Conjugation seems to have a major role in acquisition of resistance genes in *Acinetobacter*. As well *Acinetobacter* can also be a donor for multiple resistance genes as it is proved experimentally in various studies (Chopade et al., 1994; Scaife et al., 1995). Thus conjugation has gained more importance among genetic transfer mechanisms in *Acinetobacter* spp. owing to its long-term consequences like rapid development of resistance and treatment difficulties.

CHAPTER 5

5. INFECTIONS DUE TO *ACINETOBACTER* SPP.

5.1 Introduction:

*Acinetobacter baumannii* is now recognized to be the *Acinetobacter* genomic species of great clinical importance. However it is difficult to extrapolate the older literature, which reported culture *A. anitratus*, has *A. baumannii* now, with certainty. Even today, various reports of infection caused by " *A. baumannii* " do not include the necessary tests for specific identification; rather it is only presumptive identification that has been reported. With this qualification, *Acinetobacter* spp. have been isolated from different types of opportunistic infections which includes septicaemia, pneumonia, meningitis, skin and wound infection, endocarditis, ocular infections and urinary tract infection (Bergogne-Berezin 1987,1996; French, 1980; Joly-Guillou and Bergogne-Berezin, 1992).
The main sites of infection as reported by several surveys is being the lower respiratory tract and urinary tract, as this distribution sites are very similar with that of other nosocomial gram negative bacteria (Glew, 1977; Joly-Guillou et al., 1991, 1992). *Acinetobacter* species have emerged as important organisms in intensive care settings, in particular it may be related to the advanced increasingly invasive diagnostic and therapeutic procedures adopted in intensive care units of hospitals over past 20 years (Bergogne-Berezin 1991; Gerner-Smidt 1987; Hartstein et al., 1988; Ng et al., 1993; Sherertz, 1985; Siegman-Igra et al., 1993; Vandenbroucke-Grauls et al., 1988).

Isolation of *Acinetobacter* spp from clinical specimens may not necessarily reflect infection but, rather, may result from colonisation (Struelens et al., 1993) and hence it is very difficult to assess the true frequency of infection caused by these group of organisms. In a recent International multicentric study, *Acinetobacter* was ranked amongst top ten of the organisms causing septicaemia in 18 out of 44 large European hospitals (Washington, 1992). However, community-acquired pneumonia due to *Acinetobacter* species is rare as evidenced by paucity of the reports (Achar et al., 1993; Bergogue-Berezin and Towner, 1996). *Acinetobacter* species accounted for 1.4% of all nosocomial infections during 10- year period in one of the hospitals in USA (Larson et al., 1984). A more recent study revealed hospitalisation in an ICU and previous administration of antibiotics were associated with *Acinetobacter* colonization at various body sites in 3.2 to 10.8 per 1,000 patients. Here infection was accounted for 0.3% of endemic nosocomial infections in critically ill patients and for 1% of nosocomial bacteremia throughout hospital (Struelens et al., 1993). Only few reports of
seasonal incidences of *Acinetobacter* infection were reported so far, where in increase rates were in late summer and early winter (Retalliau et al., 1979; Smego, 1985). McDonald et al. (1999b) studied seasonal variations of *Acinetobacter* infection for about 10 years (1987-1996). Throughout this period, average incidence rates were significantly higher during July-October than during November-June for *Acinetobacter* infections overall (8.0 vs. 5.2; P < .01) and for bloodstream infections (2.0 vs. 1.2; P < .01) and pneumonia (9.7 vs. 6.6; P < .01).

5.2 Respiratory infections:

Numerous outbreaks of nosocomial pulmonary infection caused by *Acinetobacter* spp. in ICU's are being increasingly reported (Bergogne-Berezin et al., 1991; Buxton et al., 1978; Castle et al., 1978; Cefai et al., 1990; Hartstein 1988; Stone et al., 1985; Vandenbroucke-Grauls 1988). Their role in ventilator-associated pneumonia (VAP) is very well elucidated, which now appears to be increasing alarmingly. Regardless of the bacteriological method used to define the cause of pneumonia precisely, several studies have reported that about 3 to 5% of nosocomial pneumonias are caused by *Acinetobacter* spp (Craven et al., 1990).

