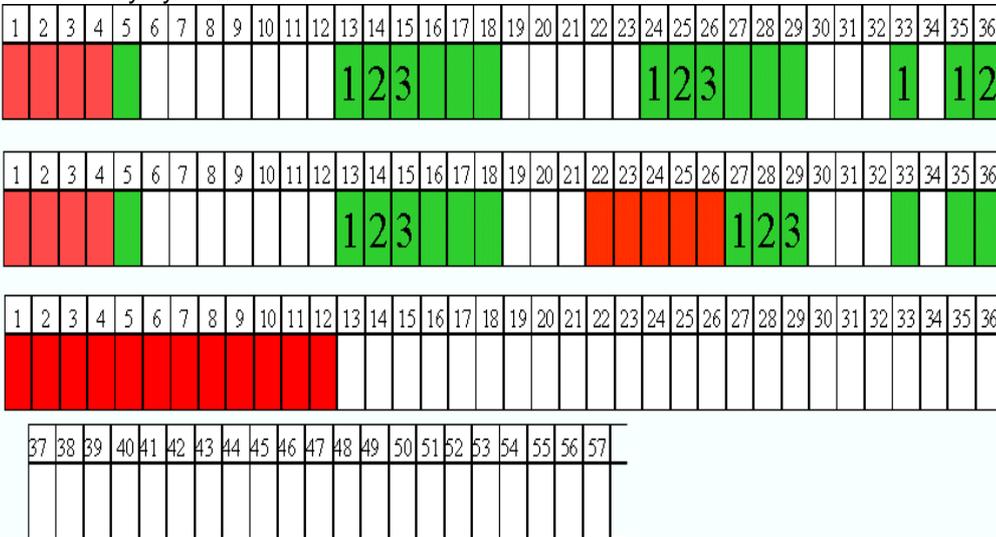
Doubtful peak



Long follicular phase

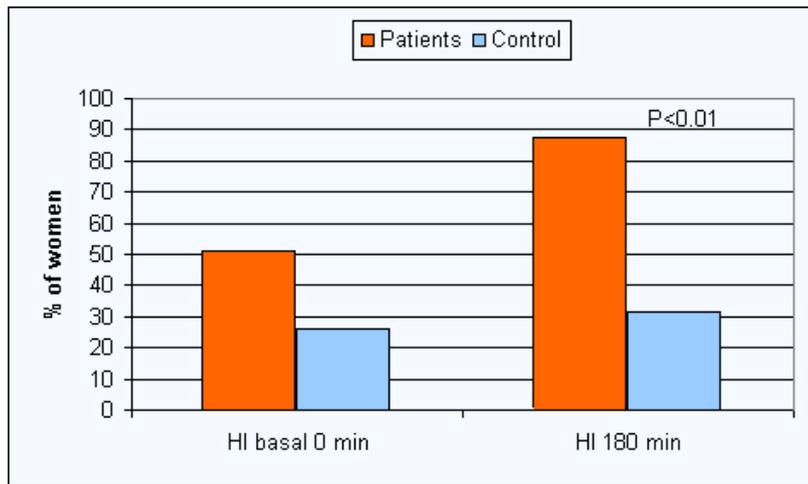


Anovulatory cycles



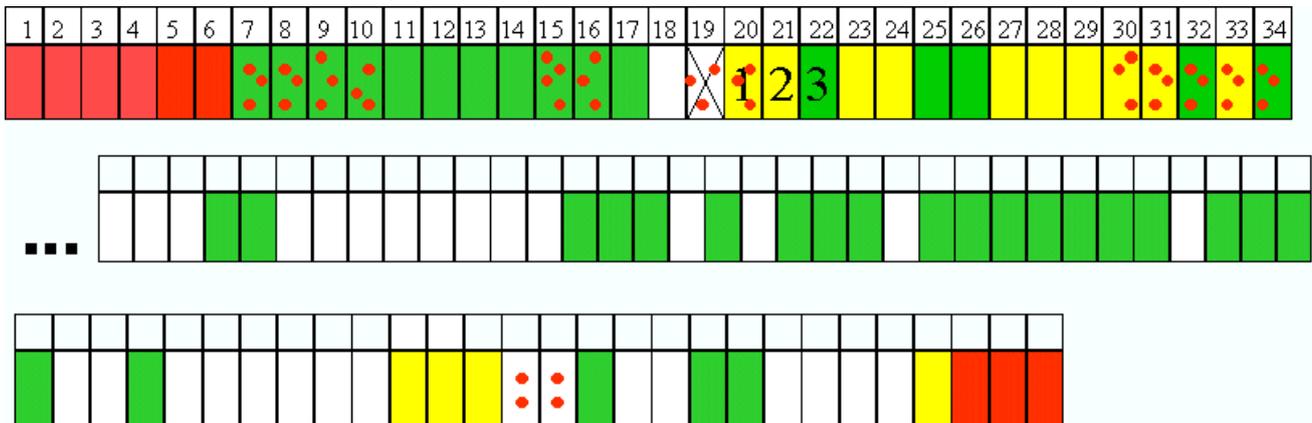
When a young woman complains because of menstrual abnormalities, the teaching of self-awareness of fertility in order to identify ovulatory dysfunctions is very important in order to be able to rule out metabolic conditions such as hyper insulinemia. Our studies have shown that in 86% of women who present with menstrual irregularities, an endocrine abnormality is present of which hyperandrogenemia is the most common (80% of cases (32). It is important to note that an impaired insulin response to oral glucose tolerance test is a commonly (80% of time) associated condition in these women (36). This requires treatment to prevent the occurrence of type II diabetes mellitus (22). Proper care, including diet, exercise and medical treatment will restore normal cyclical ovarian activity. Women who know how to recognize their mucus symptoms will be able to follow the improvement of their endocrine abnormality.

Abnormal insulin response to oral glucose tolerance test in PCO patients as compared to normal women at 0 and 180 minutes (number of women = 94)



