

# Vulvo-vaginitis and reproduction

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*Summary:* The main micro-organisms able to interfere with the reproductive function have been considered. In particular, the problems concerning the vaginal environment and its interactions with spermatozoa, immunological aspects and contraception. Lastly, reference has been made to methods of prevention and study in the field of diagnostics and of clinical management.

*Key words:* Vulvo-vaginitis; Reproduction.

## INTRODUCTION

Vulvo-vaginal inflammations represent a chapter of considerable epidemiological interest, and also one of the most frequent reasons for gynaecological consultation.

The anatomical situation, both vulvar and vaginal also helped by the presence of natural recesses, contributes to the easy development of an inflammatory process.

Then, with the beginning of widespread screening campaigns, in our country too, knowledge about an ever greater number of pathological vulvo-vaginal events pertaining to situations we may define as social, have been refined.

Woman, the object of the gynaecological discipline, is actively involved in the present historical period, in problems ex-

isting between vulvo-vaginal inflammation and reproduction.

Pathogenous agents may reach the genital organs before conception, impairing them, or afterwards causing a foetopathy or some teratological alterations.

### *Vaginal "ecological niche"*

The term ecology, as understood nowadays, is old: it was coined in 1866 by the German Ernest Haeckel, who placed it among the biological sciences. Ecology studies the relation of living organs with the environment and among themselves, forming an eco-system.

The regular vaginal pH is lower than or equal to 4.5, while a pH higher than 6 predicts an infection.

A lowering of pH towards acidity, leads to the increase of hydrogenion concentration, and it is accompanied by a release of electrons with an increase of the oxide-reduction potential, which proves unfavourable to the growth of anaerobes.

On the contrary, a raising of pH towards neutrality reduces the oxide-reduction potential and encourages the multiplication of the same anaerobes. It is precisely the regular bacterial flora present

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in a vulvo-vaginal niche which is mainly responsible for precluding access to other species, not only because its property primarily conditions the environment, but also because all the crossing micro-organisms inevitably have to compete with the "native" flora.

*Gardnerella vaginalis*, for example, which is isolable in 10-40% of asymptomatic patients, does not grow with a pH = 4. Instead it multiplies, inversely, in the presence of lactobacilli and together with the growth of the anaerobe flora, with which it synergizes.

*Neisseria gonorrhoeae* meets the scaly pluristratified epithelium of the vagina unfavourably. The infecting attack may be reached after one or two exposures, but aggressivity is generally lost with a pH lower than 6.

A feature of the vaginal niche lies in the vaginal environment, which remains practically stable, only revealing some transitory physiological fluctuations in reply to occasional events and to the variants of cycle phases.

To give two examples, vaginal pH is lowered by the introduction of the seminal fluid, but returns to its own values after about 8 hours.

Vaginal irrigations with providone-iodine also have a short duration effect, because after 30-120 minutes the vaginal flora returns to its normal composition.

#### *Protection from sexually transmitted disease and/or from infections*

Osborne and Coll. investigated 383 sexually active women, studying up to what point nine of the micro-organisms commonly transmitted by sexual intercourse might be responsible for symptomatic vaginitis.

The results were:

a) appearance of symptoms is significantly linked with the presence of micro-organisms;

b) symptomatic women contain more microbic species per person than the asymptomatic ones.

According to Osborne and Coll., the main factors may be:

1) The particular microbic contribution by the seminal fluid.

2) The temporary alkalization of vaginal pH by the ejaculate.

3) The number of partners, frequency of coitus, variety of those body parts which are in contact during sexual intercourse (each one responsible for a different property and quantity of the bacterial charge).

4) The alteration of the ecological niche with regard to the kind of contraception used.

5) Particular variations in the immunoregulation of the hostess.

#### *Correlations to the use of contraceptives*

At present, the following indications are possible:

1) Some Authors have noticed an increased risk of vulvo-vaginitis for the users of the pill, others have not confirmed this.

2) The risk of an infection deriving from the insertion of the spiral should be valued separately from the risk of infection associated with its prolonged use, though both are in relation to the ascent of germs from the vagina.

3) The finding of bacterial positive cultures 24-72 hours after the insertion of IUD, but negative at a distance of some weeks, suggests the possibility of a useful though not rapid intervention of the hostess' defences.

4) It is a common opinion that bacteria may migrate along the external surface of the spiral's filament: in fact, some epidemiological studies have indicated that there is an increased risk of pelvic inflammatory disease for spiral users.

*Aspects of vaginal biology in relation to the coital function*

It is well known that spermatozoa react to the effects of several environmental influences. In fact the great influence of vaginal pH on the motility of spermatozoa has been known at least since since 1926: motility fails if pH is 4.9 and is irrecoverable if it is 3.5.

Another factor that may modify the features of spermatozoa is microbial population. For example, *Trichomonas vaginalis* competes with spermatozoa for fructose metabolically.

Recently, Minkoff and Coll., examining the relation between the quality of vaginal flora and the sex of the conceptus, have noticed that women who are carriers of T.v., of bacterioids, or others, used to give birth to more girls – with statistically significant differences – than women who did not carry this type of micro-organism. Therefore, spermatozoa, bearers of the second chromosome X, seem to offer a greater resistance to vaginitis than bearers of chromosome Y.

