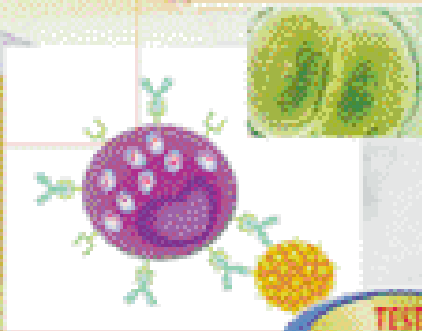


SEPTEMBER 2003 VOL 11 NO 3 ISSN 1681-5552

# the **SQUARE**

*healthcare bulletin*

- ▲ Acne Vulgaris- an Overview
- ▲ Infertility
- ▲ Pelvic Inflammatory Disease
- ▲ Anxiety Disorders
- ▲ Product Profile- Sanit®
- ▲ Medical Breakthrough



TEST  
YOURSELF 11

*Published as a service to medical professionals by*



**SQUARE**  
PHARMACEUTICALS LTD  
BANGLADESH



**IN THIS ISSUE:**

AcneVulgaris- an Overview	... Page 1
Infertility	... Page 4
Pelvic Inflammatory Disease	... Page 8
Anxiety Disorders	... Page 12
Product Profile- Sanit®	... Page 17
Medical Breakthrough	... Page 19

## "the SQUARE"

**Managing Editor**

**Omar Akramur Rab**  
MBBS, FCGP, FIAGP, FRSH

**Executive Editor**

**Latifa Nishat**  
MBBS

**Members of the Editorial Board**

**Muhammadul Haque**  
MBA

**A. H. Mahbub Alam**  
M Pharm, PhD

**Shaokat Zaman**  
MBBS

**Information Assistance**

**Md. Masudul Alam**  
MA

The views expressed in this publication do not necessarily reflect those of its editor or *SQUARE* Pharmaceuticals Ltd. Information in "*the SQUARE*" may be reprinted or translated to other languages without permission but proper credit must be given to "*the SQUARE*".

### From the Desk of Managing Editor

Dear Doctor:

Welcome to this edition of "the *SQUARE*". At first we thank you for your encouraging response regarding the new look of this healthcare bulletin! We strive to continue to bring you the most up-to-date and relevant information in a concise manner every time.

In this issue we have focused on "Acne Vulgaris"- a common skin disease that affect 85-100% of people at sometime during their lives. We also published article on "Infertility" which often creates one of the most distressing life crises that a couple has ever experienced together. In addition you will also find a feature on "Pelvic Inflammatory Disease"- a spectrum of infections of the female genital tract. Besides we highlighted the "Anxiety Disorders"- common psychiatric disorders that physicians encounter in their regular practice.

We are confident that like other previous issues you will also enjoy this issue of "the *SQUARE*" as well!

On behalf of the management of *SQUARE*, we wish you a very blissful and prosperous life.



Omar Akramur Rab

ISSN 1681-5552

Key title: The *SQUARE* (Dhaka)

Abbreviated key title: *SQUARE* (Dhaka)

# Acne Vulgaris- an Overview

Acne vulgaris is a common skin disease in the teenage years. It affects 85-100% of people at some time during their lives. Peak severity is in the late teenage years but acne may persist into the third decade and beyond, particularly in females. It is characterized by noninflammatory follicular papules or comedones and by inflammatory papules, pustules, and nodules in its more severe forms. Acne vulgaris affects the areas of skin with the densest population of sebaceous follicles; these areas include the face, the upper part of the chest, and the back.

## CLINICAL VARIANTS

- ❑ *Conglobate acne*: severe acne with many abscesses and cysts, marked scarring and sinus formation
- ❑ *Acne fulminans*: severe acne accompanied by fever, joint pains and elevated ESR
- ❑ *Acne excoriee*: refers to the effect of scratching or picking, especially on the face of the teenage girl with acne
- ❑ *Infantile acne*: it is rare and due to the sebotropic effects of maternal hormones on the infant.

## CAUSES

- Exogenous substances: chlorinated hydrocarbons, or oily cosmetics, tars, and hair pomades
- Drugs: steroids, lithium, iodides, and some antiepileptic drugs
- Congenital adrenal hyperplasia
- Polycystic ovary syndrome
- Other endocrine disorders with excess androgens production
- Genetic factors

## PATHOPHYSIOLOGY

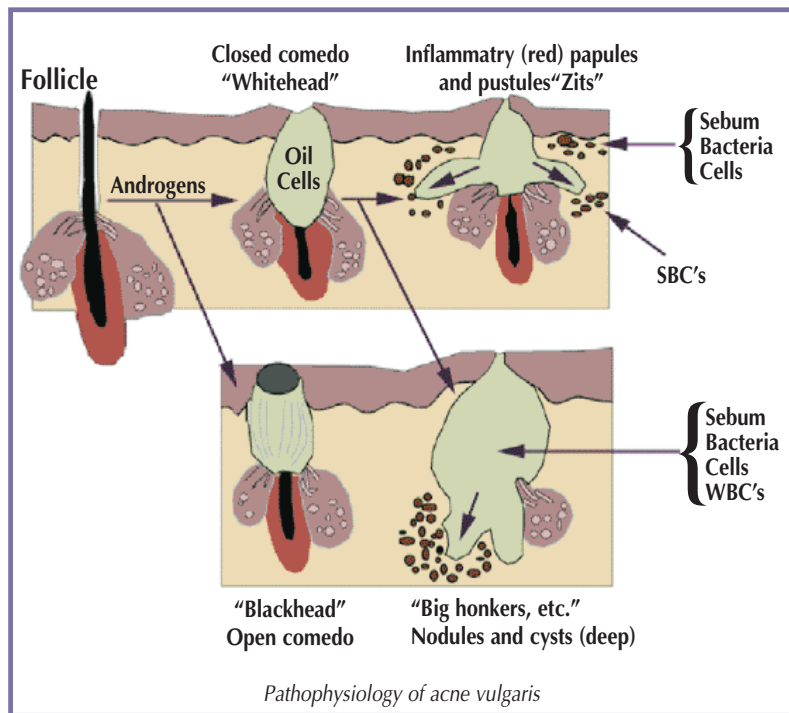
There are four pathogenetic factors

- ❑ Follicular epidermal hyperproliferation and hyperkeratinization
- ❑ Elevated sebum excretion
- ❑ Infection with *Propionibacterium acnes*
- ❑ Occlusion or blockage of the pilosebaceous unit and inflammation.

Follicular epidermal hyperproliferation and abnormal

production of keratin 6 and keratin 16 appear to be one of the primary events in the development of an acne lesion. Increasing levels of the androgen dehydroepiandrosterone sulfate (DHEAS) are correlated with the development of the microcomedon, the primary acne lesion; therefore, these levels may trigger follicular epidermal hyperproliferation. This hyperproliferation may also be stimulated by an alteration in sebum and lipid levels in acne lesions i.e. linoleic acid levels are decreased in acne lesions. Proinflammatory interleukin 1 $\alpha$  (IL-1 $\alpha$ ) and other cytokines may also contribute to follicular hyperproliferation.

Excessive production of sebum is a key factor in the development of acne vulgaris. The amount of sebum produced are strongly correlated to the degree and the



severity of the lesion. Sebum excretion is under hormonal control. Androgens stimulate sebocyte differentiation and sebum production, whereas estrogens have an inhibitory effect. Most men and women with acne have normal circulating levels of androgen hormones. An end-organ hyperresponsiveness to androgens has been hypothesized. ▶

*Propionibacterium acnes* present in many acne lesions. Although, it has not been shown to be present in the earliest stage, its presence in later lesions is almost certain. *P. acnes* stimulates inflammation by producing proinflammatory mediators i.e. interleukin 12 (IL-12), interleukin 8 (IL-8), and tumor necrosis factor (TNF) that diffuse through the follicle wall. Hypersensitivity to *P. acnes* may also contribute to develop inflammatory acne vulgaris in some individuals.

## CLINICAL FEATURES

- ❑ **Symptoms**
  - Local pain or tenderness
  - Systemic symptoms are most often absent in acne vulgaris
  - Depression and anxiety.
- ❑ **Signs**
  - Acne vulgaris may be characterized by the presence of comedones, papules, pustules, and nodules in a sebaceous distribution
  - The skin of the face is the only involved site, but lesion may be found on the skin of shoulders, upper chest and back
  - In comedonal acne, inflammation is absent
  - Inflammatory papules and comedones are present in mild inflammatory acne
  - Moderate inflammatory acne has comedones, inflammatory papules, and pustules
  - Comedones and inflammatory lesions are present in the severe form of acne vulgaris, called nodulocystic acne, and the nodules are large, more than 5 mm in diameter and scarring is often evident.

## DIAGNOSIS

- ❑ The diagnosis is depend on clinical features
- ❑ Total testosterone and DHEAS level should be assessed in a female patient with dysmenorrhea or hirsutism
- ❑ Patients with evidence of Cushing disease should have a 24-hour urine cortisol level
- ❑ In female patients with anovulation and hyperandrogenism, polycystic ovarian syndrome is likely. Lipid levels should be determined in that cases
- ❑ Skin lesion cultures to rule out gram-negative folliculitis are warranted when no response to treatment occurs or when improvement is not maintained.

## DIFFERENTIAL DIAGNOSIS

- ❑ Acne keloidalis nuchae
- ❑ Folliculitis
- ❑ Rosacea
- ❑ Syringoma
- ❑ Demodex folliculitis
- ❑ Papular sarcoidosis
- ❑ Acneiform eruptions
- ❑ Perioral dermatitis
- ❑ Sebaceous hyperplasia
- ❑ Tuberos sclerosi
- ❑ Bacterial folliculitis

## TREATMENT

Therapy should be started at an early stage to prevent scarring. Drug of choice depends on previous treatment, patient acceptability and the type of lesion. Mild acne should be treated initially with a single topical preparation. Treatment of moderate and severe acne requires the use of both systemic and topical agents.