Using specific diagnostic techniques, several investigators recently have demonstrated the increasing role played by *Acinetobacter* spp. largely by *A. baumannii* in nosocomial pneumonia for the subset of ICU patients requiring mechanical ventilation. In studies in which only mechanically ventilated patients were included and bacteriological studies were restricted to uncontaminated specimens obtained by
techniques like bronchoscopy (Fagon et al., 1989; Torres et al., 1990), of all episodes of pneumonia included at least one *Acinetobacter* species. In the above study infection frequencies in both the groups is 15 and 25% respectively. This data contradicts earlier reports of lower infection frequencies by these organism, that is 3 to 5% (Craven et al., 1990). However, the above data clearly suggest that nosocomial pneumonia caused by *Acinetobacter* spp. is now fast emerging prominent complication of mechanical ventilation. Interestingly, this ever increasing incidence is being reported despite many major advances in the management of ventilator-dependent patients and the routine use of effective disinfection procedures for respiratory equipment.

5.2.1 Predisposing factors:

A number of factors have been identified which contributes to the risk of pneumonia or colonisation of the lower respiratory tract by *Acinetobacter* spp. in the intensive care units. These include advanced age, chronic lung disease, surgery, use of antibiotics, immunosupression, presence of invasive devices such as endotracheal and gastric tubes and also the type of ventilator equipment used (Bergogne-Berezin et al., 1991; Buxton et al., 1978; Castle et al., 1978; Lortholary et al., 1995; Struelens et al., 1993).

5.2.2 Ventilator Associated Pneumonia:

Ventilator Associated Pneumonia (VAP) is usually diagnosed based on a combination of clinical, radiological and microbiological criteria. It has been documented extensively that each of these criteria taken individually has high sensitivity,
but low specificity for VAP. Many reports documented increase in specificity when these criteria were combined, however it may be still associated with unnecessary antimicrobial therapy for many patients. General criteria used to diagnose VAP have been illustrated in Table-5.1.

### Table- 5.1

<table>
<thead>
<tr>
<th>Criteria Generally Used to Diagnose VAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three or more positive out of the four below:</td>
</tr>
<tr>
<td>1. Rectal temperature &gt;38° C or &lt; 35.5 ° C</td>
</tr>
<tr>
<td>2. Blood leukocytosis (&gt; 10.10³ /mm³) and /or left shift or Blood leukopenia (&lt; 3.10³/mm³)</td>
</tr>
<tr>
<td>3. More than ten leukocytes in Gram stain or Tracheal aspirate (in high-power field)</td>
</tr>
<tr>
<td>4. Positive culture of tracheal aspirate, and</td>
</tr>
<tr>
<td>5. New, persistent, or progressive infiltrate on chest radiograph</td>
</tr>
</tbody>
</table>

For better correlation between the use of mechanical ventilators (MV) and pneumonia caused by *A. baumannii*, 159 consecutive patients who received MV for more than 72 hours in a medical-surgical ICU over a 13 month duration were studied (Trouillet et al., 1995). Fiberoptic bronchoscopy with protected-specimen brush (PSB) and bronchoalveolar lavage (BAL) was performed on each patient suspected of having pneumonia because of the presence of clinical symptoms like pulmonary infiltrate,
fever, and purulent tracheal secretions, but the diagnosis of pulmonary infection was retained only if such specimens grew $\geq 10^3$ and $\geq 10^4$ CFU of at least one microorganism per mL, respectively. Using this criterion the study reported, nosocomial pneumonia associated directly with *A. baumannii* in 19 (12%) patients of the total 159 patients studied. And the organism was present in 27% of ventilator-associated pneumonia (VAP) cases diagnosed during this study period. However, controversy regarding the use of PSB and BAL, and their advantage over routine endotracheal aspirate, as a better clinical specimen still exists. Few reports claim there is no definitive advantage of protected specimens over endotracheal aspirates (Niederman et al., 1994).