Common coition lubricants, vaseline, and also glycerine even at only 2%, should not be used by sterile women, because they are spermicidal, even saliva damages the motility and activity of the spermatozoa themselves. The increase of pH during orgasm can be considered a fact; it appears besides, an element favouring the longer preservation of an active sperm in the vaginal environment.

On this subject, it may be interesting to recall that the use of hormone contraceptives would reduce the increase of pH during orgasm, leading to a less favourable environment for spermatozoa, apart from averting the reaching of the orgasm itself.

*Production of anti-sperm antibodies*

Up to 1975, the scaly vaginal epithelium was considered “almost incompatible” with local secretion of antibodies.

However, it has been shown that the vagina, both in the human species and in others, is able to synthesize immunoglobulins in response to antigenic stimulation. However, the activation of the local immuno-system is not immediate: it probably needs 3-5 days to be realized.

In fact, the spermatic antigens introduced by coition may certainly stimulate an immunitary response by the vagina: but curiously, such an immunitary response may also be crossed, that is stimulated by antigens present in specific micro-organisms, but directed against spermatic ones.

A local treatment with cortisone could give a certain effect not specifically through the suppression of antispermatic antibodies, but by the elimination of a local inflammatory state which would make the vaginal environment less hostile towards spermatozoa.

*Maternal and foetal risks linked to the vaginal environment*

Many micro-organisms have often been recognized as risk factors for the baby if they are present in the vaginal flora, but it is generally possible to agree with those who affirm that “if the bacterial contamination of the baby is not synonymous with infection, it is also true that the higher the degree of colonization, the greater the risk of an infection”.

Positivity in the vaginal investigation for beta-haemolitical streptococcus is frequently associated with a similar infection of the urinary tract and, even if it is impossible at present to establish where it is located, it is certain that urinary colonization by this micro-organism is at least as frequent as that in the vagina. It is therefore advisable, always, to seek in urinary bacteriological examinations of the pregnant patient, suitable grounds for its isolation, too.

Another rare but not exceptional complication due to the beta-haemolitical streptococcus, is the puerperal sepsis, generally less serious than that caused by

other agents [beta-haemolytical streptococcus (group A), staphylococcus, various anaerobes, etc.].

Simple bacteraemia is, instead, more frequent. On this subject it may be interesting to bear in mind the seeming impossibility of identifying by prenatal vaginal bacteriological examinations, those patients who risk a puerperal infection.

The *Escherichia coli* is a Gram-negative bacterium, aerobe, predominant in cultures of the lower female genital tract, and it is asymptomatic: its medium frequency does not, however, reach 30%. But its presence, if consistent, should not be considered as physiological at all, but as an expression of a risk situation, as a predisposition for inflammatory episodes connected with particular environmental changes.

The papilloma virus (HPV) represents another infectious agent whose presence in the vaginal environment involves a remarkable risk of contagion for the foetus, though probably, and at the moment of birth. The foetus may swallow infected material (perhaps only in the case of condylomatosis florida) whose penetration into the tissues may be facilitated by microtraumas provoked by the rhinopharyngeal inhaling by the newborn, and such an infection is characterized by an orolaryngeal papillomatosis usually arising within the first 5 years of life and regressing at puberty.

Type 11 HPV would be the only one responsible for this infection, the risk of which has induced some to advise, and also to perform, the Caesarean section on pregnant women affected by genital infection from HPV.

#### *Maintenance of a suitable vaginal environment for receiving the foetus*

Particular condition existing in the genital sphere during pregnancy, consisting of nutritional, metabolic, endocrine and immunological alterations, also circulatory,

may assist the outbreak of vulvo-vaginal clinical situations or cause alterations in the existing ones.

In fact, at the level of the vulva and vagina, gestation causes various modifications, specially encouraged by hyperaemia and by the particular succulence of the tissues. It induces a condition in the vulva facilitating considerably the nesting of germs inside the glandular recesses and into the roots both by implantation from outside, and with conveyance by the vaginal secretion. Then, in the vagina, (by the more significant modifications due to the pregnancy, hypertrophy of the mucous membranes, reduction of Keratinization, increase of vaginal glycogen and therefore of lactic acid), the vaginal pH further diminishes, which should thus make the vagina practically sterile.

But more than infectious events, we need to remember that such modifications induce the presence of a leucorrhoeic secretion, which may be defined as physiological, having at first a translucent appearance and then taking on a dull-milky white appearance, being formed by epithelial cells often descaled during cytolysis, by mucus, Döderlein bacilli and by leucocytes.

#### *Vaginal flora and pregnancy: relations to the premature rupture of the membranes and the labour of premature birth*

Longitudinal studies during pregnancy, have shown that, with the progress of gestation, the concentration of both lactobacilli and mycetes increases; on the contrary, that of cocci aerobes (both gram positive and negative) decreases. In fact, according to the present conception, the progressive increase of lactobacilli, reducing pH, very effectively prevents the growth of pathogenous micro-organisms.

*Gardnerella vaginalis* (and also the presence of "non specific vaginitis") has been more frequently noticed in women during the labour of premature birth; but this

observation has been pointed out by some as being not statistically significant, by others as considerable.

Also, the presence of mycoplasma hominis in the vagina would not be connected with the appearance of chorion-amniosis, nor even with the light weight of these patients babies at birth.

Then to the presence of streptococcus  $\beta$  haemolyticus is associated in a statistically significant way, with the premature breaking of the membranes, which is difficult to interpret.