### Medical Care:

#### Topical treatments

- Topical retinoids are comedolytic and anti-inflammatory. They cause epidermal differentiation and, thus, normalize follicular hyperproliferation and hyperkeratinization. Topical retinoids reduce the numbers of microcomedones, comedones, and inflammatory lesions. They may be used alone or in combination with other acne medications. The most commonly used topical retinoids include adapalene, tazarotene, and tretinoin. These retinoids should be applied once daily to clean, dry skin. If irritation reported, the agents may need to be applied less frequently. Skin irritation with peeling and redness may be associated with the use of topical retinoids. The use of mild, nondrying cleansers and noncomedogenic moisturizers may help reduce this irritation. Alternate-day dosing may be used if irritation persists. Topical retinoids thin the stratum corneum, and they have been associated with sun sensitivity. Instruct about sun protection must be given to the patients.
- Topical antibiotics are mainly used against *P. acnes*. They may also have anti-inflammatory properties. Topical antibiotics are not comedolytic, and bacterial resistance may develop to any of these agents. The development of resistance is lessened if topical antibiotics are used in ►

## Acne Vulgaris- an Overview

combination with benzoyl peroxide. Commonly prescribed topical antibiotics include erythromycin and clindamycin alone or in combination with benzoyl peroxide. They may be applied once or twice a day. Gels and solutions may be more irritating than creams or lotions.

- Benzoyl peroxide is also effective against *P acnes*, and bacterial resistance to benzoyl peroxide has not been reported. Benzoyl peroxide may be used once or twice a day. It may cause allergic contact dermatitis.

### Systemic treatments

- Systemic antibiotics have anti-inflammatory properties, and they are effective against *P acnes*. The tetracycline group of antibiotics is commonly prescribed for acne. Minocycline is more effective than tetracycline due to its more lipophilic properties and less *P acnes* resistance to minocycline. The use of erythromycin in the treatment of acne has greatly reduced due to increase resistance of *P acnes* to this agent. Other antibiotics, including trimethoprim, alone or in combination with sulfamethoxazole, and azithromycin, are reportedly helpful.
- Some hormonal therapies may be effective in the treatment of acne vulgaris. Oral contraceptives increase sex hormone binding globulin, resulting in an overall decrease in circulating free testosterone. Spironolactone may also be used in the treatment of acne vulgaris. Spironolactone binds the androgen receptor and reduces androgen production. Pregnancy must be avoided while on spironolactone because of the risk of feminization of the male fetus.
- Isotretinoin is a systemic retinoid that is highly effective in the treatment of severe, recalcitrant acne vulgaris.

### Surgical Care:

- Procedural treatments include manual extraction of comedones and intralesional steroid injections.
- Additionally, some patients may benefit from superficial peels that use glycolic or salicylic acid.
- Phototherapy using red light or blue light and photodynamic therapy are being assessed as potential treatments for acne.
- The usefulness of some laser treatments in the management of acne is also being evaluated.

### Reference:

- Davidson's Principles and Practice of Medicine; 19th Edition
- Julie C Harper, MD, Assistant Professor, Department of Dermatology, University of Alabama at Birmingham
- MEREC Bulletin; National Prescribing Centre; Volume 10; Number 8, 1999

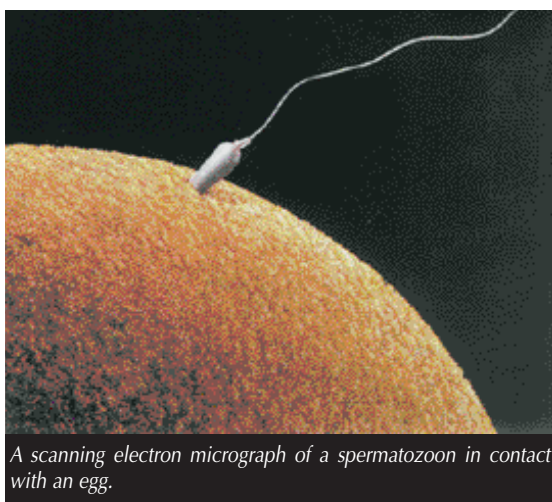
the SQUARE

The advertisement features a purple background with a large, stylized white outline of a person's head and shoulders. In the top right corner, there is a logo consisting of a square with a stylized 'A' inside, and the word 'SQUARE' written vertically to its right. Below the logo, there are three stylized white flowers. The product name 'Fona<sup>®</sup> Cream' is written in a large, white, serif font, with 'Adapalene 0.1%' written in a smaller, white, sans-serif font below it. At the bottom of the advertisement, there is a red banner with the text 'Control Acne' in white, and a black banner with the text 'without skin irritation' in white. At the very bottom, there is a green banner with the text 'We Care for Skin' in white.



Infertility often creates one of the most distressing life crises that a couple has ever experienced together. The long term inability to conceive a child can evoke significant feelings of loss. Coping with the multitude of medical decisions and uncertainties that infertility brings can create great emotional upheaval for most couples.

Infertility is usually defined as not being able to get pregnant despite trying for one year. A broader view of infertility includes not being able to carry a pregnancy to term and have a baby. Primary infertility applies to those who have never conceived, whereas secondary infertility designates those who have conceived at some time in the past. In young healthy couples having frequent intercourse, the chances of pregnancy are estimated to be only 25-30% per month. Infertility affects about 6.1 million Americans, or 10 percent of the reproductive age population, according to the American Society for Reproductive Medicine.



A scanning electron micrograph of a spermatozoon in contact with an egg.

An apparent increase in the prevalence of infertility in developed countries is suggested by analysis trends in the medical visits, which reveals an exponential increase in the number of visit for infertility in the last decade. The reasons for the increase in attention given to infertility are multiple. Couples in some cases have voluntarily delayed childbearing in favor to establishing careers and may have experience an age-related decline in fertility; in some cases the choice of prior contraception (as with use of some intrauterine devices-IUDs) may have contributed to infertility. Having an increase number of sexual

partners leads to a greater chance for exposure to sexually transmitted diseases (STDs), which may contribute to infertility; and couples are less willing to simply accept childlessness and are increasingly aware of the available services and options for resolving infertility.

## ETIOLOGY

Both partners in a relationship contribute to potential fertility, and both may be subfertile. The cause of infertility can include the man, the woman or both. A primary diagnosis of a male factor is made in about 30% of infertile couples, and the man may contribute in another 20-30%. An abnormality in the woman is responsible for the remaining 40-50% of cases.

### □ Male factor

- Endocrine disorders:
  - ▲ Hypothalamic dysfunction (Kallmann's syndrome)
  - ▲ Pituitary failure (tumor, radiation, surgery)
  - ▲ Hyperprolactinemia (drug, tumor)
  - ▲ Exogenous endrogens
  - ▲ Thyroid disorders
  - ▲ Adrenal hyperplasia
- Anatomic disorders
  - ▲ Congenital absence of vas deference
  - ▲ Obstruction of vas deference
  - ▲ Congenital abnormalities of ejaculatory system
- Abnormal spermatogenesis
  - ▲ Chromosomal abnormalities
  - ▲ Mumps orchitis
  - ▲ Cryptorchidism
  - ▲ Chemical or radiation exposure
  - ▲ Varicocele
- Abnormal motility
  - ▲ Absent cilia (Kartagener's syndrome)
  - ▲ Varicocele
  - ▲ Antibody formation
- Sexual dysfunction
  - ▲ Retrograde ejaculation
  - ▲ Impotence
  - ▲ Decreased libido

### □ Ovulatory Factor

- Central defects
  - ▲ Chronic hyperandrogenemic anovulation
  - ▲ Hyperprolactinemia (drug, tumor, congenital) ▶

- Peripheral defects
  - ▲ Gonadal dysgenesis
  - ▲ Premature ovarian failure
  - ▲ Ovarian tumor
  - ▲ Ovarian resistance
- Metabolic disease
  - ▲ Thyroid disease
  - ▲ Liver disease
  - ▲ Renal disease
  - ▲ Obesity
  - ▲ Androgen excess, adrenal or neoplastic
- **Pelvic Factor**
  - Infection
    - ▲ Appendicitis
    - ▲ Pelvic Inflammatory disease (PID)
    - ▲ Uterine adhesions (Asherman's syndrome)
  - Endometriosis
  - Structural abnormalities
    - ▲ DES (Diethylstilbesterol) exposure
    - ▲ Failure to normal fusion of the reproductive tract
    - ▲ Myoma
- **Cervical Factor**
  - Congenital
    - ▲ DES exposure
    - ▲ Mullerian duct abnormality
  - Acquired
    - ▲ Surgical treatment
    - ▲ Infection

**Age:** the effect of aging on male fertility isn't clear. Research suggests that sperm count and quality don't decline until a man is beyond age 64. Aging is an important factor in female infertility.

## DIAGNOSIS

- **Initial assessment:**

Participation of both partners in the initial assessment is ideal and can assist the physician in assessing the dynamics of the relationship. General information regarding reproduction and the timing of events may assist in correcting any misunderstandings about coital frequency, and some myths regarding infertility may be dispelled. Medical history for male or female factors responsible for infertility should be taken during the initial visit.

## Evaluation of male factors:

The initial evaluation of the male should include a general health history and a specific assessment of factors contributing to infertility.

### I. Semen analysis :

A normal semen analysis will usually exclude a significant male factor. Optimum parameters are usually observed after 2 to 3 days of abstinence, and the specimen should be received in the laboratory within 30-60 minutes of production.

### Normal Semen Parameters

Liquification	30 minutes
Count	20-250 million/mL
Motility	>50%
Volume	2-5mL
Morphology	>50% normal
Strict criteria	>14% normal
pH	7.2 - 7.8

Abnormal parameters warrant further investigation and possible referral to a urologist with special interest and expertise in infertility.

