6. PATHOGENESIS OF ACINETOBACTER INFECTIONS:

Pathogenesis is discussed and reviewed under two headings - predisposing factors and virulence factors exhibited by Acinetobacter spp., as this organism is characterised as relatively low-grade pathogen.

6.1 Predisposing Factors:

Numerous risk factors elaborated with severe infection due to Acinetobacter spp. have been identified. Some of these factors also apply to other organisms responsible for nosocomial infection. Susceptible patient populations include those who have undergone major surgery, those with severe underlying disease like malignancy, burns and immunosuppression. Another important factor is advanced age especially elderly patients. However, neonatal infection due to Acinetobacter has also been documented (Ng et al., 1989; Stone et al., 1985).

Most detailed studies of risk factors have involved studies of respiratory tract infections, and a number of factors have been suspected or identified as increasing the risk of pneumonia or colonization of the lower respiratory tract by Acinetobacter spp. (probably A. baumannii in most cases) in the ICU; these include advanced age, chronic lung disease, surgery, immunosuppression, use of antimicrobial agents, presence of
device which are invasive such as gastric and endotracheal tubes, type of respiratory equipment used (Bergogne-Berezin et al., 1991; Buxton et al., 1978; Castle et al., 1978; Lortholary et al., 1995; Struelens et al., 1993). Many of these factors are interrelated and only few studies on potential risk factors have used essential statistical modelling to define the independent risk factors (Lortholary et al., 1995).

Lortholary and co-workers studied 40 patients infected or colonized with *A. baumannii*, and these patients were compared by logistic regression analysis with 348 noninfected and noncolonized patients who were admitted in the ICU at the same time. They also demonstrated that the severity of the underlying disease, as evaluated by the APACHE II score (Knaus et al., 1985), and the presence of previous infection that needed antimicrobial treatment were the important independent risk factors for acquiring *A. baumannii* infection.

Another case control study demonstrated the duration of the ICU stay before colonization or infection with *Acinetobacter* spp. was significantly longer for infected patients than the controls (14.7 versus 5.9 days; *P*=0.002). Same study showed infected patients received respiratory therapy for significantly longer time than the controls (14.7 versus 6.6 days; *P*=0.006) (Peacock et al., 1988).

Extended ICU stay due to severe underlying disease, prolonged respiratory treatment with mechanical ventilation and prior antimicrobial therapy are all important predisposing factors to *Acinetobacter* infection. Hence judicious use of antibiotics in management of these infections in ICU should be the high priority. Indiscriminatory
use of antibiotics may alter the normal flora in patients and these may result in the selection of resistant microorganisms such as *Acinetobacter* spp.

### 6.2 Virulence of *Acinetobacter* species:

*Acinetobacter* spp. are considered to be relatively low-grade pathogens (Juni, 1978; Pedersen et al., 1970; Smego et al., 1985). However, certain characteristics of these organisms may enhance the virulence of strains involved in infection. Many studies attribute their virulence to different characteristics of the organism. Some of these include the presence of a polysaccharide capsule formed of L-rhamnose, D-glucose, D-glucuronic acid, and D-mannose (Kaplan et al., 1985). This may result in surface of strains more hydrophilic. Although some studies document *Acinetobacter* strains having high hydrophobicity, where these isolates were recovered from catheter and tracheal devices (Kaplan et al., 1985; Rosenberg et al., 1983). The presence of fimbriae and capsular polysaccharide in the bacteria imparts the property of adhesion to the bacteria. Bacterial adhesion to human epithelial cells can also contribute to virulence (Pines and Gutnick, 1984; Rosenberg et al., 1983, Rosenberg et al., 1982; Ruiz et al., 1998). Ruiz et al., (1998) concluded in their recent study that, adherence of *A. baumannii* to rat tracheal tissue, may not be related to the presence of fimbriae, but may be due to the virulence mechanism of this bacterium. One recent study found that *A. baumannii* strains originating from patients with wound infection and bacteraemia showed significantly lower aggregative properties compared to respiratory and environmental strains. Electron microscopic studies revealed more fimbriated bacterial cells among the highly aggregative *A. baumannii* strains. This
study demonstrates *A. baumannii* strains can be divided into two different groups according to their cell surface properties and source of isolation, whereas the majority of strains, from the lower respiratory tract and the hospital environment expressed strong adhesive properties (Koljalg et al., 1996). The production of enzymes in *Acinetobacter* may damage tissue lipids (Poh and Loh, 1985). Another important virulence factor is the potentially toxic lipopolysaccharide (LPS) component of the cell wall and presence of lipid A (Avril et al., 1991; Evgeny V Vinogradov et al., 1996, 1997; Garcia et al., 1999). Gracia et al., (1999) investigated different biotypes of *A. baumannii* for their pathogenicity in mouse spleen cells. All 7 LPS samples obtained from *A. baumannii* were mitogenic as it was proved by cellular proliferation experiments and six among them also induced synthesis of TNF-α.

The production of endotoxin *in vivo* by *Acinetobacter* is responsible for the disease symptoms observed during *Acinetobacter* septicaemia. Experimental studies in a murine model of *Acinetobacter* pneumonia have shown that it resembles closely to that of human pneumonia (Joly-Guillou et al., 1994). Slime production enhances the virulence during mixed infection. Above study also demonstrates that the slime is associated with cytotoxicity against neutrophils and inhibition of the migration of neutrophils into peritoneal exudate of mice. The capacity of the bacterium to assimilate the necessary iron for growth, in the human body can be an important determinant of virulence. Some strains of *Acinetobacter* are capable of producing siderophores such as aerobactin, and iron - repressible outer membrane receptor proteins. This may have a role to play in pathogenesis of the bacteria (Actis et al., 1993; Echenique et al., 1992; Smith et al., 1990; Joythishree et al 1999).