Minkoff and Al. have suggested microbial flora, as a risk factor for the premature rupture of the membranes or for the labour of premature birth, which should be checked by microbiological screening from the beginning.

#### *Mycoplasma and ureaplasma*

MYCOPLASMA. Among these, many species are recognized but are only isolated at vaginal level as saprophytic flora: Mycoplasma hominis and Mycoplasma fermentas. They present an accentuated polymorphism, spreading out from fibrous forms (from 50 microns in length) to large spherical forms, besides which they resist all the lactam antibiotics, while they are sensitive to those which stop proteinic synthesis of those preventing the attack of mRNA on polyribosomes.

For epidemiological studies, serum tests for the identification of antibodies are used; especially that of fixation of the complement. But in facing the subject of pathology from Mycoplasma, the wide diffusion of such micro-organisms, even in symptomatic patients, is always an important consideration.

Transmission seems essentially to occur by genital contagion. During the fertile period, the importance of venereal contagion is evident and therefore of the number of partners, which has been confirmed, indirectly, by variations observed since the introduction of estroprogestinic

contraception, with the consequently greater sexual freedom.

UREAPLASMS. These represent a subspecies of mycoplasmas (also called T-mycoplasma) and were observed for the first time in the male urethra. Differentiated from mycoplasma it is distinguished by the observation of metabolic activity in a culture: in effect, mycoplasma metabolize arginine, while ureaplasma metabolize urea.

It has been shown that *H. urealiticum* induces an increase of chromosome alterations (for example: breaking of segments and tetraploidies), so the possibility of miscarriages, even repeated, appears highly suspect.

#### *Granulous vaginitis and cystic colpo-hyperplasia*

There are some forms of vaginitis, typical of pregnancy, having an unknown aetiology; such as granulous vaginitis and emphysematous vaginitis.

GRANULOUS VAGINITIS. Hypertrophy of the vaginal mucous membrane produces a typical appearance that justifies such a name. On exploration a number of very small reliefs can be noted, which, may be identified by the touch as soft grains. This disease, regresses, mostly spontaneously, after the birth. The etiological agent is unknown, though a possible pathogenous role of *Trichomonas* is being discussed by some; yet others believe, instead, it is a matter of a particular aspect of gonorrhoea in reality, this latter would only rarely have been confirmed by the discovery of a gonococcus.

EMPHYSEMATOUS VAGINITIS, (also named colpo-hyperplasm). This is considered, by most of the Authors, as very frequent during pregnancy, and it seems almost its monopoly, since it disappears after the birth, even in absence of particular therapies. It is located in the upper region of the vagina, being formed by small bubbles, isolated or in groups ran-

ging in size from a grain of rice to a pea. These bubbles, with a serous content, due to strong tension (probably caused by trimethylamine), covered with a stretched and thinned mucous membrane, may easily break during the exploration or by the speculum watching, allowing vesicles contents to emerge.

### *Bartholinitis*

This may be original or secondary to other infections, complications of vulvovaginitis or other similar urogenital diseases, and it frequently appears during pregnancy. This disease also tends to relapse.

Such an infection is very often produced upwardly, through the excretive duct, where its initial location spreads fairly rapidly to the whole gland. Its etiology is prevalently bacterial. The gonococcus is present in a moderate percentage (not higher than 10% of cases). Common pyogenes are more often present, sometimes parasites or fungi. For the bacteriological examination it is preferable to take the secretion of the cervical passage rather than that one eventually covering the region where the inflamed gland is situated.

Inflammation may appear at the beginning, during or at the end of a vulvovaginal inflammation, or even suddenly.

It starts with burning, tension and a size increase of the vulva, very often unilateral, with the participation of general conditions even a high temperature. Pain is sharp and stabbing, initially vulvar, spreading subsequently to the perineum, thighs and the anus: walking is impossible and always painful, and sometimes sitting too.

Objectively, the increase of the gland can be observed, deforming and swelling the labium majus, which appears red and edematous, the rear two thirds often being involved. The emptying of the abscess is rapidly completed, the oedema is reduced, the mobile area is evidenced and it quickly opens on the outside.

There is the possibility the process spreading to the other gland, usually later, rarely at the same time.

The spontaneous emptying is not always complete, a moderate residual suppuration being possible, which would be responsible for relapses; a chronic bartholinitis would be produced.

More rarely, bartholinitis during pregnancy tends to assume a chronic course: the gland appears hard, the passage is enlarged and inflamed with possibility of purulent secretion, spontaneous or during vaginal explorations.

Therapy must be local and general; the latter is particularly suitable for acute forms, in which it must be prolonged for some days after the initial symptomatology has ended in order to prevent relapses. It should be based on the use of antibiotics, to be chosen according to the identified agent.

Local therapy, in the case of an acute bartholinitis, should be carried out by lancing the abscess. If the contents of the abscess still does not appear healthy, it will have to be helped by the usual means. The lancing must be made where flow is greatest, if possible at the limit between skin face and mucous membrane of the labium majus, after local anaesthesia.

In case the suppuration has already found a way out by itself, it may be possible to try to sterilize the passage and the cavity of the gland, by antibiotics and cortisone solutions, but results are generally disappointing. In this case (as in those cases where in spite of lancing, relapses occur), the extirpation of the gland is preferable, and, if in puerperium, it should be done after the end of this stage.