### II. Mucus studies:

The initial interaction of sperm and female genital tract can be determined by postcoital examination of the cervical mucus. A satisfactory test results in large numbers of forwardly progressive sperm seen in thin, acellular mucus and indicates a healthy sperm-mucus interaction. The absence of semen indicates an investigation of coital technique or a reevaluation of semen analysis. Intermediate results are not interpretable in terms of assigning a contributing cause of infertility if the semen analysis is normal and the mucus is favorable. When the mucus and timing appear favorable, but the sperm appear immobile, tests for autoantibodies in the male or serum antibodies in the female are indicated. When the mucus is unfavorable in appearance and amount, the timing of the test should be investigated by vaginal ultrasound to detect the presence or absence of a dominant follicle. ►

### III. Other tests:

When the initial evaluation of both of the partners does not reveal a probable cause of infertility or when repeated semen analyses are abnormal, the male factor should be investigated further. More detailed assessment of sperm function may include antibody studies, a sperm penetration assay (hamster egg penetration assay), or more sophisticated assessment of the sperm morphology such as flagellar movement, or of the capacity for the sperm to undergo the acrosome reaction can be assessed. Antibodies studies can determine the presence of autoantibodies. Use of immunobead tests can determine the class of antibody present and the antigenic site (head, tail or midpiece). Autoimmunity is more likely in men with a history of trauma, infection, or previous surgery.

### Evaluation of female factors

#### I. Ovulatory factors:

An ovulatory dysfunction contributes about 20-25% of infertility cases. The problem should be investigated by reviewing of the menstrual history including menarche. Signs and symptoms of systemic disease, particularly hypo or hyperthyroidism and physical findings of any endocrine dysfunctions, eg, hirsutism, galactorrhea, and obesity, should be noted. Serum progesterone assay should be performed in the third week of the cycle, if menstruation is regular. The follicular-phase progesterone will be less than 1 ng/mL, and values greater than 5 ng/mL are consistent with ovulation having occurred. In case of oligomenorrhea, amenorrhea, or short or very irregular menstrual cycles, evaluation of the hypothalamic-pituitary-ovarian axis is warranted, with determination of the serum concentration of luteinizing hormone (LH), follicular stimulating hormone (FSH), and prolactin.

#### II. The pelvic floor:

- a. History and pelvic examination: the pelvic factor includes any abnormalities in uterus, fallopian tubes, ovaries, and adjacent structures eg, salpingitis, appendicitis, use of IUDs, endometritis and septic abortion. Endometriosis is marked as a pelvic cause of infertility, it also worsening dysmenorrhea, dyspareunia. Any history of ectopic pregnancy, adnexal surgery, leiomyomas, or exposure to DES in

utero should be included as a pelvic factor of infertility.

- b. Hysterosalpingogram
- c. Laparoscopy

#### III. The cervical factor:

A cervical factor may be indicated by a history of abnormal Pap smears, postcoital bleeding, cryotherapy, conization, or DES exposure in utero.

### Combined factors & unexplained infertility

In about 20% of couples, combinations of factors will have been found to be suboptimal, and multiple therapies need to be arranged, either sequentially or simultaneously. For the couple with unexplained infertility, the options for testing may seem endless. In such cases, some initial tests need to be repeated.

### THERAPY FOR INFERTILITY

The choice of therapy is depend on individual circumstances, attitude towards surgery, financial status, previous experiences, and reports from friends, relatives. The costs of each possible option, in terms of time, energy, required visits, side effects, loss of intimacy, and expense, should be presented.

#### Male factor infertility

Most causes of male factor infertility require therapy in consultation with a urologist. In case of azoospermia associated with elevated serum concentration of FSH, congenital anomalies, or chromosomal anomalies, donor insemination may be offered. Hormone replacement therapy may be tried if azoospermia is due to hypothalamic or pituitary insufficiency, though the result is variable. In azoospermia due to congenital absence of vas, successful aspiration of sperm from the epididymis, with IVF (In vitro fertilization), offers potential paternity. Azoospermia secondary to vasectomy need microsurgical vasovasostomy, but the outcome depends on the quality of sperm.

When no clear etiology is found in an infertile man with normal physical findings and normal hormone profiles, a number of therapies with no clear substantiation of benefit have been suggested. Use of Clomiphene citrate is the most commonly recommended option. When occupation or environment contributes to consistently elevated scrotal temperatures, modification of these circumstances ►



should be advised. A change in exercise regimen should be recommended when excessive exercise may lead to decrease testosterone level.

Steroid therapy may be recommended to suppress the immune response in man with high levels of autoantibodies to sperm, but the risk of complication and low probability of improvement in fertility leads to recommendation for a trial of IVF. The role of varicocele in the treatment of infertility continues to be controversial.

When semen parameters are normal but results from postcoital examination is repeatedly poor, treatment with intrauterine insemination of washed concentrated sperm has been effective in overcoming an apparent barrier of infertility.

The ultimate therapy for male infertility due to unfavorable sperm parameters, or a negative sperm penetration assay, or both is IVF or GIFT (Gamete intrafallopian transfer) or ZIFT (Zygote intrafallopian transfer). When male infertility is not amenable to therapy, donor insemination offers an opportunity for pregnancy. The use of a donor raises medical, ethical, emotional, and legal issues for the potential parents and the practitioner.

### Female factor infertility

The ovulatory factor: induction of ovulation can be accomplished in 90-95% of patients with chronic anovulation and normal FSH and prolactin. Clomiphene citrate is the first option for induction of ovulation. Corticosteroids, estrogen, or midcycle human chorionic gonadotropin (hCG) may be used as supplementary medication to Clomiphene. Patients with pituitary or hypothalamic insufficiency, and patients with unexplained infertility usually respond to stimulation with human menopausal gonadotropins (hMG). Usually 85-90% of patients can be stimulated to ovulate with hMG treatment, but there is a 20% risk of multiple birth.

The pelvic factor: pregnancy will usually occur following primary conservative procedure for endometriosis, and or salpingitis. Experienced surgical assistance is required when definitive treatment cannot be done during diagnostic laparoscopy. The role of fibroids in infertility is unclear, and most surgeons reserve myomectomy for the treatment of recurrent abortion.

The cervical factor: estrogen can be given during the mid to late follicular phase of the cycle to improve the amount of mucus. If low doses of estrogen are ineffective, using of hMG shows good result. Empiric treatment of the patient and partner with doxycycline if evidence of cervicitis and inflammatory changes are present. Cervical factor patient who do not respond to the above mentioned therapies can be offered IVF or GIFT or ZIFT.

### Unexplained Infertility

There is no definitive treatment can be offered with confidence to couples with unexplained infertility. The cumulative pregnancy rate may be close to 60% over 3-5



*A laparoscope, used for the extraction of a preovulatory ovum.*

years, but the chances of pregnancy in an individual couple decrease with the duration of infertility. Most therapies have not seen to be effective than no treatment. Prior to entering IVF cycle, most programs will offer these patients 3-6 cycles of Pergonal stimulation combined with timed inseminations.

A time limit with expectation of resolution of infertility should be presented, and in some cases guidance toward acceptance of childless living, adoption, use of surrogate pregnancy, or donor insemination should be offered before extensive time and resources are expended on procedures or regimens that offer little potential.

### Reference:

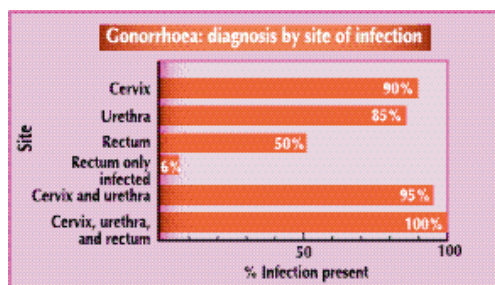
- Current Obstetric and Gynecologic Diagnosis & Treatment; 8th Edition
- Kent M. Van De graaff; Human Anatomy; 4th Edition
- US Department of Health and Human Services, Office on Women's Health

# Pelvic Inflammatory Disease

**P**elvic inflammatory disease (PID) is the single most frequent serious infection encountered by women. Each year in the United States, more than 1 million women experienced an episode of acute PID, with the rate of infection highest among teenagers. More than 100,000 women become infertile each year as a result of PID, and a large proportion of the 70,000 ectopic pregnancy occurring every year are due to the consequences of PID. It is responsible for nearly 250,000 hospitalization per year. PID comprises a spectrum of inflammatory disorders of the upper female genital tract, including any combination of endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis.

## RISK FACTORS

- ❑ **Age:** the incidence of PID is very high in sexually active women younger than 25 years, and decreases as a woman ages
- ❑ **Race:** the incidence is 8-10 times higher in nonwhite than in whites
- ❑ **Socioeconomic status:** higher in women with lower socioeconomic status is due in part to a woman's lack of education and awareness of health and disease and her accessibility to medical care
- ❑ **Contraception:** induced abortion, use of an IUD (Intra uterine device), non-use of barrier contraceptives, and frequent douching
- ❑ **Life style:** high risk behavior, such as drug and alcohol abuse, early age of first intercourse, number of sexual partners, and smoking
- ❑ **Types of sexual practice:** intercourse during menses and frequent intercourse may offer more opportunities for the admission of pathogenic organisms to the inside of the uterus
- ❑ **Disease:** 60-75% of cases of PID are associated with STDs. A prior episode of PID increases the chance of developing subsequent infections.



## CAUSES

- ❑ *N. gonorrhoeae* and *C. trachomatis* traditionally have been considered the etiologic agents of PID, alone or combined
- ❑ Recently, facultative anaerobes consistent with the endogenous vaginal and peritoneal flora have been identified as potential etiologic agents in PID. These include the followings:
  - *Gardnerella vaginalis*
  - *Streptococcus agalactiae*
  - *Peptostreptococcus species*
  - *Bacteroides species (other than B. fragilis)*
  - *Genital Mycoplasma and Ureaplasma species, coliforms*
- ❑ Other nongenital pathogens i.e. *Haemophilus influenzae*, and *H. parainfluenzae*, may be responsible for some cases of PID
- ❑ Actinomyces species have been linked to some PID cases associated with IUD usage
- ❑ In less developed countries, PID may be due to granulomatous salpingitis caused by *Mycobacterium tuberculosis* and *Schistosoma species*.

