SUMMARY
The inspiration of the present study came from the recently known modulatory effects of sex steroids, growth hormones, neuro hormones, peptide growth factors on immune cells like macrophages, natural killer cells, cytokines and immunoglobulin. Clues were also drawn from the user of neurogeneration drugs like naltrexone in chronic degenerative diseases like Alzheimer’s, multiple sclerosis and Parkinson’s disease etc. The clinical research presented in the present thesis is the treatment of some inflammatory and degenerative disease processes, which could not be cured successfully by the conventional therapy.

The cross talk among sex steroids, growth hormone, cytokine and immune cells may benefit in the control of inflammatory and degenerative processes occurring in acute and chronic diseases.

The hypothesis was tested in 57 patients referred to the author or those who directly approached him and were started on the study protocol after obtaining their consent. The institutional human ethical committee approved the study. The subjects were classified broadly into the following groups: arthritis, morbid obesity, inflammatory skin diseases, multiple organ dysfunction and failure.

> The cases were grouped according to age, sex and disease category and were compared with age and sex matched cases of the same disease categories, taken from hospital records, but treated by other routine protocols.
All the cases were assessed clinically and studied by the investigations of routine hematological, biochemical, radiological investigations.

Scanning of various organs and assessment of organ functions were done by ultrasound, computer aided tomography, magnetic resonance imaging nuclear scans as warranted by the basic disease conditions.

Hormonal assays were done in relevance to the disease, gender and the hormonal treatment schedules like hormone replacement therapy (HRT) with oestrogen and or progesterone in females and testosterone in males and the treatment schedule with recombinant growth hormone (rhGH).

The arthritic cases were given rhGH in doses of 2-4 international units (2-4 IU) at about 7 to 9 pm and on a five day week schedule or twice or thrice a week schedule. Oestrogen and progesterone combination of HRT in females and testosterone in males were given in addition wherever the respective hormone levels were found to be low. The doses were usual standard ones like 0.625mg of conjugated oestrogen or minimum dose oestradiol preparations and progesterone depot preparations given as fortnightly or monthly intramuscular shots. Testosterone was given in males usually by the intramuscular route with depot oil preparations.

The beneficial results of pain relief, healing of wounds, improvement in the pain free and wider range of movements and the improvement and
stabilization of organ function (kidney, heart and brain), evidenced by biochemical parameters were assessed subjectively and objectively.

Four male patients in the age group of 35 and 50 who had shoulder joint and hip joint osteoarthritis with radiological evidences were studied. They had no evidence of hypertension or diabetes. Their routine hematological, biochemical tests were normal and all of them had low levels of total and free testosterone, low or normal LH levels, normal FSH levels and normal cortisol and GH levels. Three of them were severely affected and bed-ridden. They were treated with testosterone enanthate preparations of long acting nature, 250 mg once in 2 weeks by intra muscular route and they were also given rhGH 3 units by subcutaneous route daily in the night for 5 days a week for 2 weeks and subsequently twice a week for 2 months. Dramatic improvement of pain relief, free and painless mobilization were achieved in these patients. Four patients, who had associated diabetes mellitus, were also taken up for the same schedule and they showed clinical relief of pain and also better stabilization of glycaemia. All the patients on follow up after 2 months showed normalization of all the hormone levels including LH and testosterone. Three patients, who were given only testosterone also had clinical improvement, which was slower and lesser than those treated with testosterone and growth hormone.

Four female patients of the age group of 43 and 45, all of menopausal phase, with low back ache and hip and knee joint arthritis were taken up for the study. All of them had low back ache, cervicoscapular joint pains, stiffness and restriction of range of movements and were unresponsive to
usual measures of NSAIDS, physiotherapy and traction. Their routine hematology and biochemistry were studied and found to be normal except low calcium levels in four subjects. All of them had low oestradiol levels, raised FSH and LH levels and normal cortisol and GH levels. None had diabetes or hypertension. They were treated with oestrogen by transdermal route daily and depot preparations of progesterone, once in 3 weeks. rhGH was given as 3 units subcutaneously daily for 5 days a week for 2 weeks and subsequently, twice a week for 2 months. All of them were completely relieved of their pains and subsequently followed up on regular HRT (with oestrogen and progesterone), exercises and relaxation therapy. Three females were given only HRT in the beginning. Their response in pain relief and stiffness was partial. They were subsequently given rhGH along with HRT and were completely relieved of pain and stiffness. All the cases were followed up after 2 months course of the study protocol and were found to have normal levels of hormones including oestradiol, progesterone and LH.