The presence of a cystic form during pregnancy demands extirpation during gestation: the operation will have to be particularly careful of haemostasis, because of the tendency to bleeding provoked inside the tissues by the alterations typical of gestation.

### *Gardnerella vaginalis*

This was discovered by Leopold in 1953. Morphologically, it looks like a short stick, gram-negative and fairly polymorphic.

In the next few years, different suggestions were presented. One considered the micro-organism as the main, if not the only, aetiological agent, of « non specific vaginitis ». This was characterized by a malodorous homogeneous and rosy leucorrhoea, by alterations of vaginal pH (higher than 4.5) and by the discovery of the « clue cells » (paving cells completely covered with small coccobacilli), even in the absence of inflammatory reaction, and near absence of lacto-bacillar flora. Another opinion, on the contrary, considered *Gardnerella* as a component of the general vaginal flora, being present in 10-40% of cases.

A third suggestion considered the symbiosis between *Gardnerella* and anaerobic flora responsible for « non specific vaginitis ».

Proliferation of anaerobes is followed by an increased production of amines, which confer the typical « bad fish » odour of the vaginal secretion. This smell may be intensified by adding potassium hydroxide at 10%, which makes amines volatile and therefore the smell of the « fishy test », on the occasion of the prompt smear.

Trimethylamine is specially responsible for the smell.

### *Vulvo-vaginal Candida*

The vaginal *Candida* is, like *Trichomoniasis*, a typical disease of the fertile period.

One woman in 2 or 3 proves to a carrier of *Candida Albicans* and is destined to show vaginitis in a relatively short time; besides, 40-60% of the partners of women with vulvo-vaginitis from *Candida* prove to be affected from balanitis. The optimum pH varies from 5.5 to 6.5.

Mycetes are eukariote micro-organisms characterized by a substance called thallus, which is formed by fibres called « ife » with a maximum length of 20-30 micron. A group of ife originates a « mycelium », and the thus formed mycetes are named « moulds ».

There is, besides, a second group including fungi with a unicellular thallus called « leavens », while « blastospores » are the result-cell forming them.

When blastospores meet subsequent gemmations, remaining united among themselves, they produce lengthened formations called « pseudoife ».

In each case of vulvo-vaginal *Candida*, the isolated species is « *Candida albicans* ». In a very low percentage, of cases, 6 other species are admitted as being pathogenic: *Candida stellatoidea*, *C. tropicalis*, *C. Krusei*, *C. pseudotropicalis*, *C. guilliermondi* e *C. parapsilosis*.

The well known aphorism, suggesting mycotic vulvo-vaginitis is easy in cure but difficult in recovery is as true as ever, in spite of the great availability of medicines new existing on the market, which may be given both topically and orally.

The incidence of *Candida* during pregnancy increases from 10% in the first quarter, to 50% in the third and its presence at the moment of the birth has 40-80% of probability of being transmitted to the new-born.

Therefore an antimycotic therapy ought to be given to each pregnant woman four weeks before her term as a precautionary measure.

The flourishing and development of mycosis is helped during pregnancy by different factors, such as the abundance of glycogen in the vagina, the lowering of vaginal pH, and the increase of sexual steroids.

The subjective symptomatology is represented by a white-yellowish leucorrhoea in clots, comparable to curdled milk.

Pregnant women complain of itching and burning, as from scalding. Objectively, the vulva is red, oedematous and sometimes covered with a whitish dried up mush; the vaginal mucous membrane appears red with some secretion zones on the walls; the uterine neck is usually undamaged.

Diagnosis is facilitated by:

– the direct examination, facilitated by the typical blastospores and the filaments of mycetes;

– culture: using particular grounds (Sabouraud, Nickerson-Carr's).

The therapy also feels the effects of the evolutionary particularities of mycosis which, like trichomoniasis, often presents relapses during pregnancy and only recovers after the birth.

The objective of the therapy is the destruction of fungus and the modification of vaginal pH (more effective here than in trichomoniasis), that can be obtained by trying to raise it through the introduction of alkaline solutions in the vagina (sodium bicarbonate).

Locally, the destruction of fungus may be obtained by some applications of gentian-violet at 2%, of Millian's solution or by glycerine, boric acid and sodium borate mixture.

Today, specific therapy is practised orally and locally.

#### *Infestation from trichomonas vaginalis*

Trichomonas, different from other flagellata, does not pass through the cystic phase: they remain, in the form of trophozoites. They are 10-20 micron long, have a pear shaped body, with a single front nucleus, 3-5 flagella directed forward and one back, which forms the edge of a waving membrane. They reproduce by longitudinal division.

Trichomonas tenax is instead a parasite of the oral cavity, that does not survive the intestinal passing; it may be transmitted by tools or kisses.

T.V. is an anaerobe micro-organism that utilizes carbohydrates polymers as substrata. Electrons released during glycolysis have as last acceptors hydrogenions, which change so into hydrogen, giving a foamy appearance to secretions.

The T.V. competes with lactobacilli, and its growth is therefore helped by any increasing of pH.

Though it may live between pH 4.9 and 7.5, optimum values for its development are contained between 5.5 and 5.8. Trichomoniasis is an infestation that prefers the years of sexual maturity.