## CLINICAL FEATURES

- ❑ **Symptoms**
  - The insidious or acute onset of lower abdominal and pelvic pain
  - Pain is usually bilateral, but occasionally unilateral
  - Sensation of pelvic pressure may be present
  - Back pain radiating down one or both legs
  - In most cases, symptoms appear shortly after the onset or cessation of menses
  - There is often an associated purulent vaginal discharge
  - Nausea with or without vomiting may occur
  - Headache and generalized lassitude are common
- ❑ **Signs**
  - Fever >38°C (100.4°F) is diagnostic for salpingitis, but research confirmed acute salpingitis with laparoscopically in only 30% of women
  - Distended abdomen
  - Bowel sound may be hypoactive or absent
  - Inflammation of the periurethral or Bartholin glands
  - Purulent cervical discharge ▶

- Extreme tenderness on movement of the cervix and uterus and palpation of the parametria
- **Laboratory findings**
  - Leukocytosis with a shift to the left is usually present; however the W.B.C. count may be normal
  - Elevated ESR
  - Elevated C-reactive protein
  - Polymorphonuclear leukocytes may contain in purulent cervical smear
  - Culdocentesis generally is productive of "reaction fluid"
  - The cloudy peritoneal fluid reveals leukocytes with or without gonococci or other organisms
  - Culture and sensitivity test of the organisms from culdocentesis may be done, penicillinase production should also be confirmed.
- **Radiograph**
  - X-ray abdomen may show signs of ileus, air may be seen under the diaphragm with a rupture of tubo-ovarian or pelvic abscess

## Diagnostic criteria

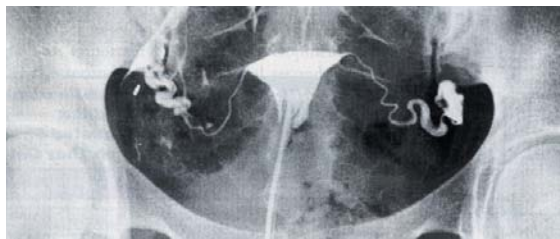
Many episodes of PID go unrecognized. Although some cases are asymptomatic, others are undiagnosed due to the difficulties to recognize the implications of mild or nonspecific symptoms or signs e.g., abnormal bleeding, dyspareunia, or vaginal discharge (atypical PID). Acute PID is difficult to diagnose because of the wide variation in the symptoms and signs. Diagnosis of PID usually is based on clinical findings. The clinical diagnosis of acute PID also is imprecise.

The essentials of diagnosis of acute salpingitis-peritonitis are the followings:

- Onset of lower abdominal and pelvic pain, usually following onset or cessation of menses and associated with vaginal discharge, abdominal, uterine, adnexal, and cervical motion tenderness, plus one or more of the followings
  - Temperature above 38°C (100.4°F)
  - Leukocyte count greater than 10,000/mL
  - Inflammatory mass (on examination / USG)
  - Gram-negative intracellular diplococci in cervical secretions
  - Purulent material (WBC) from peritoneal cavity (culdocentesis or laparoscopy)

## □ The definitive criteria for diagnosing PID:

- ▲ Histopathologic evidence of endometritis on endometrial biopsy,
- ▲ Transvaginal sonography or other imaging techniques showing thickened fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex, and
- ▲ Laparoscopic abnormalities consistent with PID.



A hysterosalpingogram showing the cavity of the uterus and lumina of the fallopian tubes.

## DIFFERENTIAL DIAGNOSIS

- ▲ Acute appendicitis
- ▲ Ectopic pregnancy
- ▲ Ruptured corpus luteum cyst with hemorrhage
- ▲ Diverticulitis
- ▲ Infected septic abortion
- ▲ Torsion of an adnexal mass
- ▲ Degeneration of a leiomyoma
- ▲ Endometriosis
- ▲ Acute urinary tract infection
- ▲ Regional enteritis
- ▲ Ulcerative colitis

## COMPLICATIONS

- ◆ Pelvic peritonitis or generalized peritonitis
- ◆ Prolong adynamic ileus
- ◆ Severe pelvic cellulitis with thrombophlebitis
- ◆ Abscess formation (pyosalpinx, tubo-ovarian abscess, cul-de-sac abscess) with adnexal destruction and subsequent infertility
- ◆ Intestinal adhesions and obstruction
- ◆ Rarely- dermatitis, gonococcal arthritis, or bacteremia with septic shock

## PREVENTION

Approximately 15% of women with asymptomatic gonococcal cervical infection develop acute salpingitis. Detection and treatment of those women and their sexual ▶

partners should therefore prevent a substantial number of cases of gonococcal pelvic infection. Early diagnosis and eradication of minimally symptomatic disease i.e. cervicitis, urethritis also usually prevent salpingitis.

## TREATMENT

All patients with PID require antibiotics. The CDC (Center for Disease Control and Prevention recommends several parenteral and oral regimens in the 1998 Guidelines for Treatment of Sexually Transmitted Diseases. PID treatment regimens must provide empiric, broad-spectrum coverage of likely pathogens. Antimicrobial coverage should include *N. gonorrhoeae*, *C. trachomatis*, anaerobes, Gram-negative facultative bacteria, and *streptococci*. Treatment should be initiated as soon as the presumptive diagnosis has been made, because prevention of long-term sequelae has been linked directly with immediate administration of appropriate antibiotics.

Criteria for hospitalization according to CDC:

- ◆ Surgical emergencies such as appendicitis cannot be excluded
- ◆ The patient is pregnant
- ◆ The patient does not respond clinically to oral antimicrobial therapy
- ◆ The patient is unable to follow or tolerate an outpatient oral regimen
- ◆ The patient has severe illness, nausea and vomiting, or high fever
- ◆ The patient has a tubo-ovarian abscess; or
- ◆ The patient is immunodeficient (i.e., has HIV infection with low CD4 counts, is taking immunosuppressive therapy, or has another disease).

Most clinicians favor at least 24 hours of direct inpatient observation for patients who have tubo-ovarian abscesses, after which time home parenteral therapy should be adequate. Clinical experience should guide decisions regarding transition to oral therapy, which may be accomplished within 24 hours of clinical improvement.

### Parenteral Regimen A

Cefotetan 2 g IV every 12 hours,  
OR  
Cefoxitin 2 g IV every 6 hours,  
PLUS  
Doxycycline 100 mg IV or orally every 12 hours.

### Parenteral Regimen B

Clindamycin 900 mg IV every 8 hours,  
PLUS  
Gentamycin loading dose IV or IM (2 mg/kg of body weight), followed by a maintenance dose (1.5 mg/kg) every 8 hours. Single daily dosing may be substituted.

### Alternative Parenteral Regimens

Ofloxacin 400 mg IV every 12 hours,  
PLUS  
Metronidazole 500 mg IV every 8 hours.  
OR  
Ampicillin/Sulbactam 3 g IV every 6 hours,  
PLUS  
Doxycycline 100 mg IV or orally every 12 hours.  
OR  
Ciprofloxacin 200 mg IV every 12 hours,  
PLUS  
Doxycycline 100 mg IV or orally every 12 hours,  
PLUS  
Metronidazole 500 mg IV every 8 hours.

Ampicillin/sulbactam plus doxycycline has good coverage against *C. trachomatis*, *N. gonorrhoeae*, and anaerobes and appears to be effective for patients who have tubo-ovarian abscess. Both IV ofloxacin and ciprofloxacin have been investigated as single agents. Because ciprofloxacin has poor coverage against *C. trachomatis*, it is recommended that doxycycline be added routinely. Because of concerns regarding the anaerobic coverage of both quinolones, metronidazole should be included with each regimen.

### Oral Treatment

As with parenteral regimens, clinical trials of outpatient regimens have provided minimal information regarding intermediate and long-term outcomes. The following regimens provide coverage against the frequent etiologic agents of PID, but evidence from clinical trials supporting their use is limited. Patients who do not respond to oral therapy within 72 hours should be reevaluated to confirm the diagnosis and be administered parenteral therapy on either an outpatient or inpatient basis.

### Regimen A

Ofloxacin 400 mg orally twice a day for 14 days,  
PLUS  
Metronidazole 500 mg orally twice a day for 14 days. ►

## Regimen B

Ceftriaxone 250 mg IM once,

OR

Cefoxitin 2 g IM plus Probenecid 1 g orally in a single dose concurrently once,

OR

Other parenteral third-generation cephalosporin (e.g., ceftizoxime or cefotaxime),

PLUS

Doxycycline 100 mg orally twice a day for 14 days. (Include this regimen with one of the above regimens.)

## Alternative Oral Regimens

Amoxicillin/clavulanic acid plus doxycycline was effective in obtaining short-term clinical response in a single clinical trial; however, gastrointestinal symptoms might limit the overall success of this regimen. Several recent investigations have evaluated the use of azithromycin in the treatment of upper-reproductive tract infections.

## Follow-Up

Patients receiving oral or parenteral therapy should demonstrate substantial clinical improvement within 3 days after initiation of therapy. Patients who do not demonstrate improvement within this time period usually require additional diagnostic tests, surgical intervention, or both.

## Management of Sex Partners

Sex partners of patients who have PID should be examined and treated if they had sexual contact with the patient during the 60 days preceding onset of symptoms in the patient. The evaluation and treatment are imperative because of the risk for reinfection and the strong likelihood of urethral gonococcal or chlamydial infection in the sex partner. Male partners of women who have PID caused by *C. trachomatis* and/or *N. gonorrhoeae* often are asymptomatic. Sex partners should be treated empirically with regimens effective against both of these infections. Even in clinical settings in which only women are treated, special arrangements should be made to provide care for male sex partners of women who have PID. When that is not feasible, sex partners should be referred for appropriate treatment.

## Special Considerations

### Pregnancy

Because of the high risk for maternal morbidity, fetal wastage, and preterm delivery, pregnant women who have suspected PID should be hospitalized and treated with parenteral antibiotics.

