## Current Dermatological Therapy

A series of articles on the current dermatological therapy will feature in the pages of the journal. Articles are contributed this year by Dr. P. Sugathan, M.D, Associate Professor, Department of Dermatology & Venereology, Medical College Hospital, Calicut.

# ACNE VULGARIS - 'THE BOILS OF LUST'

"What is your fortune my pretty maid?
My face is my fortune sir, she said"

— Nursery rhyme

Indeed the face is still the fortune of many maids unless it is pock marked by that chronic inflammation of the pilosebaceous units of the face, which we call acne vulgaris. The colloquial term '*Kama — Kuru*' (Boils of lust) is possibly based on the casual observation that in the majority of individuals the onset of acne coincides with the development of secondary sexual characters. That acne is certainly an androgen dependent disease, there is no doubt[1] but it is preposterous to assume that acne patients are 'over sexed' because available laboratory data do not corroborate it[2,3,4]. However in women with acne the urinary excretion of 5 alpha-androstane-3 alpha 17 beta-diol was found to be higher[5,6] This reflects the rate of formation of dihydrotestosterone, the active form of androgens.

It is safe to assume that acne vulgaris is primarily a problem of teenagers of affluent societies. The average age of onset is about 16 though it is not unusual to encounter it during the second or third decade of life. Soft living and unrestricted eating habit appear to contribute to the genesis or aggravation of acne[7]. But strong and conflicting opinions abound whether diet significantly influences the course of acne[8,9,10]. If acne means only few comedones and papules its incidence is close to 100%. The true incidence of acne vulgaris depend upon many variables. In the Medical College Hospital, Calicut it is 0.3% per annum. Higher incidence is reported from other countries[11].

The first significant study on the pathologic dynamics of acne vulgaris was that of Strauss and Kligman[12]. Formally developed and evolved into the 'free fatty acid (FFA) hypothesis', it still stands as the best workable explanation currently available for the pathogenesis of acne[13]. The FFA hypothesis postulates that under androgenic stimulation the sebaceous glands undergo hypertrophy and produce more sebaceous lipids. The increased flow of sebaceous lipids and perhaps the androgen itself induce hyperkeratosis of the infundibulum of the hair follicle and result in stasis of sebaceous lipids. Corynebacterium acnes, an anaerobic diphtheroid colonize in this lipids. This organism produces an extracellular enzyme called lipase which cleaves the triglycerides into

glycerol and FFA. Glycerol may serve as an energy source for the organism and the FFA by-products are comedogenic and induce inflammation[14-18]. Coagulase negative staphylococci are also found normally in the sebaceous follicles and similarly show lipolytic activity, in vitro[19]. Except for the presence in greater quantity of a minor component of fatty acid octa-deca-5-8 dienoic acid[20] the composition of sebum in acne vulgaris is not different from the normal. The role of lipase in the aetiopathogenesis of acne vulgaris is questioned. Based on the results of studies with a specific enzyme inhibiting organophosphate, O, O-Dimethyl-O-(3, 5, 6, trichloro-2 pyridyl) phosphate (DH-818) Fulton[21] favoured the previous hypothesis of Kligman[22] that acne is a genetic disease of altered keratinization and the initial fault is a 'retention hyperkeratosis'. Electron-microscopic observations of Knutson[23] also indicate that follicular keratinization is abnormal in acne patients. Thus the old concept of Sutton[24] that the fault of acne is in the terrain and not the flora is gaining acceptance.

Whatever be the arguments at the academic level regarding the aetiopathogenesis of acne vulgaris, therapeutically we have come a long way from the second century axiom 'Tempos varos curat' : Time cures acne[25]. Based on our understanding of the current concept of the pathogenesis of acne a rational approach to therapy may be devised[26]. No two Dermatologists give the same instructions and carry out the same therapeutic proceedures in acne vulgaris. So, here, I shall emphasize my own views.