Crude mortality rates of 30 to 75% have been reported for nosocomial pneumonia caused by *Acinetobacter* spp. with highest rates encountered in ventilator-dependent patients (Bergogne-Berezin et al., 1991; Fagon et al., 1993; Torres et al., 1990). Hence the prognosis associated with this *Acinetobacter* infection is considerably worse than that associated with other gram positive or gram-negative bacteria, with the exception of *Pseudomonas aeruginosa*.

Fagon et al., (1989) reported a study where in the diagnosis was retained only if PSB specimens grew $> 10^3$ CFU of at least one organism per mL, mortality associated with *Acinetobacter* or *Pseudomonas* pneumonia was $> 75\%$, compared with only 55% for pneumonia caused by other organisms ($P < 0.05$). Sanchez-Nieto et al. (1998), found no differences in mortality and morbidity when comparing invasive (PSB, BAL) [33%] versus non-invasive quantitative endotracheal aspirates (QEA) [27%] diagnostic management of mechanically ventilated patients with nosocomial pneumonia. Above
study evaluates the impact of bronchoscopy against the QEA specimens and confirms least differences between the two methods. Niederman and co-workers (1994) drew the same conclusions, and reinforced that there is no need of invasive diagnostic testing for routine management of suspected VAP.

In a cohort study conducted by Fagon et al., (1993), in which patients who had developed pneumonia caused by *Acinetobacter* spp. and other organisms were matched carefully with control subjects. The matching was for the severity of underlying illness and other important variables such as age, ventilatory support, and duration of exposure to risk. The attributable mortality in cases of infection caused by nonfermentative gram negative organisms exceeded 40%, with a corresponding relative risk of death of 2.5.

Recent studies mainly indict two important predisposing factors such as prolonged MV, prior antibiotic therapy for the pneumonia caused by *Acinetobacter* spp. Trouillet et al. (1998) showed patients who were ventilated ≥ 7 days and who had received previous antibiotic therapy were readily prone to infection by multidrug resistant *A. baumannii*.

In the study by Fagon and co-workers (1989), majority (89%) of patients who developed pneumonia caused by MDR *Pseudomonas* or *Acinetobacter* species had received antimicrobial therapy prior to the onset of pneumonia, whereas only 17% of the pneumonias occurred in patients without such antibiotic therapy.
5.2.3 Community Acquired Pneumonia:

Apart from nosocomial pneumonia, *Acinetobacter* spp. can be potentially fatal cause of community-acquired pneumonia (CAP) (Achar et al., 1993), however only a small number of cases have been reported in the literature. Since 1955 there have been only 45 cases of community-acquired *Acinetobacter* pneumonia described in the literature all over and majority are reported from developing countries (Achar et al., 1993; Cordes et al., 1981; Anstey et al., 1992). The major risk factors for this infection among patients seem to be heavy cigarette smoking with chronic lung disease, alcoholism, diabetes mellitus and impaired immunity. Community-acquired pneumonia due to *Acinetobacter lwofii* in a patient infected with the human immunodeficiency virus has been diagnosed recently (Domingo et al., 1995). However, recently one unusual case of pneumonia due to *A. baumannii* that was acquired in the community by an individual with no underlying risk factors has been reported (Bick et al., 1993). Interestingly, majority of cases (>70%) showed blood culture positivity in contrast to nosocomial pneumonia where in bacteraemia may not be a characteristic feature. However, the diagnosis of CAP is also been established by culture of the organisms from pleural fluid, pulmonary aspirate and sputum (Barnes et al., 1988).

*A. baumannii* as a cause of community acquired infection has been increasingly reported. *A. baumannii* CAP in a patient with HIV patient has been reported recently (Megarbane et al., 2000).
5.3 **Bacteremia:**

Blood stream infections caused by non-fermentative gram negative bacilli have been associated with a high mortality (Emori and Gaynes 1993). Blood stream infections due to *Acinetobacter* were documented first in 1950s (Rocha and Guze, 1957; Sorrel and White, 1953), soon many reports followed, however all cases reported *Bacterium anitratum* as causal organism for septicaemia. These reports were based on old nomenclature. Although differentiation between blood specimen contamination by skin inhabitants and true bacteremia is rather difficult, the most common *Acinetobacter* species causing significant bacteremia is now recognised as *A. baumannii* in adult patients (Siefert et al., 1993).