### HIV Infection

Differences in the clinical manifestations of PID between HIV-infected women and HIV-negative women have not been well delineated. In early observational studies, HIV-infected women with PID were more likely to require surgical intervention. In a subsequent and more comprehensive observational study, HIV-infected women who had PID had more severe symptoms than HIV-negative women but responded equally well to standard parenteral antibiotic regimens. In another study, the microbiologic findings for HIV-infected and HIV-negative women were similar, except for higher rates of concomitant *Candida* and HPV infections and HPV-related cytologic abnormalities among HIV-infected women. Immunosuppressed HIV-infected women who have PID should be managed aggressively by parenteral antimicrobial agents.

## PROGNOSIS

A favorable outcome is directly related to the promptness and type of therapy. The incidence of infertility is directly related to the severity of tubal inflammation judged by laparoscopic examination. A single episode of salpingitis has been shown to cause infertility in 12-18% of women. Tubal occlusion was present in only about 10% of those patients regardless of whether or not there had been a gonococcal or nongonococcal infection. Nongonococcal infection predisposed more commonly to ectopic pregnancy, and thus carried a worse prognosis for subsequent viable pregnancy. Follow-up care and education are necessary to prevent reinfection and complications.

### Reference:

- Current Obstetric and Gynecologic Diagnosis & Treatment; 8th Edition
- Center for Disease Control and Prevention -1998 Guidelines for Treatment of Sexually Transmitted Disease
- Stephanie Abbuhl, MD, Medical Director, Associate Professor, Department of Emergency Medicine, University of Pennsylvania School of Medicine
- Department of Health and Human Services; National Institute of Allergy and Infectious Diseases; National Institute of Health, Bethesda, Maryland 20892
- ABC of sexually Transmitted Diseases; 3rd Edition



Anxiety disorders are most common of all mental disorders. These disorders fill people's lives with overwhelming anxiety and fear. Stress, fear, and anxiety all tend to be interactive. The principal components of anxiety are psychologic (tensions, fears, difficulty in concentration, apprehension) and somatic (tachycardia, hyperventilation, palpitation, tremor, sweating). Other organ systems (e.g: gastrointestinal) may be involved in multiple system complaints. Anxiety disorders are chronic, relentless, and can grow progressively worse if not treated. Effective treatments for anxiety disorders are available, and research is yielding new, improved therapies that can help most people with anxiety disorders lead productive, fulfilling lives.

Followings are the different forms of anxiety disorder:

- Panic disorder
- Obsessive-compulsive disorder (OCD)
- Post-traumatic stress disorder (PTSD)
- Social phobia (or social anxiety disorder)
- Specific phobias, and
- Generalized anxiety disorder (GAD)

Each anxiety disorder has its own distinct features, but they are all bound together by the common theme of excessive, irrational fear and dread.

## PANIC DISORDER

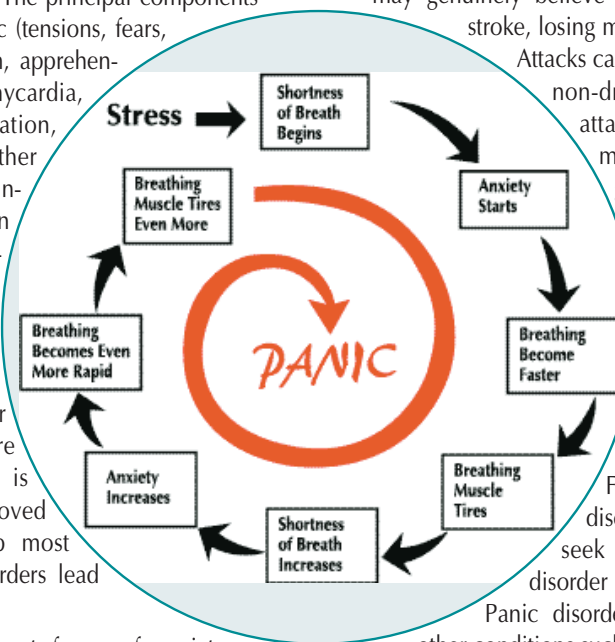
People with panic disorder have feelings of terror that strike suddenly and repeatedly with no warning. They can't predict when an attack will occur, and many develop intense anxiety between episodes, worrying when and where the next one will strike. In between times there is a persistent, lingering worry that another attack could come any minute. When a panic attack strikes one may feel palpitation, sweaty, weakness, faintness, or dizziness, hands may tingle or feel numb,

and might feel flushed or chilled. Chest pain or smothering sensations, a sense of unreality, or fear of impending doom or loss of control may be occurred. One may genuinely believe of having a heart attack or stroke, losing mind, or on the verge of death.

Attacks can occur any time, even during non-dream sleep. While most attacks average a couple of minutes, occasionally they can go on for up to 10 minutes. In rare cases, they may last an hour or more. Panic disorder is twice as common in women as in men. It can appear at any age in children or in the elderly-but most often it begins in young adults.

For those who have panic disorder, though, it's important to seek treatment. Untreated, the disorder can become very disabling.

Panic disorder is often accompanied by other conditions such as depression or alcoholism, and may spawn phobias, which can develop in places or situations where panic attacks have occurred. Some people's lives become greatly restricted-they avoid normal, everyday activities such as grocery shopping, driving, or in some cases even leaving the house. Or, they may be able to confront a feared situation only if accompanied by a spouse or other trusted person. Basically, they avoid any situation they fear would make them feel helpless if a panic attack occurs. When people's lives become so restricted by the disorder, as happens in about one-third of all people with panic disorder, the condition is called agoraphobia. A tendency toward panic disorder and agoraphobia runs in families. Nevertheless, early treatment of panic disorder can often stop the progression to agoraphobia. Studies have shown that proper treatment-a type of psychotherapy called cognitive-behavioral therapy, medications, or possibly a combination of the two-helps 70 to 90 percent of people with panic disorder. Significant improvement is usually seen within 6 to 8 weeks. Cognitive-behavioral approaches teach patients how to view the panic



situations differently and demonstrate ways to reduce anxiety, using breathing exercises or techniques to refocus attention, for example. Another technique used in cognitive-behavioral therapy, called exposure therapy, can often help alleviate the phobias that may result from panic disorder. In exposure therapy, people are very slowly exposed to the fearful situation until they become desensitized to it. Some people find the greatest relief from panic disorder symptoms when they take antidepressants and, or benzodiazepines.

## **OBSESSIVE-COMPULSIVE DISORDER (OCD)**

Obsessive-Compulsive Disorder is characterized by anxious thoughts or rituals that can't be controlled. The disturbing thoughts or images are called obsessions, and the rituals performed to try to prevent or dispel them are called compulsions. There is no pleasure in carrying out the rituals but only temporary relief from the discomfort caused by the obsession. A lot of healthy people can identify with having some of the symptoms of OCD, such as checking the stove several times before leaving the house. But the disorder is diagnosed only when such activities consume at least an hour a day, are very distressing, and interfere with daily life. Most adults with this condition recognize that what they're doing is senseless, but they can't stop it. Some people, though, particularly children with OCD, may not realize that their behavior is out of the ordinary. OCD strikes men and women in approximately equal numbers and afflicts roughly 1 in 50 people. It can appear in childhood, adolescence, or adulthood, but on the average it first shows up in the teens or early adulthood. A third of adults with OCD experienced their first symptoms as children. The course of the disease is variable-symptoms may come and go, they may ease over time, or they can grow progressively worse. Evidence suggests that OCD might run in families. Depression or other anxiety disorders may accompany OCD. And some people with OCD have eating disorders. In addition, they may avoid situations in which they might have to confront their obsessions. If OCD grows severe enough, it can keep someone from holding down a job or from carrying out normal responsibilities at home, but more often it doesn't develop to those extremes. A combination of behavioral treatment and drugs like clomipramine, fluoxetine is often helpful for most patients. Some individuals respond best

to one therapy, some to another. Behavioral therapy, specifically a type called exposure and response prevention, has also proven useful for treating OCD. It involves exposing the person to whatever triggers the problem and then helping him or her forego the usual ritual-for instance, having the patient touch something dirty and then not wash his hands. This therapy is often successful in patients who complete a behavioral therapy program, though results have been less favorable in some people who have both OCD and depression.

## **POST-TRAUMATIC STRESS DISORDER (PTSD)**

Post-Traumatic Stress Disorder (PTSD) is a debilitating condition that follows a terrifying event. Often, people with PTSD have persistent frightening thoughts and memories of their ordeal and feel emotionally numb, especially with people they were once close to. PTSD, once referred to as shell shock or battle fatigue, was first brought to public attention by war veterans, but it can result from any number of traumatic incidents. These include kidnapping, serious accidents such as car or train wrecks, natural disasters such as floods or earthquakes, violent attacks such as a mugging, rape, or torture, or being held captive. The event that triggers it may be something that threatened the person's life or the life of someone close to him or her. Or it could be something witnessed, such as mass destruction after a plane crash. Whatever the source of the problem, some people with PTSD repeatedly relive the trauma in the form of nightmares and disturbing recollections during the day. They may also experience sleep problems, depression, feeling detached or numb, or being easily startled. They may lose interest in things they used to enjoy and have trouble feeling affectionate. They may feel irritable, more aggressive than before, or even violent. Seeing things that remind them of the incident may be very distressing, which could lead them to avoid certain places or situations that bring back those memories. PTSD can occur at any age, including childhood. The disorder can be accompanied by depression, substance abuse, or anxiety. Symptoms may be mild or severe- people may become easily irritated or have violent outbursts. In severe cases they may have trouble working or socializing. In general, the symptoms seem to be worse if the event that triggered them was initiated by a person- such as a rape, as opposed to a flood. Ordinary events can serve as ►

reminders of the trauma and trigger flashbacks or intrusive images. Not every traumatized person gets full-blown PTSD, or experiences PTSD at all. PTSD is diagnosed only if the symptoms last more than a month. In those who do have PTSD, symptoms usually begin within 3 months of the trauma, and the course of the illness varies. Some people recover within 6 months, others have symptoms that last much longer. In some cases, the condition may be chronic. Occasionally, the illness doesn't show up until years after the traumatic event. Antidepressants and anxiety-reducing medications can ease the symptoms of depression and sleep problems, and psychotherapy, including cognitive-behavioral therapy, is an integral part of treatment. Being exposed to a reminder of the trauma as part of therapy—such as returning to the scene of a rape—sometimes helps. And, support from family and friends can help speed recovery.