T.V. may be transmitted:

a) sexually (the man being as the vector and woman as the reservoir);

b) by direct contact, particularly through toilet objects (T.V. does not survive in a dry environment, it is destroyed by exposure to the sun and by heat at 40°; it survives for 30 minutes in tap warm water and for 6 hours in the seminal fluid);

c) through the birth.

The infestation from T.V. may have the following effects:

a) it may be asymptomatic;

b) it may cause inflammation;

c) it may cause infertility, being responsible for both 20% of prostatitis and ostato-vesicolitis, and for damaging the motility and vitality of the spermatozoa.

During pregnancy, it is quite frequent (20-25% of all vulvo-vaginitis) or according to Hoehne even 54%. Such a high frequency might be due to different causes: in fact, it might be a question of an abnormal proliferation of the parasite in women infected before pregnancy, or of an infestation during gestation, because the abundance of glycogen typical of the vagina, during pregnancy, helps its development.

Subjective symptomatology is known: presence of an abundant, bad smelling, white-greenish or yellow-greenish coloured, foamy leucorrhoea. Itch, burning, urological signs such as dysuria, pollakiuria, and cystalgia are associated with it.



Objectively, a reddening and an oedema of the vulva can be observed whose skin covering appears stretched, with lesions from scratching and intertrigo particularly located into the groin-crural zone and in nearby ones. The vaginal mucous membrane looks like a strawberry, being hyperemic and oedematous, and sometimes presents some erosion zones, which may also spread to the neck. Another typical aspect of *Trychomonas* (T.) during pregnancy, is its evolution. It frequently presents relapses, while recovery is only possible after the birth.

Diagnosis is based on the clinical examination that must be confirmed by laboratory research. Let us quote:

- prompt examination by putting one drop of secretion on a heated slide, and then diluting it by a physiological solution the parasite can be recognized by its typical aspect and movements. Its colour can also be seen by the base with colouring agents which leave T. colourless (bright blue, fuchsine);

- instead, the examination after the colouring by agents such as gram, May Grunwald-Giemsa, Shorr, Indian ink, will reveal the existence of the parasite, but it evidences a complex associated microbic flora;

- cultures, among which the Roiron-Ratner is the most used.

Therapy, because of the particular evolution of the disease, tending to relapse, must aim at both the destruction of the parasite and the causes of relapses and their suppression, particularly of the reasons for urinary manifestations.

The patient's partner should also be treated and he should extent the therapy to a general treatment in addition to the local one.

### *Gonococcal vulva-vaginalis*

*Gonococcus* is a gram-diplococcus coffee grain shaped; average sizes are  $1.5 \times 1.8$  micron; optionally resulting as an anaerobe, while the optimum pH is between

6.8 and 7.7 and it proves to have an attraction for glucose.

Gonococcal vulvo-vaginitis may be due to recent infective intercourse, or to an infection preceding the pregnancy where the gonococcus, previously nestling inside some paravulvar glands, resumes its virulences from different causes, some of which are connected with the pregnancy itself.

In the first case the symptomatology will be stronger: vulvar phenomena will predominate, compared with vaginal ones. Subjectively, there will be itch, burning, miction problems with dysuria. Objectively, swelling and reddening, can sometimes be observed in vulva; the labiae will be swollen and sometimes covered with a purulent exudate; the urethral orifices, and also those of the Skene and Bartholini glands are red, with a swollen mucous membrane up to the occlusion. In less acute forms, germs must be sought through fractuosities of mucous membrane, internal glandular orifices and also in the urethral orifice.

Though it is rare, the gonococcal infection has to be sought with care during pregnancy, it being sometimes capable of causing very serious consequences for both mother and foetus. For the new-born, the gonococcus ophthalmitis is particularly worrying, it is due to infection of the eyeball caught through the infected birth canal. Today with prophylaxis required by law, and carried out systematically, it be can fortunately be considered exceptional.

Lastly, we must remember how gonococcal forms, and perhaps even more those from ordinary phyogenous germs, are helped during pregnancy by the existence of chronic infections of the cervix and of venereal papilloma growths. A mutual influence often seems to exist between the two infections with a worsening of the subjective and objective symptomatology. Vegetation, in fact, by the double influence of pregnancy and bacterial infection, become particularly luxuriant and exube-

rant, proliferating in size and surface, invading the vagina and spreading to the vulvo-perineal region.

### *Chlamydia Trachomatis (CHT)*

To speak of the vaginal localization of Chlamydia (CHT) would not be completely accurate, since it is not located inside the vaginal epithelium, but in the cylindrical cervical or metaplastic cells: however, being a sexually transmitted disease or intrapartum disease, it must be referred to in such a paper.

Therefore, it is a bacterium that has no characteristics in common with gram-negative bacteria, but a set intracellular parasitism. It can be subdivided into 15 serotypes. The development cycle of Chlamydia is represented by the infecting form or "elementary body", which, by a process of phagocytosis, penetrates the cell, where it modifies into a "reticular body". Reticular bodies multiply into the cell by binary scission, subsequently transforming themselves into "elementary bodies" which causing the breaking of the infected cell, wander freely into the environment and start new cycles.

At the level of the female genital organs, Chlamydia locates in the cylindrical or metaplastic cells of the cervical area, where it mainly causes cervicitis or endocervicitis.