Hypothyroidism is a less frequent (about 2%) (32) cause of ovarian dysfunction but it and hyperthyroidism, have to be considered. Different types of ovarian dysfunction can be observed in patients with thyroid disorders. Menorrhagia (15) is frequently associated to hypothyroidism. Although there is no specific pattern of ovarian activity associated to these endocrine abnormalities they should always be kept in mind and eliminated as a possible cause.

### *Menorrhagia*

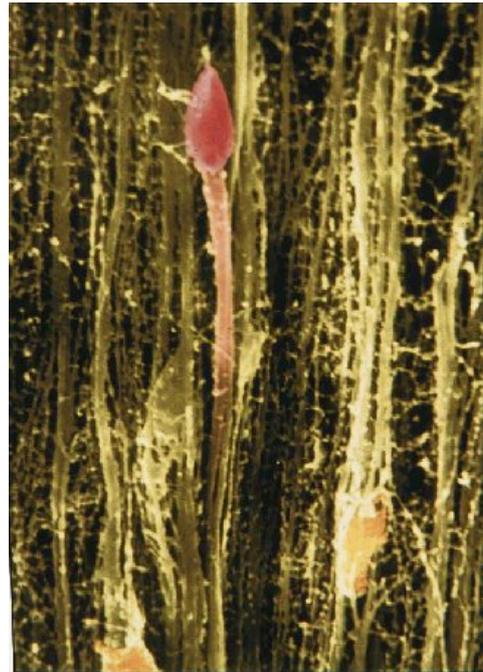


Women with ovulatory dysfunctions associated to irregular cycles and abnormal mucus patterns will not usually resume normal cycling spontaneously without appropriate treatment. Follow up studies have shown that in the absence of treatment these conditions only worsen with time (22, 23).

Other conditions, such as premature ovarian failure may also be a cause of fertility disorders presenting with irregular mucus patterns in response to fluctuating estrogen levels. These conditions are also observed in the perimenopausal period, where some cycles show an ovulatory pattern. As the condition worsens, anovulatory cycles will predominate.