## PHOBIAS

Phobias occur in several forms. A specific phobia is a fear of a particular object or situation. Social phobia is a fear of being painfully embarrassed in a social setting. And agoraphobia, which often accompanies panic disorder, is a fear of being in any situation that might provoke a panic attack, or from which escape might be difficult if one occurred.

### Specific Phobias

Many people experience specific phobias, intense, irrational fears of certain things or situations—dogs, closed-in places, heights, escalators, tunnels, highway driving, water, flying, and injuries involving blood are a few of the more common ones. Phobias aren't just extreme fear; they are irrational fear. Adults with phobias realize their fears are irrational, but often facing, or even thinking about facing, the feared object or situation brings on a panic attack or severe anxiety. Specific phobias strike more than 1 in 10 people. No one knows just what causes them, though they seem to run in families and are a little more prevalent in women. Phobias usually first appear in adolescence or adulthood. They start suddenly and tend to be more persistent than childhood phobias; only about 20 percent of adult phobias vanish on their own. When children have specific phobias—for example, a fear of animals—those fears usually disappear over time, though they may continue into adulthood. No one knows why

they hang on in some people and disappear in others. If the object of the fear is easy to avoid, people with phobias may not feel the need to seek treatment. Sometimes, though, they may make important career or personal decisions to avoid a phobic situation. When phobias interfere with a person's life, treatment can help. Successful treatment usually involves a kind of cognitive-behavioral therapy called desensitization or exposure therapy, in which patients are gradually exposed to what frightens them until the fear begins to fade. Three-fourths of patients benefit significantly from this type of treatment. Relaxation and breathing exercises also help reduce anxiety symptoms.

### Social Phobia

Social phobia is an intense fear of becoming humiliated in social situations, specifically of embarrassing oneself in front of other people. It often runs in families and may be accompanied by depression or alcoholism. Social phobia often begins around early adolescence or even younger. The most common social phobia is a fear of public speaking. Sometimes social phobia involves a general fear of social situations such as parties. More rarely it may involve a fear of using a public restroom, eating out, talking on the phone, or writing in the presence of other people, such as when signing a check. Although this disorder is often thought of as shyness, the two are not the same. Shy people can be very uneasy around others, but they don't experience the extreme anxiety in anticipating a social situation, and they don't necessarily avoid circumstances that make them feel self-conscious. In contrast, people with social phobia aren't necessarily shy at all. They can be completely at ease with people most of the time, but particular situations, such as walking down an aisle in public or making a speech, can give them intense anxiety. Social phobia disrupts normal life, interfering with career or social relationships. About 80 percent of people who suffer from social phobia find relief from their symptoms when treated with cognitive-behavioral therapy or medications or a combination of the two. Therapy may involve learning to view social events differently; being exposed to a seemingly threatening social situation in such a way that it becomes easier to face; and learning anxiety-reducing techniques, social skills, and relaxation techniques. The medications that have proven effective include antidepressants, MAO ▶

inhibitors. People with a specific form of social phobia called performance phobia have been helped by drugs called beta-blockers. For example, musicians or others with this anxiety may be prescribed a beta-blocker for use on the day of a performance.

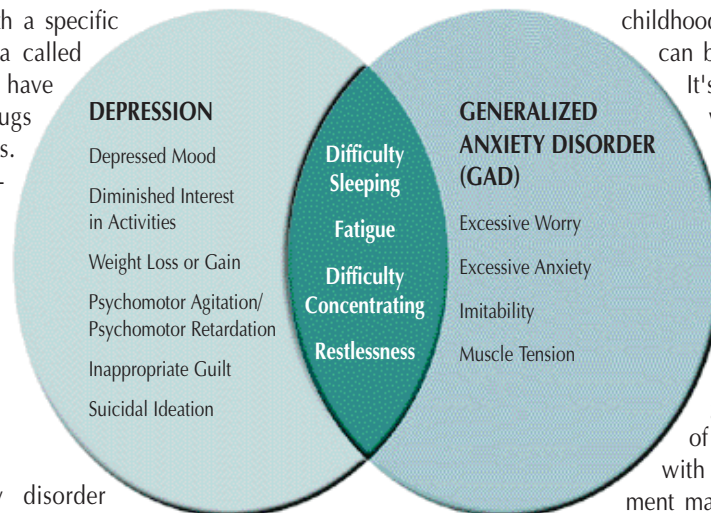
## GENERALIZED ANXIETY DISORDER (GAD)

Generalized anxiety disorder (GAD) is much more than the normal anxiety people experience day to day. It's chronic and exaggerated worry and tension, even though nothing seems to provoke it. Having this disorder means always anticipating disaster, often worrying excessively about health, money, family, or work. Sometimes, though, the source of the worry is hard to pinpoint. Simply the thought of getting through the day provokes anxiety. People with GAD can't seem to shake their concerns, even though they usually realize that their anxiety is more intense than the situation warrants. People with GAD also seem unable to relax. They often have trouble falling or staying asleep. Their worries are accompanied by physical symptoms, especially trembling, twitching, muscle tension, headaches, irritability, sweating, or hot flashes. They may feel lightheaded or out of breath. They may feel nauseated or have to go to the bathroom frequently. Or they might feel as though they have a lump in the throat.

Many individuals with GAD startle more easily than other people. They tend to feel tired, have trouble concentrating, and sometimes suffer depression, too.

Usually the impairment associated with GAD is mild and people with the disorder don't feel too restricted in social settings or on the job. Unlike many other anxiety disorders, people with GAD don't characteristically avoid certain situations as a result of their disorder. However, if severe, GAD can be very debilitating, making it difficult to carry out even the most ordinary daily activities.

GAD comes on gradually and most often hits people in



childhood or adolescence, but can begin in adulthood, too.

It's more common in women than in men and often occurs in relatives of affected persons. It's diagnosed when someone spends at least six months worried excessively about a number of everyday problems. In general, the symptoms of GAD seem to diminish with age. Successful treatment may include a medication called buspirone. Research into the effectiveness of other medications, such as benzodiazepines and antidepressants, is ongoing. Also useful are cognitive-behavioral therapy, relaxation techniques, and biofeedback to control muscle tension.

Research into the effectiveness of other medications, such as benzodiazepines and antidepressants, is ongoing. Also useful are cognitive-behavioral therapy, relaxation techniques, and biofeedback to control muscle tension.

## DRUGS USED IN ANXIETY DISORDERS

The major classes of medications used for various anxiety disorders are described below.

### Antidepressants

A number of medications that were originally approved for treatment of depression have been found to be effective for anxiety disorders

- **Selective serotonin reuptake inhibitors (SSRIs)**, the newest antidepressants act in the brain on serotonin. SSRIs tend to have fewer side effects than older antidepressants. Nausea, sexual dysfunction may be reported by some of the patients, when they first start taking SSRIs, but that usually disappears with time. An adjustment in dosage or a switch to another SSRI will usually correct bothersome problems. Fluoxetine, sertraline, fluvoxamine, paroxetine, and citalopram are among the SSRIs commonly prescribed for panic disorder, OCD, PTSD, and social phobia. SSRIs are often used to treat people who have panic disorder in combination with OCD, social phobia, or depression. Venlafaxine, a drug closely related to the SSRIs, is useful for

treating GAD. These medications are started at a low dose and gradually increased until they reach a therapeutic level.

- **Tricyclic antidepressants (TCA)** are started at low doses and gradually increased. Tricyclics have been around longer than SSRIs and have been more widely studied for treating anxiety disorders. For anxiety disorders other than OCD, they are as effective as the SSRIs, but many physicians and patients prefer the newer drugs because the tricyclics sometimes cause dizziness, drowsiness, dry mouth, and weight gain. When these problems persist or are bothersome, a change in dosage or a switch in medications may be needed. Tricyclics are useful in treating people with co-occurring anxiety disorders and depression. Clomipramine, the only antidepressant in its class prescribed for OCD, and imipramine, prescribed for panic disorder and GAD, are examples of tricyclics.
- **Monoamine oxidase inhibitors (MAOIs)**, are the oldest class of antidepressant medications. The most commonly prescribed MAOI is phenelzine, which is helpful for people with panic disorder and social phobia. Tranylcypromine and isopropcarb-oxazid are also used to treat anxiety disorders. People who take MAOIs should be put on a restrictive diet because these medications can interact with some foods and beverages, including cheese and red wine, which contain a chemical called tyramine. MAOIs also interact with some other medications, including SSRIs. Interactions between MAOIs and other substances can cause dangerous elevations in blood pressure or other potentially life-threatening reactions.

## Anti-Anxiety Medications

High-potency benzodiazepines relieve symptoms quickly and have few side effects, although drowsiness can be a problem. Because people can develop a tolerance to them-and would have to continue increasing the dosage to get the same effect- benzodiazepines are generally prescribed for short periods of time. One exception is panic disorder, for which they may be used for 6 months to a year. People who have had problems with drug or

alcohol abuse are not usually good candidates for these medications because they may become dependent on them.

Some people experience withdrawal symptoms when they stop taking benzodiazepines, although reducing the dosage gradually can diminish those symptoms. In certain instances, the symptoms of anxiety can rebound after these medications are stopped. Benzodiazepines include clonazepam, which is used for social phobia and GAD; alprazolam, which is helpful for panic disorder and GAD; and lorazepam, which is also useful for panic disorder.

Bupirone, a member of azipirones, is a newer anti-anxiety medication that is used to treat GAD. Possible side effects include dizziness, headaches, and nausea. Unlike the benzodiazepines, bupirone must be taken consistently for at least two weeks to achieve an anti-anxiety effect.

## Other medications

Beta-blockers, such as propranolol, are often used to treat heart conditions but have also been found to be helpful in certain anxiety disorders, particularly in social phobia.

