CHAPTER V

SUMMARY AND CONCLUSIONS
Majority of the coagulase positive and alpha haemolysin positive strains, 26 out of 27, were found to be pathogenic to mice. With coagulase positive, alpha haemolysin negative strains there was a significant difference in pathogenicity as well as mortality in mice. The size of the lesions were also smaller than of the first group. However, 50 per cent of the coagulase negative strains were also pathogenic, indicating that coagulase production cannot be the sole factor determining the pathogenicity of a strain.

When purified alpha lysin was added to coagulase positive, alpha lysin negative strains their virulence was significantly more enhanced than when coagulase was added to coagulase negative, alpha lysin positive strains. It appears that both coagulase and alpha lysin production are the two most important characters determining pathogenicity. It has been concluded from present observations that coagulase production is an important factor for the initiation of infection. It serves to protect the organism from the first line of defense and thereby helps in multiplication and formation of adequate concentration of other toxic metabolites. The tissue injury which is the essence of infection and which initiates the classical inflammatory response is attributed to alpha lysin.

Of the other active agents production of hyaluronidase, leucocidin and fibrinolysin all seem to play a secondary role. In enhancing the primary effects of coagulase and alpha lysin
all of them alone or in combination are effective bacterial agents which are able to modify the local tissue environment in favour of invasion, both local and distant.

The fact that hyaluronidase production is a character which is equally distributed in strains obtained from active lesions as well as those from carrier indicate its secondary role. It is also significant that coagulase negative strains obtained from active lesions produce effective concentrations of hyaluronidase. Taken as a whole there is a close parallelism between coagulase, alpha lysin and hyaluronidase activities. Such strains which elaborate all those three are relatively more virulent. That experimental lesions could be produced by hyaluronidase negative strains which are both coagulase positive and alpha lysin positive and many hyaluronidase positive strains were non-pathogenic to mice - confirms the secondary importance of this enzyme in the total armamentarium of staphylococcic products. It has been concluded that hyaluronidase activity, when present, is an added parasitic factor which helps in dissemination. On the other hand, excess of hyaluronidase production may have a reverse effect by diluting the concentration of bacterial population.

The leucocidin activity follows almost a similar pattern and comparative analysis of its relation to pathogenicity vis-à-vis coagulase and alpha lysin activities indicates a secondary role. It is of interest that the closest correlation of leucocidin
production is with capacity to produce alphalysin. The adjuvant role of leucocidin in helping the invading organisms against leucocytes and thereby ensuring an environment for uninterrupted bacterial multiplication must be regarded as an important though secondary virulence factor.

The fibrinolytic activity closely followed that of leucocidin. It seems to have a secondary role which appear to be more important like hyaluronidase for local and systemic dissemination.

The analysis of other well recognised characters like production of acid phosphatase, lipase, gelatinase, Muller's phenomenon, beta and delta haemolysins are shared by the pathogenic, coagulase positive, alpha lysin positive strains. They seem to be associated with the overall biochemical make up of pathogenic staphylococci but they do not seem to play any important or significant role in pathogenicity.

It has been postulated that the ultimate potentiality of any strain of producing a number of agents mostly proteinous in nature, may depend on their capacity to synthesise or utilise certain specific amino acids. Amino acid analysis of different strains of organisms having different biological properties do not however indicate any significant difference in their basic amino acid pattern. It is however significant that mouse passage of some of the strains resulted in the appearance of new amino acid like aspartic acid along with emergence of an important biological character viz. production of alpha lysin. This correlation appears
It seems reasonable therefore to conclude that some amino acid like aspartic acid is related in some way with the capacity of a strain either inherent or acquired for producing alpha lysin, one of the most important pathogenic armamentarium in the parasite.

The sugar reactions, viz. the capacity of fermentation both aerobically and anaerobically glucose and mannitol are shared by the majority of pathogenic strains. There is a much closer correlation between ability to ferment glucose with coagulase activity. While over 50 percent of coagulase negative strains were able to ferment mannitol only 1 percent of these strains were able to ferment glucose.

An attempt to correlate virulence with antibiotic resistance indicate that there is no relationship between development of such resistance with any significant alteration in the basic biological character of pathogenic staphylococci. Contrary to some reports majority of the single or multiple drug resistant strains were coagulase positive. Drug resistance, however, is significantly lower in coagulase negative strains.

Mouse passage leads to increase in virulence as indicated by acquirement of new character like production of alpha lysin. There was no alteration however in some of the strains and in others there was decline in one or the other virulence factors.

In an attempt to demonstrate the role of host factors it has been confirmed that previous experience with small inoculum renders the host hypersensitive and more prone to acquire infection
when challenged subsequently with a small dose which otherwise is innocuous. Repeated exposure of large doses leads to acquired resistance.

One may conclude therefore that staphylococci produces a battery of enzymes. Some of them are of primary importance in determining their pathogenicity. Others are more like adjuvant factors which enhances the effects. Once the organism has gained a foot-hold and has produced tissue destruction, a number of other characters which are shared by these strains seem to complete the complex biochemical make up of the organism and cannot be directly related to any one of its important biological properties viz. of pathogenicity and virulence. The results confirms that the production of disease is a summation of opposing forces, one the inherent or acquired characters in the host and the other, the potential biochemical make up of the parasite and its capacity to produce metabolite of wide variety which help the bacteria in the initiation of infection like coagulase activity, in producing tissue injury like alpha toxin, in paralysing local defenses as leucocidin and in helping dissemination such as hyaluronidase and fibrinolytic activity. It must be conceded that the host factors play an equally important role which determines whether under a given conditions actual disease will be produced irrespective of the potential pathogenic character of the bacterium. Any condition which alters the reaction of the host, non-specific or specific, genetic or acquired resistance, and development of hypersensitivity determines the ultimate outcome of infection.