Four menopausal women of the age group 40 and 50 with severe and extensive pemphigus and three female cases of the same age group with severe and extensive psoriasis were also included in the study. After their routine hematological and biochemical workup, their hormonal status was assessed. All of them had normal thyroid functions, high FSH and LH levels, low oestradiol and GH levels. They were treated with HRT with transdermal oestrogen daily and depot preparations of progesterone (once in three weeks by intramuscularly) and rhGH by subcutaneous route of three units daily for 5 days a week for one month and subsequently twice a week for 2 months.
The consistent effect of weight reduction in morbid obesity patients by the use of recombinant growth hormone can be explained by the following postulations.

1. Cortisol-sparing and anti-lipogenic effects of growth hormone in morbid obesity patients who have a pseudo-cushing status of cortisol action.

2. Resistance of insulin receptors to insulin are also reverted to normal response by growth hormone (with its beneficial effects on lipid metabolism).

3. Obesity dulls the action of hormones like thyroxine and leptin and hence the adipocytes go into a steady state of heightened avidity for fatty acids. This is often spoken of as adipocyte inflammatory state and growth hormone helps to revert this inflammation.
Since all of them had earlier irregular use of cortisone they were weaned off the cortisol doses and the sluggish hypothalamic-pituitary-adrenal axis, by ACTH injection of 40 units intramuscularly once a week for 5 weeks. All the patients were completely relieved of their skin lesions (infected and non-infected) in two months and were followed up subsequently on HRT with oestradiol and progesterone. Their follow up of hormone levels were normal.

Three male subjects of the age group of 35 and 45, and four female subjects of the same age group (all menopausal) with morbid obesity of 130 kilograms and above were taken up for study. All of them had trunkal obesity, exertional dyspnoea and abrasive skin lesions of the groin, making their day-to-day mobility difficult and weight reduction by exercise impossible. Their clinical work up of cardiac status and metabolic parameters were normal. Ventilatory insufficiency was evident in pulmonary function test. Their hormone levels were normal, except low normal testosterone and oestradiol levels. They were treated with rhGH by subcutaneous route in the night five days a week for two months. All of them showed reduction of weight of 15 to 30 kilograms in two months and amelioration of breathlessness and healing of intertrigenous skin lesions, making them freely moving about and being able to perform easy exercises for burning of calories for further weight reduction. More than anything was the improvement and total change of their attitude, self-image and confidence.

Four male and three female cases of diabetes mellitus with secondary complications in skin, joints, retina and peripheral nerves, who were
developing multi system complications like cardiac, renal and stroke related sequelae, were taken up for the study protocol and were treated additionally with rhGH and HRT schedules. All of them improved significantly in their multiple organ functions.

Seven cases of multiple organ failure, receiving critical care treatment in intensive care units (for stroke, myocardial infarction and post head injury and post trauma conditions) were taken up for the study protocol and were given recombinant growth hormone. Two of them, females, on initial hormone replacement schedule alone, showed only partial improvement in clinical condition and so after 10 days of initiating the treatment with hormone replacement, they were also given additional GH and they showed all round betterment of clinical and biochemical parameters.

The findings of the study support the hypothesis. It is postulated that the non-classical actions of hormones like growth hormone, testosterone, oestrogen and progesterone can be used in clinical settings of disease processes, involving inflammation, degeneration and cell apoptosis. These hormones can help to revert, arrest and improve such disease processes and thus help to improve basic disease condition in cases like rheumatoid and osteoarthritis and the secondary complications of diabetes mellitus in various organ systems. Though this treatment schedule is not a specific measure against the major diseases mentioned, this certainly helps the underlying basic disease process, namely inflammation and degeneration in a very big way. This method of management is not known or recognized hitherto.