Clinical manifestations of bloodstream infections may range from benign transient bacteremia to fulminant disease with septic shock associated with an overall mortality as high as 46% (Seifert et al., 1995; Smego et al., 1985). Many earlier reports describe causal agent of bacteremia as *A. anitratus* or *A. calcoaceticus* subsp. *anitratus*. This should be interpreted with caution; one cannot assume that these organisms would now be identified as *A. baumannii* since strains that oxidise glucose might be one of the other genospecies of genus *Acinetobacter* that can also oxidize glucose according to recent taxonomy. Summary of clinical data from many reported series of *Acinetobacter* bacteremia are given in tables-5.21 and 5.2b.

One of the largest series of bacteremia was reported in Germany, wherein new molecular classification was used to describe the organism (Seifert et al., 1995). They
<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Frequency of Nosocomial acquisition (%)</th>
<th>Frequency of ICU acquisition (%)</th>
<th>No. of Patients / Episodes</th>
<th>Species Identification</th>
<th>No. of Strains</th>
<th>Major portals of Entry</th>
<th>Septic shock (%)</th>
<th>Mortality Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glew et al.</td>
<td>1977</td>
<td>100</td>
<td>89</td>
<td>9</td>
<td>A. anitratuS</td>
<td>9</td>
<td>Respiratory tract: 44% Catheter: 56%</td>
<td>78</td>
<td>44</td>
</tr>
<tr>
<td>Raz et al.</td>
<td>1982</td>
<td>89</td>
<td>25</td>
<td>8</td>
<td>A. anitratuS</td>
<td>8</td>
<td>Respiratory tract: 12% Urinary tract: 12% Chest tube: 12%</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Smego</td>
<td>1985</td>
<td>89</td>
<td>44</td>
<td>18</td>
<td>A. anitratuS</td>
<td>16</td>
<td>Respiratory tract: 39% Abdomen: 22% Skin/soft tissue: 11% Catheter: 11% Urinary tract: 6%</td>
<td>22</td>
<td>28</td>
</tr>
<tr>
<td>Rolston et al.</td>
<td>1985</td>
<td>100</td>
<td>NA</td>
<td>95</td>
<td>A. anitratuS</td>
<td>48</td>
<td>Respiratory tract: 80% Abdomen: 2% Skin/soft tissue: 4%</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Fuchs et al</td>
<td>1986</td>
<td>NA</td>
<td>0</td>
<td>29</td>
<td>A. anitratuS</td>
<td>14</td>
<td>Catheter: 90%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sakata et al.</td>
<td>1989</td>
<td>100</td>
<td>100</td>
<td>19</td>
<td>A. anitratuS</td>
<td>19</td>
<td>NA</td>
<td>0</td>
<td>11</td>
</tr>
</tbody>
</table>
Table 5.2b Review of clinical data from series of earlier reports of *Acinetobacter* bacteremia.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Frequency of Nosocomial acquisition (%)</th>
<th>Frequency of ICU acquisition (%)</th>
<th>No. of Patients / Episodes</th>
<th>Species Identification</th>
<th>No. of Strains</th>
<th>Major portals of Entry</th>
<th>Septic shock (%)</th>
<th>Mortality Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leonov et al.</td>
<td>1990</td>
<td>100</td>
<td>100</td>
<td>12</td>
<td><em>A. calcoaceticus</em></td>
<td>12</td>
<td>Catheter: 33%</td>
<td>NA</td>
<td>8</td>
</tr>
<tr>
<td>Beck-Sague et al.</td>
<td>1990</td>
<td>100</td>
<td>100</td>
<td>69</td>
<td><em>A. baumannii</em></td>
<td>69</td>
<td>Catheter: 100%</td>
<td>NA</td>
<td>41</td>
</tr>
<tr>
<td>Gomez Garces et al.</td>
<td>1990</td>
<td>100</td>
<td>70</td>
<td>19</td>
<td><em>A. anitratus</em></td>
<td>17</td>
<td>Respiratory tract: 42%</td>
<td>NA</td>
<td>30</td>
</tr>
<tr>
<td>Moreno et al.</td>
<td>1990</td>
<td>100</td>
<td>48</td>
<td>40</td>
<td><em>A. anitratus</em></td>
<td>40</td>
<td>Respiratory tract: 13%</td>
<td>NA</td>
<td>22</td>
</tr>
<tr>
<td>Chen et al.</td>
<td>1991</td>
<td>96</td>
<td>58</td>
<td>48</td>
<td><em>A. calcoaceticus</em></td>
<td>48</td>
<td>Respiratory tract: 36%</td>
<td>15</td>
<td>46</td>
</tr>
<tr>
<td>Tilley et al.</td>
<td>1994</td>
<td>83</td>
<td>NA</td>
<td>52</td>
<td><em>A. anitratus</em></td>
<td>47</td>
<td>Respiratory tract: 40%</td>
<td>NA</td>
<td>33</td>
</tr>
<tr>
<td>Seifert et al.</td>
<td>1995</td>
<td>100</td>
<td>91</td>
<td>87</td>
<td><em>A. baumannii</em></td>
<td>87</td>
<td>Respiratory tract: 31%</td>
<td>30</td>
<td>44</td>
</tr>
</tbody>
</table>
confirmed higher mortality rates of *Acinetobacter* bloodstream infections and their higher frequency of nosocomial acquisition. *A. baumannii* bloodstream infections are also most common among patients with severely impaired host defense and breakdown of natural defense barriers such as skin and mucous membranes (Bergogne-Berezin et al., 1987). In the above study vast majority of patients had prior surgery, polytrauma or full-thickness burns. This is contrary to early reports where it is frequently observed in cancer patients (Fuchs et al., 1986; Rolston et al., 1985).