In women, 20% of the cases are asymptomatic; in 30% an isolated leucorrhoea or some sub-acute vulvo-vaginitis can be noted. But the most serious complication is salpingitis, because of its sterility risk.

The infection from Chlamydia Trachomatis is sexually transmitted; also, the passage through the birth canal of an infected mother may cause a conjunctivitis or an "interstitial pneumonia".

The incidence of genital infections caused by Chlamydia Trachomatis during pregnancy oscillates between 2% and 15-30%, with a threshold of 8% in western countries.

Among the possible effects of infection on the evolution and outcome of a pregnancy it is possible to result an increase in the percentage of prematurity, perinatal mortality and low birth weight. It also has a possible role in determining spontaneous miscarriages.

In order to prevent infection from Chlamydia and its extremely serious consequences, special vigilance must always be given to the following patients at risk:

- all patients suffering from gonorrhoea;
- male patients suffering from post-gonococcal urethritis, epididymitis, Reiter syndrome or rectal inflammations;
- all pregnant women;
- women suffering from cervicitis and mucopurulent cervico-vaginitis, urethral syndrome, endometritis or salpingitis;
- the new-born children of infected mothers;
- new-born children with conjunctivitis from inclusions and/or pneumonia;
- all patients suffering from venereal lymphogranuloma, with trachoma or conjunctivitis from inclusions;
- all sexually active individuals, women particularly, noting the clinical signs carefully.

### *Human Papillomavirus (HPV)*

Papillomatous vegetation, or pointed condylomas, frequent during pregnancy, are acute inflammations, more frequent in the vulva than in the vagina, and etiologically different, prevalently attacking the skin derm papillae causing hypertrophy. This soft vegetation, initially spreads, tends then to unite generating some cabbage shaped arborizations which may extend above the surface and increase so that they may also totally invade the vagina and nearby regions, preventing the vaginal exploration.

Cytologically, the infection from HPV is characterized by two kinds of cells which may be variously connected:

– Koilocytes are the cellular pathognomic elements of the lesion from HPV. They are the cells of the intermediate and superficial layers of the Malpighi epithelium, characterized by nuclear degenerating alterations and by a light halo, perinuclear, optically empty, well delimited, irregular, also a dense peripheral cytoplasm. They often have a double nucleus and rarely more.

– Diskeratocytes are small scaly cells of superficial layers, with an enlarged and very dense nucleus. Cytoplasm contains keratin, and assumes an intense colouring at Papanicolaou.

Histologically, different kinds of alterations from HPV are distinguished at cervical level:

– Pointed condyloma: more frequently found at vulvar or perianal level, it is characterized by papillomatosis, acanthosis, parakeratosis and Koilocytosis;

– Level condyloma: the architecture of the tissue is preserved: the cells of the basic layers keep a regular polarization, intermediate layers contain several Koilocytes and the superficial ones show some signs of diskeratotic alterations;

– Inverted condyloma: this is a level lesion developing inside the glands and substituting the epithelial column. Such a disease is mostly transmitted by sexual contact, and may be increasing because of the reduction in the use of barrier contraceptives (prophylactic) that protect from contagion.

Some conditions altering the immunological state, such as pregnancy and resorting to estroprogestinic contraceptives, may help the infection and the growth of lesions. It usually appears in the fertile period. During pregnancy, the extension of condylomas to the vagina is frequently jointed by tension and pain. Condyloma vegetation rarely reaches such dimensions as to justify the choice of the Caesarean section. The new-born may become infected during the passage through the birth canal and later present a laryn-

geal papillomatosis or a perinatal papillomatosis. There is no kind of prophylaxis or specific therapy but the use of beta-interferon and immunomodulating medicines whose effectiveness and innocuousness during pregnancy still remain to be tested.

The HPV infection may show itself at vulvar level under two main aspects:

– condylomatosis florida: if it is located on the skin, as a whitish hyperkeratotic excrescence, small and crescent shaped or, if it locates on the mucous membrane, as a wide based formation, papillar, with a whitish-pearly wrinkled surface;

– micro-papillomatosis: as papillar excrescences, small, multiple, smooth, translucent with a white apex and a clearly visible vascular axle. These are mainly located at the level of the internal face of the labia minora and on the vestibule. Cryotherapy obtains good results particularly in resistant forms.

Chemotherapy gives good results with the resins of podophyllum for local applications, repeated at a distance of days: this cellular poison leads to vacuolization, to the gathering into large blocks of chromatin and to cytotoxicity.

Vulvar condylomas are not to be mistaken for the physiological papillomatosis producing pinky filiform digitations, wide-spread, bilateral and asymmetrical.

According to the situation, it will be decided whether to do the HIV test or not: nor must they be mistaken for Bowen's papulosis which attacks young women (of 20-30 years).

The clinical aspects, in this case, are very polymorphic and sometimes deceptive. In general, papulosis appears in the form of multicentric lesions, flat, pigmented, especially in the perineum and perineal zones. It is often due to an infection from HPV 16. The treatment should be based on the elimination of lesions (Electrocoagulation, Cryotherapy, Trichloroacetic acid, Laser CO<sub>2</sub>). The malignant potential is low.

### *Genital herpes*

This is a neurotropic epithelial virus, of medium size similar to Herpes labialis, CMV (cytomegalovirus) and the virus of chickenpox zoster. It is formed by a DNA core, a proteinic capsid and a lipoglycic wrapper of proteins: due to an HSV 2 genital simplex virus in 90% of cases, or more rarely to an HSV 1 herpes simplex virus (labial and herpetic keratitis).