## References

- Current Medical Diagnosis & Treatment: 2003
- U.S. Census estimated residential population age 18 to 54 on July 1, 1998.
- National Institute of Mental Health of USA, 1998.
- British Journal of Psychiatry Supplement, 1998; (34): 24-8.
- American Journal of Psychiatry, 1990; 147(6): 685-95; 1995; 152: 973-81.
- Psychopharmacology Bulletin, 1997; 33(3): 381-90.
- Journal of Psychopharmacology, 2000; 14(2 Suppl 1): S5-S12.
- Annual Review of Psychology, 2000; 51: 445-79.
- Canadian Journal of Psychiatry, 1999; 44(1): 34-9.
- Journal of Anxiety Disorders, 1988; 2: 227-41.
- Behavior Genetics, 1995; 25(6): 499-515.
- Social Psychiatry and Psychiatric Epidemiology, 1990; 25(6): 314-23.
- Archives of General Psychiatry, 1992; 49(4): 267-72.
- Biological Psychiatry, 1998; 44(12): 1229-38.
- Annals of the New York Academy of Sciences, 821.
- The New York Academy of Sciences, 1997.
- Psychiatric Clinics of North America, 1997; 20(4): 741-68.
- National Academy of Sciences USA, 1999, 96(9): 5263-7.
- Scientific American Medicine. Volume 3.
- Healthon/WebMD Corp., 2000, Sect. 13, Subject. VIII.



# Product Profile

17

Sanit<sup>®</sup> tablet

## COMPOSITION

Sanit<sup>®</sup> tablet: Each film coated tablet contains Nortriptyline 10 mg (as Nortriptyline HCl BP) and Fluphenazine HCl BP 0.5 mg.

## PHARMACOLOGY

Nortriptyline hydrochloride is a tricyclic antidepressant. Nortriptyline inhibits the uptake of norepinephrine and serotonin at nerve terminals. In contrast to its parent compound amitriptyline which is equally potent in inhibiting the uptake of norepinephrine and serotonin, Nortriptyline has a greater effect on norepinephrine reuptake than on serotonin reuptake.

Fluphenazine is a tranquilizer of the phenothiazine type with piperazine side chain. Fluphenazine primarily acts as a neuroleptic drug whose main therapeutic effect is believed to reside in potent dopamine (specially D<sub>2</sub>) receptor antagonism. Due to the nature of the two active constituents and the larger inter and intra subject variability seen in trials, accurate and consistent pharmacokinetic data are not available. This can be illustrated by the fact that studies of nortriptyline hydrochloride have produced half life values ranging from 16 to 38 hours. In the case of Fluphenazine hydrochloride these values have been 10 to 16 hours.

## INDICATION

Sanit<sup>®</sup> provides effective therapy in the management of patients exhibiting mild to moderate anxiety, tension and/or agitation with or without co-existing depression.

Various forms of neurosis (anxiety, hysteria, depression, neurasthenia), disorder of sleep are amenable to treatment with Sanit<sup>®</sup>.

Sanit<sup>®</sup>, in addition, patients exhibiting general neurotic feelings, fear, mild to moderate depression and mild to moderate anxiety have responded well to Sanit<sup>®</sup>.

## DOSAGE AND ADMINISTRATION

*Adult:* One Sanit<sup>®</sup> tablet three times daily. The course of the treatment should be limited to three months. If the patient does not respond after 4 weeks, an alternative treatment should be given.

*Children:* Not indicated for the treatment of children.

*Elderly:* Elderly patients should be started on one Sanit<sup>®</sup> tablet twice daily. If one tablet three times a day required subsequently three tablets may be given.

## CONTRAINDICATION AND PRECAUTION

Phenothiazines and tricyclic antidepressants have been shown to lower the threshold for electrically induced convulsions in animals; hence, this combination is not recommended for patients with a history of epilepsy or brain damage. This combination is further contraindicated in patients with blood

dyscrasias, severe cardiac insufficiency, renal or liver damage. It is inadvisable to give monoamine oxidase inhibitors (MAOIs) with this combination, nor should they be given in two weeks after cessation of treatment with MAOIs.

This combination should be given with caution to patients with glaucoma and to those who have a propensity for urinary retention. This combination should be used with caution in patients with cardiac failure, especially when there is evidence of rhythm disturbance and in patients with recent myocardial infarction.

## SIDE EFFECT

Tardive dyskinesias have been reported in phenothiazine therapy, usually after prolonged courses given at doses adequate to control psychotic illness. Consequently, treatment with this drug should be limited to three months.

Dryness of mouth, drowsiness, faintness and constipation. Occasionally tachycardia, nasal congestion, blurred vision and excitement are seen.

Extrapyramidal reactions are unlikely to occur with this dose of fluphenazine alone, and it is probable that the anticholinergic activity of nortriptyline affords protection against such effects. As with all neuroleptic drugs the presence of unexplained hyperthermia could indicate neuroleptic malignant syndrome. In this event, this combination and associated neuroleptic treatment should be discontinued until the origin of the fever has been determined.

## DRUG INTERACTION

Interaction with barbiturates, alcohol and narcotic drugs may occur, so central nervous depressants should be administered with caution. This combination may diminish the anti-hypertensive effect of an adrenergic blocking agent and could potentiate the pressor response to locally injected sympathomimetic agents.

## USE IN PREGNANCY AND LACTATION

Do not use during pregnancy, especially in the first and last trimesters unless there are compelling reasons. There is no evidence as to drug safety in human pregnancy, nor are the results of animal studies conclusive. Breast feeding is not recommended for women receiving this combination.

## OVERDOSE

Overdose should be treated symptomatically and supportively. Extrapyramidal symptoms are amenable to anti-parkinsonian drugs.

In severe hypotension, circulatory shock should be managed.

## PHARMACEUTICAL PRECAUTION

Store below 25°C. Protect from light & moisture.

## HOW SUPPLIED

Sanit<sup>®</sup> tablet: Box containing 10x10 tablets in blister pack.



## Correct answers of the 'Test Yourself - 12'

1. c & d    2. c & d    3. b & d    4. c    5. b & d    6. b & c

The following are the 10 winners of the "Test Yourself -12"; they have been selected through lottery.