*A. baumannii* bloodstream infections in general are hospital acquired. *Acinetobacter* species can be found either as a single pathogen or as part of polymicrobial bacteremia. Among adults, immunocompromised patients form the largest group. In these patients, the source of bacteremia is quite often the respiratory tract infection, with the highest rate of nosocomial blood stream infection occurring during the second week of hospitalisation. Some of the most common predisposing factors seem to be malignant disease, trauma, and burns.

As far as predisposing risk factors for adults are concerned, surgical wound infections caused by *Acinetobacter* spp. have been described, and such infections may lead to bacteraemia. Pneumonia was the most common source of bacteremia. Numerous reports in the literature describe bacteremia in burn patients (Graber et al., 1962; Green et al., 1983). Many studies confirm the correlation between vascular catheterization and infection (Rolston et al., 1985; Seifert et al., 1993). Insertion site change at every 48 h may reduce the risk of *Acinetobacter* infection. In one study *Acinetobacter* infection was associated with use of transducers (Beck-Sague et al., 1990). Treatment in ICU,
mechanical ventilation, hyper alimentation and prior broad-spectrum antimicrobial therapy are also major determinants or predisposing factors according to some studies (Beck-Sague et al., 1990; Bergogne-Berezin et al., 1987; Peacock et al., 1988; Smego, 1985)

In general, the underlying conditions seem to determine the prognosis of the infection. The prognosis of patients with malignant disease and burns is rather poor (Tilley et al., 1994), but trauma patients have a better prognosis. Prior antibiotic therapy is associated with the selection of resistant strains. The mortality rate in one of the study (Tilley et al., 1994) was unusually high (33%), as the study comprised of a highly compromised group. Recent study (Cisneros et al., 1996) concludes that most A. baumannii are multidrug resistant. Nosocomial A. baumannii bacteremia may cause severe clinical disease that is associated with a high mortality, as the mortality rate was 34% in the above study. Here independent factors associated with high mortality, were the use of inappropriate antimicrobial therapy and presence of disseminated intravascular coagulation (DIC) among patients.