The cell-mediated immunitary response plays an important part in herpetic manifestations.

Clinical situation:

– in men: initially it results in a small gathering of vesicles, then in small pointed erosions on an erythematous plaque (in 20% of cases, the first infection is asymptomatic);

– in women: hyperalgetic acute vulvovaginitis, with high temperature and alteration of the general conditions and inflammatory inguinal adenopathy.

After intercourse with an infected person and an incubation of about a week, some painful vesicles appear, gathered or separated. Generally, the vesicles evolve into pustules that erode later.

Subsequently, within 10-12 days, there is the formation of scabs, before the epithelium can be re-formed.

Superinfection from common germs and from *Candida Albicans* is frequent.

The clinical aspects must be known:

1) the first episode of no primary genital herpes;

2) the first episode of primary genital herpes;

3) the recurrence or relapsing of genital herpes: often painful, it is noticed in 10% of cases, showing the persistence of HSV in the genital regions. Generally, the anamnesis assures diagnosis (vesicles, periodicity, predisposing factors: psychological stress, immuno-depression, antibiotics);

4) asymptomatic genital herpes.

Herpes in the new-born (1/7500 births in USA) is very serious (50% of deaths, 50% of serious consequences for survivors) because of the liver, septicaemic or meningo-encephalic spread which makes Caesarean section advisable for women with herpetic vesicles at the moment of the birth, when a premature breaking of the membranes occurs.

Laboratory tests: histopathology and cytopathology, electronic microscopy, immunofluorescence, hybridization by soundings of RNA or DNA nucleic acids associated with enzymes which join viral DNA producing a visible reaction product, immunocenzymic methods, monoclonal antibodies.

### *The infection from HIV*

AIDS is by now a problem all doctors have to cope with. The genetic information of the virus may be contained both in DNA and in RNA. Tests in search of anti-HIV antibodies at present allow the revelation of contamination from HIV 2 in a percentage of cases varying between 90 and 95%.

The search for antibodies may be made by different methods: the most common and widely used are represented by the immunoenzymic method (ELISA) and by immunoblotting (Western Blot). The contagion occurs by parenteral or mucous membrane exposure to infected blood, by sexual intercourse with individuals who are carriers of retrovirus, and by infected mothers to the foetus.

The number of men with infection from HIV now being higher, women have a greater chance of meeting an infected partner and become infected, too. Besides, the possibility that the virus is sexually transmitted from men to a women, seems higher than that from women to men. Lastly, the foreseeable spreading of the infection through heterosexual intercourse, might involve a parallel increase of cases of vertical transmission of the infection particularly among women.

The prophylactic has been shown capable of reducing by at least 10 years the eventuality of a contagion during intercourse with a seropositive individual. The presence of inflammatory or ulcerous disease of the genitals are considered alienating elements of contagion.

The risk of contagion by a single vaginal sexual intercourse has been evaluated at between 1:100 and 1:500.

Vertical transmission: it is known that all babies who are born of seropositive mothers present anti-HIV antibodies: this, in reality, is only due to the passive transfer of antibodies, and does not mean that all babies are born infected.

In risky sexual intercourse, in addition to the use of the preservative, some spermicidal creams, containing 9 nonoxilo, might be used. Experimentally, such preparations have shown a virucide action, but the irritant effect at the local level has not yet been evaluated.

It is evident that there is a high risk that fertilizing intercourse with a seropositive partner may lead to an infection occurring in a woman undemonstrable until the sixth month of pregnancy. The virus crosses the placenta at about the eighth week of gestation, and this seems to be the most frequent procedure by which the infection is transmitted from the mother to the child.

The contagion may occur not only during pregnancy, but at the moment of birth, too, and probably also through suckling. Maternal antibodies also cross the placental barrier, being able to stay in the baby's organism till the 15th to 18th month of life. For such reasons all babies born of infected mothers are seropositive at birth and diagnosis of anti-HIV antibodies cannot be formulated on the base of researching examinations before 18 months have passed. After this period, seropositivity is no longer linked to the persistence of maternal antibodies any more, but to active production by the baby's organism, in response to the

infection occurred. Such an eventuality occurs in about 20-30% of cases; in the remaining 70-80%, though born seropositive, babies are not infected, and the title of maternal antibodies is progressively reduced till it becomes negative. At present there do not exist clinical, viral or immunological parameters allowing for prediction as to the transmission, or not, from an infected mother to her newborn.

It has not been shown that HIV can cause embryofetopathy, spontaneous miscarriage or prematurity. The babies of seropositive mothers generally are born within the right time limits, with normal anthropometric data and without clinical signs that can be attributed to HIV infection.

The birth of underweight babies seems to be linked more to toxic dependence or to the clinical conditions of the mother than to the infection itself. The incubation time relapsing between the origin and the development of the disease in infected babies varies from 6 months to 6 years. In most cases symptomatology generally appears at the seventh month, and 80% of babies show signs of the disease in the first 2 years of life. Mortality is about 20% in the first year, and the survival is about five years from birth.

#### *Prevention - Informing and Avoiding*

– Information is certainly an effective means of prevention.

– Information means spreading information at all possible levels: high school, industry, family consultation structures and lastly by the mass-media and by all possible forms of commercials.