In fertile women, naturally occurring midcycle cervical mucus studied with scanning electron microscopy, shows an arrangement of parallel fibers oriented along the main axis of the mucus sample, probably corresponding to the S subtype (2). Sperm transport maybe facilitated by this normally occurring condition. At midcycle, cervical mucus is greater in quantity, has more mucin and less protein and has higher water content than in the luteal phase (19). This increase in the amount of mucin in the cervical canal, because of its hydrophilic character, probably functions to retain or hold water in place at the cell surface, keeping in this way the cervical canal patent for sperm migration. Also this increase in mucin at a period of high water content could help in the protection of the cervix. Pathogens or other toxins may be trapped by the mucin thus preventing their entry into the uterus and Fallopian tubes (12).

Future research is needed to establish mucus ultra structure and biochemical properties under different endocrinological abnormalities. Also, the function of the specific mucins and mucus types remains to be determined as well as their possible alterations.



## Gynecologic Disorders

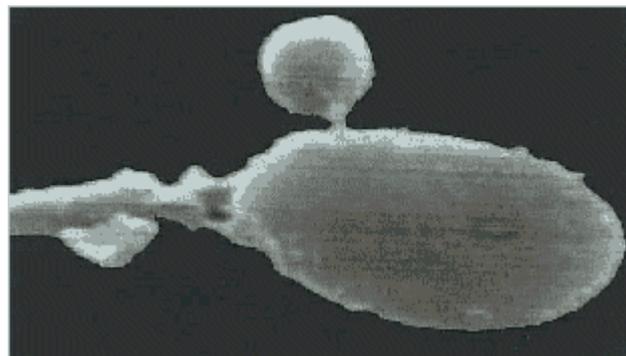
### *Genital Tract Infections*

Menstrual disorders and alteration in the mucus pattern can also be caused by gynecologic disorders such as anatomical abnormalities, neoplasia or inflammatory diseases.

The second most frequent cause of fertility disorders are inflammatory processes, usually secondary to genital tract infections (GTI), which predominantly have an origin in sexually transmitted diseases. Microbial mucin degrading enzymes are associated with sexually transmitted infections and produced by the offending micro organisms. These enzymes will alter the mutually beneficial cohabitation that normally exists between commensals such as Lactobacillus, which use glycogen as an energy source and contribute to normal mucin turnover by the production of mucin degrading enzymes such as sialidase. Mucin molecules would be partly or completely degraded by the microbial enzymes. These molecules dictate the rheological properties which determine the amount and viscosity of the mucus, so these properties will change in response to enzymes produced by microbial organisms in the genital tract (37).

A woman who knows her own mucus pattern in times of health will be able to early recognize a GTI. These will usually cause a continuous discharge whose characteristics will depend upon the etiologic agent causing the infection. In general, an ovulatory pattern is identifiable, but it is associated with a creamy, sticky BIP. Symptomatic infections (itching and a characteristic discharge) are usually caused by fungi, bacteria or parasites. Chlamydia trachomatis infections, with an incidence of 13% in infertile couples and often associated with tubal pathology, (30, 34) will be asymptomatic or present with continuous moistness and variable degrees of pelvic pain. This infection may also show a mucopurulent discharge associated with the mucus discharge. The recognition of this infection and timely treatment may prevent fertility disorders.

Human spermatozoa from infected male patient with Ct



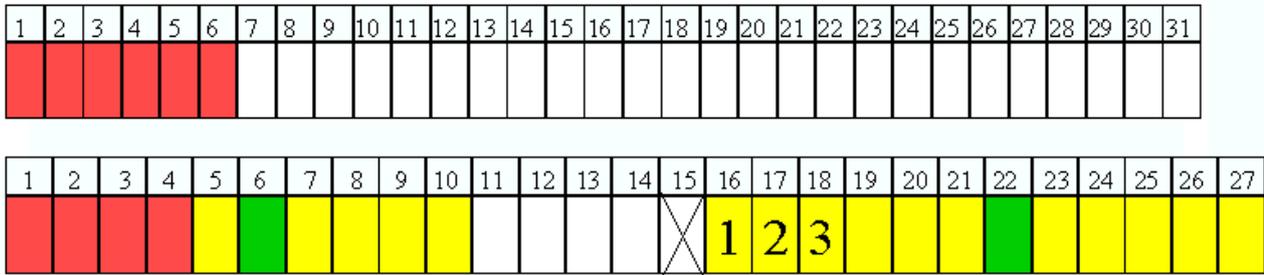
Continuous discharge: Symptomatic infections caused by fungi, bacteria