A. baumannii bloodstream infection only infrequently arises from an endogenous source. However, sporadic cases of blood culture positive community-acquired pneumonia with high mortality have been reported recently in patients with underlying conditions such as cigarette smoking and chronic pulmonary disease (Anstey et al., 1992) as well as in a healthy host (Bick et al., 1993). Although A. baumannii is hailed as common cause of Acinetobacter bacteremia, other species like A. johnsonii and A. junii is also been implicated as a cause of bacteremia. Acinetobacter species other than A. baumannii are almost exclusively involved in
devise-related bacteremia (Seifert et al., 1994). One study reported 13 cases of vascular catheter related bloodstream infection due to A. johnsonii. The clinical course of this A. johnsonii bacteremia is usually benign (Seifert et al., 1993). Kappstein et al. (2000) reported an outbreak of bacteraemia in paediatric oncology patients caused by Acinetobacter junii.

A second important group of patients consist of neonates. One report describes 19 neonates with Acinetobacter septicaemia in the neonatal ICU monitored for a period of 30 months (Sakata et al., 1989). All cases were of late-onset type septicaemia in infants hospitalized for prolong periods, with mortality rate of 11%. The predisposing risk factors for septicaemia were low birth weight, previous antibiotic therapy, mechanical ventilation (MV), and the presence of neonatal convulsions. The second report (Ng et al., 1989) describes an outbreak of septicaemia due to Acinetobacter in a neonatal ICU, which was confined to 7 babies receiving parenteral nutrition. In them 5 required MV and all had signs of septic shock. Third report from Israel (Regev et al., 1993) had nine cases of Acinetobacter sepsis in ICU over period of 31 months, and the clinical course was fulminant in four babies who eventually died. The fourth outbreak was from Bahamas, where in three deaths was recorded out of 8 confirmed bacteremia cases.

In another study (Iqbal Hossain et al., 1998), children ≤ 5 year old (paediatric group) were screened for community-acquired bacteremia (CAB) as well as nosocomial bacteremia (NB) where in, out of total 138 significant cultures 91 (66%) were obtained from CAB and 47 (34%) were from NB. Here 16% mortality was attributed to
Acinetobacter bacteraemia. Above reports confirms that Acinetobacter spp can be a cause of severe nosocomial blood stream infection in neonatal intensive care units.

5.3.1 Clinical features of Acinetobacter bacteremia:

The most common sign associated with the onset of A. baumannii bacteremia is fever. The maximum temperature may range from 34.1-41.7° C. The mean duration of fever is 4 days (range3hr-16d). Majority will exhibit leukocytosis and a few manifests with leukopenia. Thrombocytopenia, severe sepsis, septic shock and DIC are some common manifestations of Acinetobacter bacteremia. Some specific symptoms of sepsis such as fever (temperature above > 37°C), chills and hypotension are prominent features (Seifert et al., 1995; Cisneros et al., 1996).

5.4 Meningitis:

Secondary meningitis is the predominant form of Acinetobacter meningitis, although sporadic cases of primary meningitis have been reported, particularly following neurosurgical procedures or head trauma (Berk and McCabe, 1981). Until 1967, there were about 60 reported cases of Acinetobacter meningitis, most of these were community acquired. Many of these reports used old nomenclature to describe the causal agent. However, since 1979 majority of cases have been nosocomial infections, with almost all caused probably by A. baumannii. Mortality rates from different studies range from 20 to 27%. Most patients have been adult men and had undergone lumbar punctures, myelography, ventriculography, and other neurosurgical procedures,
although two cases described patient having posttraumatic otorrhoea without intervention (Siegman-Igra et al., 1993; Venkataraman et al., 1999). A case of Acinetobacter meningitis associated with a ventriculoperitoneal shunt with concomitant tunnel infection where in A. baumannii was isolated from CSF has been described (Seifert et al., 1995). Predisposing factors include the presence of a continuous connection between ventricles and the external environment, a ventriculostomy, or a CSF fistula. In addition, the presence of an indwelling ventricular catheter for more than five days is an important risk factor. Heavy use of antimicrobial agents in the neurosurgical ICU is one important risk factor. One outbreak subsided immediately only when the selective pressure of antibiotics was reduced (Siegman-Igra et al., 1993).