– Preventive and really valid research, requires the formulation of easily usable protocols, giving the real measure of the frequency and penetration of the individual pathological vulvo-vaginal entities.

– The traditional field where the specialist works has also been widened; in the connections between vulvo-vaginitis

and reproduction, the consideration of woman and the environment, well-being and disease as parts of a dynamic eco-system, may be today, in our opinion, particularly favourable to effective work in preventive and social medicine.

#### *Advice*

1) Abstinence from non-protected intercourse during treatment.

2) Explaining to the couple the importance of checks, and if necessary, treatment in order to interrupt the transmission, both internally and externally, and to safeguard their reproductive capacity.

3) Remembering that the agents of sexually transmitted diseases may be passed on in other ways than sexual intercourse.

4) Always seeking protection from fortuitously encountered sexual intercourse.

5) Remembering that even steady and faithful couples are often subject to infections.

#### *A study programme must include at least:*

a) *In the field of laboratory analysis:* the search for improvement in culture techniques in order to assure greater response, and shorten the response times, and must also stress the importance of even newer diagnostic parameters.

b) *In the field of instrumental diagnostics:* the search and study for new research techniques and the widening of the existing ones.

c) *In the clinical-epidemiological field:* clinical and statistical research as to the real incidence of various pathological situations, in order to obtain data referring to our regions, regarding risks of recurrence, and useful indications as to pathologies towards which more organizational and research effort should be directed in order to improve prevention and diagnosis.

#### CONCLUSIONS

This is an extremely interesting theme for both its medical and social implications, a theme subject to quicken continual technical and scientific innovation, particularly in the field of diagnostics and prevention.

The main micro-organisms able to interfere with the reproductive function have been considered. In particular, the vaginal environment has been studied in its interaction with the seminal fluid, with contraceptives, with sexually transmitted diseases, and with the vulvo-vaginal infectious pathologies specially in reference to reproduction.

Particularly, problems inside the vaginal environment, interactions with spermatozoa, immunological problems and contraception have been considered.

Finally, most importantly, prevention.

#### REFERENCES

- Carr-Hill R. A., Hall M. H.: "The repetition of spontaneous preterm labour". *Br. J. Obstet. Gynecol.*, 1985, 92, 921-8.
- Catlin B. W.: "Gardnerella vaginalis: characteristics, clinical considerations, and controversies". *Clin. Microbiol. Rev.*, 1992, 5, 213-37.
- De Punzio C., Masoni S. et al.: "Typical and atypical lesions of herpes genitalis". *Eur. J. Gynaecol. Oncol.*, 1990, 11, 195-201.
- Drutz D. J.: "Lactobacillus prophylaxis for Candida vaginitis". *Ann. Intern. Med.*, 1992, 116, 419-20.
- Eschenbach D. A.: "Bacterial vaginosis: emphasis on upper genital tract complications". *Obstet. Gynecol. Clin. North Am.*, 1989, 16, 593-610.
- Faro S.: "Bacterial vaginitis". *Clin. Obstet. Gynecol.*, 1991, 34, 582-6.
- Faro S.: "Vaginitis and pregnancy". *J. Reprod. Med.*, 1989, 34, 602-4.
- Hammil H. A.: "Trichomonas vaginalis". *Obstet. Gynecol. Clin. North Am.*, 1989, 16, 531-40.
- Hanna N. F., Taylor-Robinson D. et al.: "The relation between vaginal pH and the microbiological status in vaginitis". *Br. J. Obstet. Gynecol.*, 1985, 34, 123-6.

- Hughes V. L., Hillier S. L.: "Microbiologic characteristics of *Lactobacillus* products used for colonization of the vagina". *Obstet. Gynecol.*, 1990, 75, 244-8.
- Kent H. L.: "Epidemiology of vaginitis". *Am. J. Obstet. Gynecol.*, 1991, 165, 1168-76.
- Mardh P. A.: "The vaginal ecosystem". *Am. J. Obstet. Gynecol.*, 1991, 165, 1163-8.
- Martius J., Eschenbach D. A.: "The role of bacterial vaginosis as a cause of amniotic fluid infection, chorioamnionitis and prematurity". *Arch. Gynecol. Obstet.*, 1990, 247, 1-13.
- Pokorny S. F.: "Prepuberal vulvovaginopathies". *Obstet. Gynecol. Clin. North Am.*, 1992, 19, 39-58.
- Rosenberg M. J., Phillips R. S. *et al.*: "Vaginal douching. Who or why?". *J. Reprod. Med.*, 1991, 36, 753-8.
- Roy S.: "Nonbarrier contraceptives and vaginitis and vaginosis". *Am. J. Obstet. Gynecol.*, 1991, 165, 1240-4.
- Schell C. L., Harris J. H. *et al.*: "Report on *Gardnerella* vaginitis". *Mil. Med.*, 1992, 157, 37-40.
- Sobel J. D.: "Vulvovaginitis". *Dermatol. Clin.*, 1992, 10, 339-59.
- Sparks J. M.: "Vaginitis". *J. Reprod. Med.*, 1991, 36, 745-52.
- Thomason J. L., Gelbart S. M. *et al.*: "Vaginitis in reproductive-age women". *Curr. Opin. Obstet. Gynecol.*, 1990, 2, 656-61.

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