*Congratulations from "the SQUARE" Editorial Board*

**Dr. Syed Altaf-uz-Zaman** MBBS  
Medical Officer  
BRAC, Shushastho, Valuka, Major Vita  
Mymensingh

**Capt. Jesmin Akhter** MBBS  
Medical Officer  
Mymensingh Girls Cadet College  
Mymensingh

**Dr. Habibur Rahman** MBBS, MPH  
UH&FPO  
Chandina, Comilla

**Dr. Syed Amanul Islam** MBBS  
MO, Digholia THC  
Digholia, Khulna

**Dr. Rokhana Begum (Molly)** MBBS  
Gynae Ward  
Mohammad Ali Hospital  
Bogra

**Dr. D K Biswas** MBBS, DTM&H  
West Bakalia  
D.C. Road, Chawkbazar  
Chittagong

**Dr. Jiban Krishna Sarker** MBBS  
MO, Upazila Health Complex  
Dhobaura, Mymensingh

**Dr. Fauzia Akhtar Huda** MBBS  
Lifeline Hospital, Munshipara  
Dinajpur

**Dr. Sandipan Ghose** MBBS  
MO, Upazila Health Complex  
Bagha, Rajshahi

**Dr. Md. Hossanuzzaman** MBBS, FCGP  
233/6, B.B. Road  
Press Club Bhaban, Narayanganj



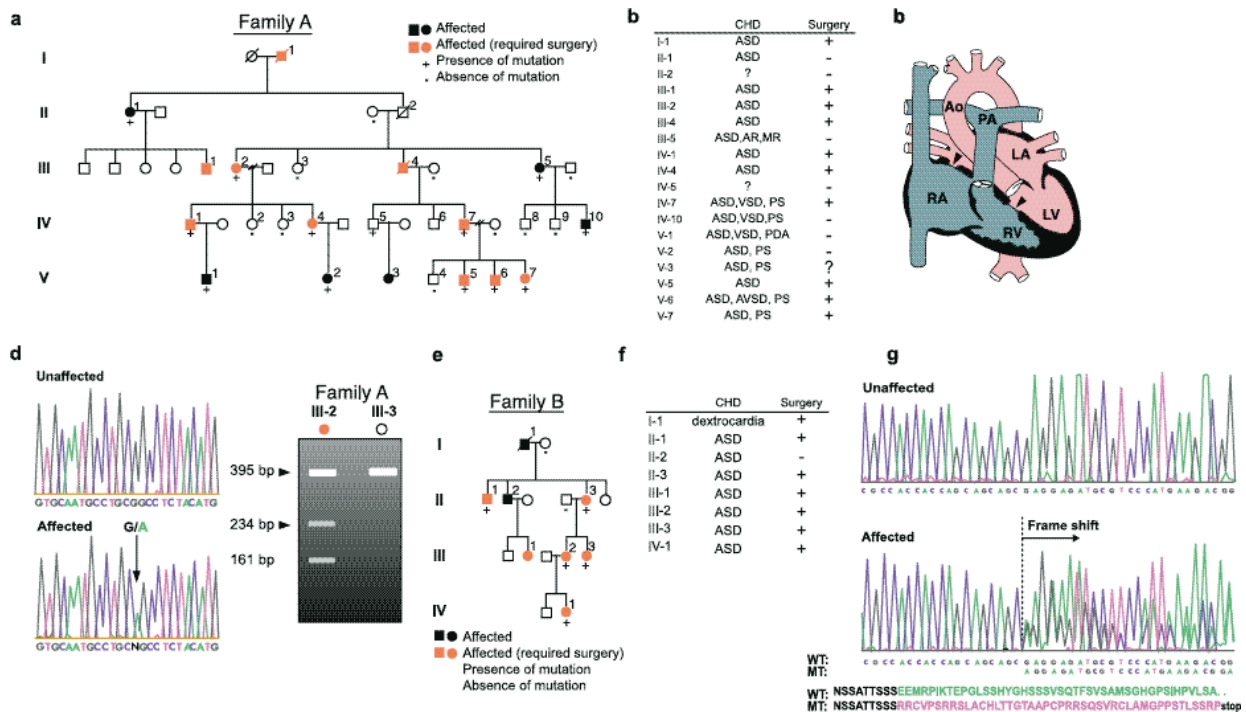
# Test Yourself

13

- The followings are true for PID except:
  - PID may be due to granulomatous salpingitis caused by *Mycobacterium tuberculosis*.
  - Transvaginal sonography, laparoscopic abnormalities are only definitive criteria for PID
  - Intestinal obstruction, abscess formation, pelvic peritonitis are common complications of PID.
  - Treatment should be started as soon as the presumptive diagnosis has been made.
- All the following points are true for the treatment of PID except:
  - All patients of PID require antibiotics.
  - Antimicrobial coverage should include *N. gonorrhoeae*, *C. trachomatis* and *Streptococci*.
  - Patients not responding to oral therapy within 48 hours should be reevaluated to confirm diagnosis.
  - Patient receiving treatment should show substantial clinical improvement within three days after initiation of treatment.
- All the followings are correct for infertility except:
  - Pituitary failure, mumps, orchitis, thyroid disorder, PID are some of the causes of infertility.
  - Semen analysis, mucus studies, antibody studies, sperm penetration assay are the male factors evaluation tests.
  - Normal Pap smears, postcoital bleeding, cryotherapy are the cervical factors in infertility.
  - Clomiphene citrate is the only option for ovulation induction.
- The following points are true for Acne Vulgaris except:
  - The lesion may be found on the skin of shoulders, upper chest and back.
  - Adapalene, tretinoin and tazarotene are most commonly used systemic agents for acne treatment.
  - The tetracycline group of antibiotics is generally prescribed for acne.
  - Bacterial resistance is uncommon with topical antibiotics for the treatment of acne.
- The followings are correct for Sanit® (Nortriptyline) except:
  - Effective in mild to moderate anxiety, tension and/or agitation.
  - Used in various forms of neurosis and sleep disorders.
  - In the patients with general neurotic feelings and fear.
  - The usual adult daily dose is one tablet and treatment should be limited to three months.
- All the points mentioned below are true for anxiety disorders except:
  - Panic attack may occur any time, even during dream sleep.
  - OCD strikes men and women in approximately equal numbers and it never run in families.
  - PTSD is diagnosed only if the symptoms last more than one month.
  - Fluoxetine, sertraline, paroxetine etc. are among the SSRIs commonly prescribed for panic disorder, OCD, PTSD.

## Gene Discovery Could Save Babies' Lives

A new genetic discovery could one day allow to save the lives of babies born with heart defects. Scientists have identified a gene that may underlie many of the inherited disorders. About 1% of babies are born with congenital heart defects, the leading cause of death in non-infected newborn infants. The risk jumps to 5% for parents who already have an affected child. One of the main disorders occurs when walls separating the heart's four chambers do not form properly. The US scientists found that mutations in the gene GATA4 can lead to these conditions, known as cardiac septal defects. They believe interfering with the gene's effects could prevent the problem occurring before a child is born. Scientists said the work could also help in future screening of people with heart defect genes. The risk of a baby being born with a heart problem if either parent has the mutant form of GATA4 is 50 per cent. So far, only one other gene has been linked with congenital heart disease. Scientists are still trying to find others.

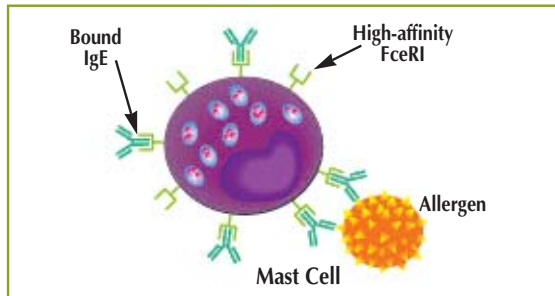


**Figure 1** GATA4 mutations segregate with familial cardiac septal defects. *a*, Kindred with five generations (indicated in Roman numerals) affected by congenital heart defects (CHDs). Participating members of each generation are indicated numerically. III-1, V-3 and deceased family members were not available for mutation analysis. *b*, Types of CHDs and need for surgical repair in affected family members. Echocardiography or operative data were available for all subjects except for I-1, II-2 and IV-5. *c*, Atrial and ventricular septal defects, indicated by arrowheads, in schematic and echocardiogram of a representative family member. Ao, aorta; AR, aortic regurgitation; ASD, atrial septal defect; AVSD, atrioventricular septal defect; LA, left atrium; LV, left ventricle; MR, mitral regurgitation; PA, pulmonary artery; PDA, patent ductus arteriosus; PS, pulmonary stenosis; RA, right atrium; RV, right ventricle; VSD, ventricular septal defect. *d*, Sequence chromatogram displaying G to A transition of nucleotide 886, generating a new PstI restriction enzyme site in exon 3 of GATA4 that resulted in the appearance of 234-bp and 161-bp fragments of a 395-bp PCR product in affected members of family A. *e*, Second pedigree affected by CHDs, as described in *f*. *g*, Sequencing revealed a single nucleotide deletion that was linked to disease and altered the GATA4 sequence after amino acid 359, resulting in a premature stop codon. The wild type (WT) and predicted mutant (MT) protein sequences are shown. Two (II-2 and III-1) affected members were not available for the mutation study.

Nature: Vol, 424: N 6947: 2003. ►

## The First Biotechnology Drug for Asthma

The U.S. Food and Drug Administration have recently approved a bioengineered medication omalizumab. The drug is used to treat the patients with severe acute asthma, who are not responding to inhaled steroids and



allergy injections and who even require oral steroids to keep them out of the hospital. It is the second line of treatment, recommended only after first-line treatments have failed. The drug is not approved for the children under the age of 12 years; and it is known to work and approve only for patients with moderate to severe, allergy-related asthma. Omalizumab prevents to release chemical mediators from the mast cells and basophils by inhibiting the binding of IgE antibodies to the high-affinity IgE receptor (FcεRI) on the surface of mast cells and basophils. Reduction in surface-bound IgE on FcεRI-bearing cells limits the degree of release of mediators of the allergic response. Treatment with the drug also reduces the number of FcεRI receptors on basophils in atopic patients. The drug will be given by injection about once a month. Dosage depends on the body weight of the patients. It is the first biotechnology drug for asthma, the likely price at \$ 1,000 per month or \$ 10,000 per year.

*HealthDay News; June 25, 2003*

## Gene for Cancer Breakthrough

Scientists have made a breakthrough in cancer treatment after unlocking the secret of a gene which combats the condition. The naturally occurring human gene called Alternate Reading Frame (ARF), appears to shield healthy cells from sinister signals which may otherwise turn them cancerous. A team of scientists at the University of Dundee found that mimicking the action of the keystone molecule known as ARF, could herald an exciting anti-cancer treatment. The ARF could kill cancerous cells

outright, or at least make them more sensitive to chemotherapy. The scientists investigated whether ARF, which controls the growth of and destroys damaged cells, could prevent some of the critical stages in the development of cancer. They found that feeding it to cancer cells knocked out the action of NF-kappaB, a molecule which encourages the transformation of healthy cells to cancerous ones.

*Internet; 24th July, 2003*

## End of Human Infertility!

Scientists say artificially created sperm and eggs could spell the end of infertility in 10 years. They believe it will be achieved by combining stem cell technology and fertility treatment. Stem cells are the body's unprogrammed "master" cells. Those taken from early-stage embryos can potentially be made to develop into any tissue in the human body. Scientists at the cutting edge of fertility research think it is only a matter of time before the technique is used to re-build sperm and egg cells. Researchers believe in future everybody who is infertile can be helped and able to take cells and reconstruct the equivalent of sperm and eggs."



Stem cells

*ANANOVA: Thursday July 24, 2003.*

## Adhesive to Mend Lung!

Surgeons in Newcastle have saved the life of a three-year-old boy by mending his punctured lung with surgical adhesive in a procedure similar to fixing a tyre. The procedure, carried out on Hassan Chaudhary, is believed to have been the first time the operation was performed in Britain. The youngster's lungs collapsed during treatment for a serious infection and doctors told his parents, that he might not survive. His left lung collapsed while he was being treated for the infection, which had already destroyed his right lung. The heart surgeon, and his specialist team in Newcastle inflated the boy's left lung using a small "balloon" and glued up the puncture in the lung wall to stop it deflating. The operation was a complete success, is now expected to make a full recovery.

*ANANOVA: Monday July 21, 2003.*



**Friendly to Patient - Wider in Action**

**Robic**<sup>®</sup>  
Ornidazole 500 mg tablet

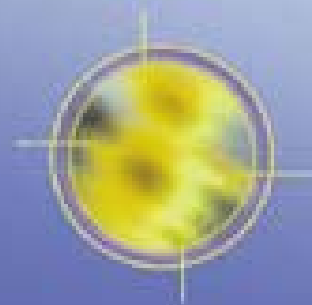


**Excellent Cure Rates**

- ★ 100% in vaginal trichomoniasis
- ★ 94.6% in amoebic liver abscess
- ★ 90% in intestinal amoebiasis

**Devoid of metallic after-taste**

**Overcoming all drawbacks**



**Trevox**<sup>®</sup>

Levofloxacin 250 & 500 mg tablet



*The patient friendly fluoroquinolone*



**SQUARE...**

**... is replacing**

**Canesten<sup>®</sup> cream with**

**Afun<sup>®</sup> Cream**

Clotrimazole 1% BP



healthcare bulletin **the SQUARE** September 2003, Vol 11; No 3

Medical Services Department, **SQUARE PHARMACEUTICALS LTD.**, Corporate Headquarters, SQUARE CENTRE  
48, Mohakhali Commercial Area, Dhaka-1212, Tel : 8827729 - 38, 8817729 - 38, Fax : 880 -2-882 8608 / 882 8609  
E-mail : square@bangla.net, Web Page : <http://www.square-bd.com>, Omar Akramur Rab <omar@squaregroup.com>

Production PharmaScope