The above report from Siegman-Igra et al. (1993) describes 25 cases of CNS infections due to A. baumannii secondary to invasive procedures and it constitutes the largest reported series of hospital-acquired meningitis due to Acinetobacter. Most of these cases occurred in the neurosurgical ICU over a 5-year period, with an increased rate during summer. The majority of infections were associated with indwelling ventriculostomy tubes or CSF fistulae in patients receiving antimicrobial therapy. Environmental sampling failed to reveal the source of the microorganism. The study reported a mortality rate of 20%. This group also reviewed the literature for Acinetobacter meningitis and the overall mortality rate was 23%. These rates are strikingly similar to the 27% mortality due to acinetobacter meningitis reported as early as 1967 (Donald and Doak, 1967). The study concluded that the main predisposing factors for infection are the indwelling ventriculostomy tubes, which connects the ventricles to the external environment and duration of connection as well as heavy use.
of antimicrobial agents in ICU. Removal of indwelling catheters and reduction in usage of antimicrobial agents subsided this 5-year extended outbreak. The authors believed that indiscriminate use of antimicrobial agents was an important factor in the selection of Acinetobacter as the main residential flora of the ICU, and long-term openings into the CNS served as easy portals of entry for the Acinetobacter.

A particularly interesting outbreak of meningitis caused by Acinetobacter was described in a group of children with leukemia (Kelkar et al., 1989) following the administration of intrathecal methotrexate. Of the twenty children who received intrathecal methotrexate, 8 returned within 2 to 19 h of treatment with signs and symptoms of acute meningeal irritation. Acinetobacter organisms were isolated from the CSF of 5 of these patients, as well as from the methotrexate solution. Three of the children died as a result of meningitis and five recovered. The outbreak was caused by the use of inappropriately sterilized needles.

One comprehensive study from Ludhiana, India (Pearce et al., 1993) reports 5.6% incidence of acinetobacter meningitis. A total of 10,468 CSF samples from cases of meningitis in different age groups were cultured during 1988-1991. Acinetobacter calcoaceticus was isolated in 12 of 211 positive bacterial cultures. All strains were 100% resistant to ampicillin, cotrimoxazole and tetracycline. 50% were resistant to cephazolin, gentamicin and kanamycin. However, all were susceptible to chloramphenicol. The above study used old nomenclature for the identification purposes.
Jimenez-Mejias et al., (1997) studied 8 cases of MDR *A. baumannii* meningitis and their outcome. All the patients had fever, neck stiffness or meningeal signs, low consciousness level and their CSF had typical features of acinetobacter meningitis. Seven isolates obtained from these cases were resistant to imipenem. All patients were treated with ampicillin / sulbactum. Six patients were cured and 2 died of meningitis. Authors concluded that ampicillin / sulbactum may be effective as therapy for meningitis caused by *A. baumannii* resistant to imipenem and other β-lactams drugs.

5.4.1 *Clinical features of Acinetobacter meningitis:*

According to Siegman-Igra et al. (1993), important clinical features manifested due to *Acinetobacter* meningitis were as follows. Most of the patients had temperatures of ≥ 38 °C, White Blood Cell count of more than 11,000/mm³, pleocytosis with 90% Polymorphonuclear leukocytes and the cell count ranging from 60 to 26,000 cells/mm³. Increase in protein level (average, 185mg/dL) and with decreased glucose level.

Jimenez-Mejias et al., (1997) diagnosed seven acinetobacter meningitis cases with following clinical features. Leukocytosis (18,817± 6.101/μL) with a polymorphonuclear predominance was noted. In all CSF specimens, pleocytosis (4,383 ± 6,927 cells/μL) with a polymorphonuclear predominance, an elevated protein level (415 ± 219 mg/dL), and a low glucose level (14 ± 15 mg/dL) were noted.

5.5 *Urinary tract infections:*

*Acinetobacter* spp as a cause of urinary tract infection is infrequent, if not rare. Infection occurs most commonly in elderly debilitated patients, in patients confined to
ICUs, and in patients with permanent indwelling urinary catheters. 80% of patients were males (Pedraza et al., 1993), perhaps reflecting the higher prevalence of catheters usage in this population as a result of prostatic enlargement. However, not every isolation of this organism from the indwelling catheters can be ascertained as actual infection (Hoffmann et al., 1982). Muller-Serieys et al (1989) reported 33 cases of nosocomial infections that developed during 1987 in the surgical intensive care unit and in the urology department. *Acinetobacter* was isolated from urinary tract infections was as high as 43 per cent among those cases. Yasodhara et al., (1997) isolated majority of *Acinetobacter* spp from urine sample when compared to all other clinical specimens. Villers et al. (1998) reported high incidence of urinary isolates among all the patients in their study (31%). In one report from Pedraza et al. (1993) in two years, 114 urinary strains of *A. baumannii* were isolated in 57 patients with traumatic spinal cord injury. They also observed a higher incidence among males (46 males, 11 females). Only 6 patients presented with clinical signs directly related to *A. baumannii* infection.