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25

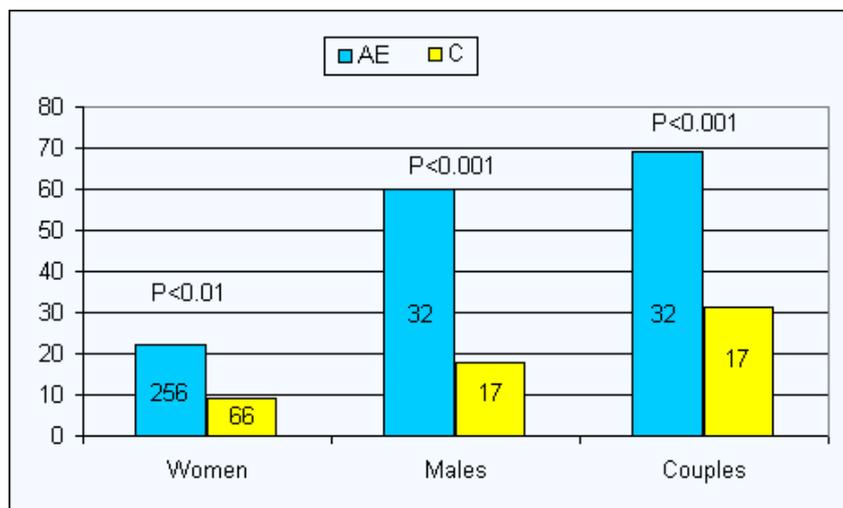
It has been shown that these infections provoke pelvic inflammatory processes and are associated with spontaneous abortions. Recent studies (20) have shown that the mesh spacing between mucin fibers is large enough for small viruses as human papiloma virus (HPV), associated to cervical neoplasia, to

diffuse unhindered through mucus. Bacterial vaginosis related bacteria, micoplasmas, trichomonas vaginalis, and gardnerella among others, must also be considered when unusual mucus patterns or menstrual irregularities occur. In this situation, both members of the couple should be treated in order to restore the healthy condition.

Continuous discharge: Symptomatic infections caused by virus(HPV), Chlamydia



Incidence of Chlamydia trachomatis in groups of males females and couples with or without first trimester spontaneous abortions



### Contraceptive Pill

Fertility disorders may also be iatrogenic, caused by contraceptive pills or by hormonal therapy. Women coming off the pill may present cycles with short luteal phases, absence of a well defined mucus pattern, indicating anovulation, (21) poor mucus response due to damaged cervical epithelium and a poor menstrual flow due to alterations of the endometrial lining. Major cycle disturbances lasting for up to seven cycles (cycle length > 35 days or luteal phase of < 10 days, monophasic basal body temperature or anovulatory cycles) occur frequently in women, after discontinuation of the birth control pills. It has also been shown that in comparison with formerly used mechanical anti-conception methods; pill users have lower monthly percentages of conception during the first three months and a somewhat lower percentage between the fourth and tenth months after discontinuation of the pill (13, 14, and 16).

### Conclusion

Self knowledge acquired by learning the BOM is an invaluable tool for women willing to achieve a healthy reproductive system state. Thus, identification of medical and environmental causes of abnormal menstrual cycle patterns may provide clues to the causes of the most frequent fertility disorders. Early diagnosis of these alterations, as can be achieved through self fertility awareness, will not only improve fertility disorders, but may help in the diagnosis and treatment of other pathologies such as metabolic conditions, endocrine disorders, anatomical alterations, pelvic inflammatory diseases or even neoplasia. Moreover, the menstrual cycle pattern should be taken into consideration in the clinical decision-making process.

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