

# Community-acquired pneumonia — factors influencing intensive care admission

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## Summary

The mortality rate in critically ill patients with pneumonia who require invasive vital organ support, including mechanical ventilation, in an intensive care unit (ICU) remains above 50%. The contribution of these costly life support systems to the survival of patients with extensive pneumonia is a matter for debate. The high mortality rate in this group of patients can be attributed in part to the fact that they are frequently referred for ICU care when their condition has already deteriorated to the point of no return. A retrospective study over 18 months of 34 cases of community-acquired pneumonia (17 patients required ventilatory support in the respiratory ICU) was undertaken to identify criteria which would justify early admission to an ICU. These were first-line clinical and biochemical factors, three of which were present in all patients on admission to hospital: (i) bronchopneumonia or lobar pneumonia involving more than two lobes ( $P < 0,001$ ); (ii) respiratory rate  $> 30/\text{min}$  ( $P < 0,001$ ); and (iii) partial arterial oxygen pressure  $< 8 \text{ kPa}$  ( $P < 0,001$ ). Other systemic factors associated with a poor prognosis and admission to the ICU were clinical signs of septicaemia, abnormal liver function and low serum albumin value. A scoring system for severity of pneumonia based on these factors is proposed. The possibility of an improved prognosis in a potentially reversible disease can become a reality if this approach is employed prospectively.

*S Afr Med J* 1988; 73: 77-81.

Pneumonia is a major cause of morbidity and mortality and is currently the fifth most common cause of death in the USA.<sup>1,2</sup> The impact of intensive care unit (ICU) support on the mortality rate in patients critically ill with pneumonia has, however, been questioned.<sup>3</sup>

Hook *et al.*<sup>3</sup> recorded a mortality rate of 76% in patients with bacteraemic pneumococcal pneumonia who required ICU

management. When mechanical ventilation was necessary the rate rose to 80% and if additional pharmacological blood pressure support was required it increased to 93%. In patients with bacterial pneumonia who develop the adult respiratory distress syndrome (ARDS) or respiratory failure the mortality rate has been reported to be 50% and 71% respectively.<sup>4,5</sup> The reasons for this exceptionally high figure are numerous and several high-risk factors have been identified in patients with pneumonia. These include: (i) age  $> 50$  years;<sup>6-9</sup> (ii) leucopenia (white cell count  $< 4 \times 10^9/\text{l}$ );<sup>5,10</sup> (iii) alcoholism;<sup>6,10,11</sup> (iv) multiple lobe involvement;<sup>5,11</sup> (v) chronic heart and lung disease; (vi) malignant disease; (vii) diabetes; and (viii) any factor affecting the immune system, such as malnutrition.<sup>2,6,12,13</sup>

These prognostic factors have not changed significantly in the last 25 years, but the therapeutic and supportive measures (such as reliable mechanical ventilators, pharmacological cardiovascular support, dialysis and invasive haemodynamic monitoring), have improved markedly. The contribution of these sophisticated and expensive life-support systems to survival in the critically ill patient with pneumonia has been questioned by many physicians because of their cost-effectiveness and the shortage of ICU beds. Many patients with pneumonia are referred for ICU management in a moribund condition and this may be one of the important reasons for the high mortality rate in patients who eventually require mechanical ventilation.

Since guidelines for the early recognition of patients with pneumonia who require ICU care are not at present available, a retrospective study of the clinical and biochemical parameters as well as complications which influence morbidity and mortality of all patients with community-acquired pneumonia (CAP) admitted to the respiratory ICU at Tygerberg Hospital was conducted. A scoring system for severity of pneumonia based on these factors was found useful for identifying patients with CAP who require more aggressive management.

## Patients and methods

The study group consisted of 34 adult patients with CAP, 17 of whom were managed in the respiratory ICU (group I) and 17 in a general medical ward (group II). The control group (group II) were patients with pneumonia, toxically ill and justifying admission to the medical ward. They were managed by different physicians during the same period as the patients in group I. Patients were selected randomly from hospital records and were matched for age, sex and race. Records of all patients were reviewed, all relevant clinical, haematological, bacteriological, biochemical and radiological manifestations on admission were documented as well as complications during their stay in hospital. The diagnosis of CAP was made on a combination of clinical (history, symptoms and signs), radiological and bacteriological (sputum Gram stain and culture, blood cultures and serology) data. All patients admitted to the ICU (group I) required endotracheal intubation and mechanical ventilation with positive end-expiratory pressure. Invasive haemodynamic monitoring was essential in all these patients and all but 2 needed pharmacological blood pressure support. The control group were treated with appropriate antibiotics and other supportive measures as required.