5.6 Other Miscellaneous infections:

A few rare cases of native-valve infective endocarditis (IE) caused by *Acinetobacter* spp have been reported (Gradon et al., 1992). Gardon et al., (1992) reviewed around 15 cases of both native-valve and prosthetic valve infective endocarditis reported till date and drew some important points regarding their manifestations. The possible inciting risk factors are identified as dental procedures and open heart surgery. The presence of transient maculopapular rash involving the palms...
and soles but not on the face may be possible early clinical clue for to the diagnosis. Among patients with native-valve infective endocarditis, disease appears to be more aggressive than the prosthetic valve form. Although there are variations in the clinical course and manifestation, *Acinetobacter* IE does not differ much clinically from IE caused by other microorganisms. A rare case of infective endocarditis caused by *A. haemolyticus*, first of its kind has also been reported (Castellanos et al., 1995).

Patients undergoing continuous ambulatory peritoneal dialysis (CAPD) are prone to peritonitis caused by *Acinetobacter* spp. However it is difficult to ascertain all such cases as nosocomial, but technique failure and diabetes mellitus are the important underlying predisposing risk factors. The most common symptoms are abdominal pain or cloudy dialysate and in some cases fever may be present. Studies suggest that most patients were responding to antibiotic therapy and hence interruption of CAPD was not warranted. (Lye et al., 1991; Valdez et al., 1991).

*Acinetobacter* cholangitis and septic complications following percutaneous transhepatic cholangiogram and percutaneous biliary drainage have been reported, primarily among elderly patients with obstructive jaundice caused by malignant disease or choledocholithiasis. In one study, 13.5% of patients undergoing transhepatic cholangiography or biliary drainage developed infection, with the most common isolates being *Enterobacter cloacae* and *Acinetobacter* spp (Sacks-Berg et al., 1992).

Eye infections following trauma have been described (Mark and Gaynon 1983; Melki and Sramek, 1992). Corneal perforation due to *Acinetobacter* have been reported (Prashanth and MadhavaRanga, 2000; Wand et al., 1975). *Acinetobacter* keratitis has
been reported in association with soft contact lens wear (Herbst et al., 1972; Kent et al., 1990), penetrating keratoplasty (Zabel et al., 1989), and in patient with chronic lymphatic leukaemia (Presley and Hale, 1968). Exposure keratitis followed by *Acinetobacter* infection have some common predisposing factors such as immunocompromised conditions of patients, prolonged hospitalisation and severe underlying diseases like diffuse lymphoma, prostatic carcinoma (Marcovich and Levartovsky, 1994).

Other, rare case reports of infections due to *Acinetobacter* spp include typhilitis after autologous bone marrow transplantation (Nagler et al., 1992), osteomyelitis and extremity infections following injury (Dietz et al., 1988; Martin et al., 1988), and suppurative thyroiditis along with bacteremic pneumonia (Eugene Hsin Yu, 1998).

Lam et al., (1997) described a case of active systemic lupus erythematosus (SLE) complicated with a large amount of pericardial effusion with diastolic collapse of right ventricle suggestive of tamponade. Isolates from surgical drainage of pericardial fluid showed *A. baumannii* exhibiting multiple antibiotics resistance. Septic pericarditis and tamponade is considered rare. Most of the reported cases of septic pericarditis in SLE were due to *Staphylococcal aureus*, and *A. baumannii* has never been reported before. Hunt et al., (2000) recently documented an unusual case, where in there was formation of pneumatoceles secondary to *Acinetobacter* pneumonia.