Motivation : Unless the patient is sufficiently motivated, no treatment is likely to be successful. A simple explanation regarding the nature of the disease and the aims of treatment is essential to dispel any illusion the patient may have about the disease. This is very vital as the pimply young sitting in front of you may be influenced by friends, parents and of course the persuasive commercial publicity. The first point to be stressed is that the treatment of acne is "tailor made". There are no magic cures out of the bottle for acne. A careful family history and personal history, particularly of diet and drugs, may be useful. The severity of the disease is assessed on the basis of grading from 1 to 4. Actual counting of the number of lesions may be ideal but unnecessary unless you are doing some sort of investigative work. Therapeutic modalities may be divided into local treatment, physical therapy and systemic treatment.

Acne excoriee des jeunes filles is the clinical designation for the illdefined hyperpigmented lesions with excoriation marks mostly on the forehead and cheeks. It is the mark of self mutilation by a neurotic young person, who has practically no acne. Strict instructions to abstain from picking the face and local application of calamine lotion is all that is required.

Cleanliness : There are r pid adherents to the liberal and frequent use of soap and water as the treatment of acne. Excessive use of soap even in acne patients is harmful and antibacterial soaps do not have any superiority over the others[27], in the management of acne. Excessive use of soap may in fact favour the formation of comedones[28]. Reasonable personal hygiene is all that is required. Any one who does not care for that won't turn up for treatment of acne anyway.

Exfolients : 'Dry and peel' used to be the dictum in the past and it still is. The time honoured combination is sulphur precipitated and salicylic acid in calamine lotion, water or alcohol. Precipitated sulphur though discredited[29] is certainly useful as a drying agent. The concentration of sulphur

and salicylic acid required vary from 1 to 25%. It is best to start from the lowest concentration and build up the intensity[30]. Commercially available calamine lotion dries up rather fast, which will alter the concentration of the ingredients. Success with this modality of treatment requires the help of an honest dispensing chemist. The medicine should be dispensed in wide mouthed containers. The patient should be instructed to paste a strip of paper vertically on the bottle to mark the fluid level. If drying up is noticed it may be reconstituted with water. Test application on a small area is a wise precaution, each time the prescription is refilled or renewed. Resorcinol may also be used instead of salicylic acid. The choice is based on availability of the chemical or personal preference. I have no personal experience with Eu de Alibour.

Retinoic acid was introduced in 1969[31] for the treatment of acne. It is an irritant and causes significant erythema and peeling. This irritant effect speeds up cellular turnover, increases the rate of production of loose horny cells in the follicular canal, thus preventing formation of new comedones and tend to unseat existing ones[32]. Initial reports from India[33-36] and Singapore[37] showed that it is most effective in grade I and II types of acne. In the pigmented people post-inflammatory hyperpigmentation may be a problem. It is available as a cream in India. The lotion in disposable foil packs were found to be more acceptable and useful in my experience. It is best avoided in patients who are out door workers and it is useless in acne of grade III and IV.

Benzoyl peroxide is a very useful new addition in the treatment of acne. It is a potent precursor of free-radical oxygen and benzoic acid. On the skin the sulphydryl type of amino acids (cysteine and homocysteine) initiate the break down of benzoyl peroxide with the release of free-radical oxygen. This penetrates into follicle and reduces FFA by its cidal action on corynebacterium acnes population. Combined therapy with topical tretinoin and benzoyl peroxide gel, applied at different times of the day, result in greater clinical improvement than with either drug alone[38,39]. Benzoyl peroxide is the most elegant, though expensive, local medication now available for the treatment of acne. It is effective in all types of acne except grade IV.

The latest in the field of topical anti-acne preparations are the antibiotics. Tetracycline HCL in ethanol-water-solution with n-decyl Methyl sulfoxide as a penetration enhancer is found to be effective[40]. Erythromycin gluceptate as a 2% alcoholic solution[41] and Clindamycin phosphate[42,43,44] are also reported to be effective topically. This precludes the prolonged use of systemic antibiotics and its inherent adverse effects. Further, it is argued that local application achieves a greater concentration of the antibiotic at the site of activity. Yellowish staining of the skin is an undesirable side effect with tetracycline HCL.

Comedo extraction: As inflammation is a tissue reaction to the comedo lipids it is logical to assume that removal of this might improve acne. I don't think comedo extractor is a popular instrument even with the dermatologists. There are instruments with cups too deep and opening too large or too small and their thickness interferes hopelessly with visualization. No self-respecting dermatologist will tolerate working with this equipment. This difficulty can be overcome by using a sterile No. 19 needle which can be used also for a tiny episiotomy from the mouth of the follicle outwards wherever required. This procedure

helps to pop out the comedo without applying undue pressure. It is a jeweller's job and a tedious one but the results of meticulous attention repay the pains[24]. The needle can also be used for draining small pustule. I prefer to aspirate the cystic lesions. Intralesional triamcinalone acetonide 0.25 to 10 mgm/ml is the ideal. The dose is 0.05 ml to 2.5 ml depending on the size of the lesion. I prefer a mantoux syringe and No. 26 BD needles to a dermojet for this injections.

Dermabrasion, though often mentioned as a treatment for the scars of acne is not very popular even in the west. With our patients intractable post-inflammatory hyperpigmentation is a problem. Carbon dioxide snow with acetone and powdered sulphur and liquid nitrogen are reported to be effective, but only in experienced hands. In a country like India with abundant ultra violet light I don't think there is any place for it in the treatment of acne. Superficial X-rays were very popular once but the serious sequelae and dangerous complications that may ensue rules out its use in an otherwise benign dermatosis.

Systemic treatment: Systemic antibiotics particularly tetracyclines, erythromycin and clindamycin have proven efficiency in the treatment of acne. It is most effective in grade III and IV. Bacterial inhibition, reduction of lipase elaboration, reduction of FFA, chelation of enzymes and metallic ions have all been demonstrated to be the mechanism of action of antibiotics[45]. Either one or all these can be considered as possible reason to use antibiotics in the treatment of acne. Even though photosensitivity and dose related Diabetes insipidus may be cited as contraindications, for long term therapy, safety data on long term therapy for 3 to 6 months is abundant. However, I like to use tetracycline HCL for grade III and IV type of acne only. After clinical response is visible the dose is reduced to 250 mgm per day, thus avoiding side effects of prolonged therapy, like moniliasis, colitis and gram negative folliculitis.

Long acting sulphonamides and oral hypoglycaemic agents as well as diuretics are largely useless in the treatment of acne. However DDS in the dose of 50 to 100 mgm daily was found to be a useful adjuvant to the usual antibiotics in the treatment of grade IV acne. This is perhaps due to the antiinflammatory effect of the drug. Short courses of systemic steroids may have to be administered at times in severe and extensive grade IV acne, keeping in mind the known complication of systemic steroid therapy such as steroid acne.

Antiandrogens: As oestrogen is the natural antagonist of androgens attempts were made early to use it for the treatment of acne vulgaris. Undesirable side effects precluded its use in the male patients. When the 'pill' became a reality every one believed that it is the definitive solution for the acne problem at least in the females. However irreversible chloasma and other serious systemic side effects have now made it less popular even among the gynaecologists! It can't be used in a teenager for obvious reasons. The ideal patient for the pill in my judgement is a newly married girl suffering from acne who would also like to avoid pregnancy; thus justifying the risks involved.

Drugs which interfere with the action of androgens at their target organs are called antiandrogens[46]. They are potentially useful in the treatment of acne vulgaris and other androgen dependent diseases like hirsutism and male-pattern baldness. The mechanism of action of androgens are complex and poorly understood. Available data indicate that androgens are first converted into more active dihydrotestosterone (DHT) by an enzyme

5-alpha reductase. It is then bound to a receptor protein present in the target cell cytoplasm. This receptor-DHT complex then moves into the cell nucleus, where it stimulates RNA synthesis. Subsequent physiological changes in the receptor organ are brought about by this RNA. Therefore two classes of antiandrogens are possible. Those which inhibit the end-organ reduction of testosterone to DHT and those which interfere with the binding of DHT to the receptor protein. 4 androsten-3-one-17 beta-carboxylic acid is an example of the former and cyproterone, cyproterone acetate, 17 alpha Methyl B-nortestosterone, and flutamide examples of the latter. Unfortunately none of these drugs show any end-organ specificity, and exhibit multiple antiandrogenic effects, thus limiting their clinical usefulness. If we succeed in developing an antiandrogen which affect only the skin the treatment of acne vulgaris may become meaningful and successful. The search continues.

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