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Accepted 10 Feb 1987.

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The diagnosis of ARDS was made according to well-known criteria.<sup>14</sup> All patients had arterial partial oxygen pressures ( $P_{aO_2}$ ) of  $\leq 6,6$  kPa on a fractional inspired oxygen concentration ( $F_{iO_2}$ )  $> 50\%$  during mechanical ventilation, diffuse pulmonary infiltrates and a normal to low wedge pressure at the time of diagnosis of ARDS. The diagnoses of multi-organ failure<sup>15</sup> and diffuse intravascular coagulation<sup>16</sup> were made according to accepted criteria. The diagnosis of stress diabetes was made with a blood glucose level above 11,1 mmol/l on more than two occasions during a period of normal kilojoule intake.

A patient was considered clinically septicemic on admission when at least three of the following five factors were present: (i) mean blood pressure  $< 75$  mmHg; (ii) central venous pressure  $< 2$  cm  $H_2O$ ; (iii) confusion; (iv) laboratory evidence of pre-renal uraemia; and (v) metabolic acidosis (total bicarbonate content of arterial blood ( $HCO_3^-$ )  $< 20$  mmol/l). A patient was considered to be an abuser of alcohol when a bottle of wine (or equivalent) or more was consistently consumed per day. Abnormal laboratory parameters were defined as: leucopenia — white cell count  $< 4 \times 10^9/l$ ; low serum albumin —  $< 30$  g/l; abnormal liver function — one or more of the following: bilirubin  $> 17$  mmol/l, aspartate transaminase  $> 40$  U/l, alanine transaminase  $> 53$  U/l or alkaline phosphatase  $> 85$  U/l; abnormal renal function — serum urea  $> 6,5$  mmol/l and/or serum creatinine  $> 120$  mmol/l. All  $P_{aO_2}$  values reported were on an  $F_{iO_2}$  of 0,4 and the alveolar-arterial oxygen gradient was calculated from  $P_{aO_2}$  and partial arterial carbon dioxide pressure ( $P_{aCO_2}$ ) utilising the simplified alveolar gas equation (respiratory quotient assumed to be 0,8).<sup>17</sup>

Differences between groups were compared by the chi-square analysis with Yates' correction, and Student's paired  $t$ -test when appropriate; a  $P$  value of  $< 0,05$  was considered a significant difference. All values are presented as the mean  $\pm$  SEM.

## Results

The two groups studied were comparable as regards race, sex and age (group I —  $39 \pm 2,6$  years, range 18 - 57 years; group II —  $39,8 \pm 4,0$  years, range 17 - 69 years). Factors known to predispose to a poor prognosis in pneumonia were similar in the two groups (Table I). Alcohol abuse, age  $> 50$  years and underlying heart and lung disease appeared more commonly in the control group but there was no statistically significant difference between the groups.

**TABLE I. FACTORS ASSOCIATED WITH POOR PROGNOSIS IN PATIENTS WITH CAP**

Prognostic factor	Group 1			Group II
	Total	Died	Survived	
Age $\geq 50$ yrs	2	0	2	5
Alcohol abuse	6	4	2	9
Leucopenia ( $\leq 4 \times 10^9/l$ )	2	1	1	1*
$\geq 2$ lobes involved	10	4	6	6
Broncho-pneumonia	7	4	3	4
Heart, lung disease	3	2	1	7
Malignant disease	1	0	1	0
No risk factor	0	0	0	2

\*Patient died.

Seven patients in group I and 4 in group II were diagnosed as having bronchopneumonia on clinical and radiological grounds. The remaining 23 patients presented with the clinical and radiological picture of lobar pneumonia (group I —  $3,5 \pm 0,4$  lobe involvement, group II —  $1,5 \pm 0,3$  lobe involvement ( $P < 0,009$ ) (Table II)). In group I a definite bacteriological diagnosis was made in 70% of patients with 47% positive blood cultures. The corresponding figures for group II were significantly lower — 23% and 17% respectively. The principal reason for negative cultures was that antibiotics were administered before collection of speci-

**TABLE II. CLINICAL, LABORATORY AND BACTERIOLOGICAL DATA ( $\pm$  SEM) ON ADMISSION OF PATIENTS WITH CAP**

	Group I	Group II	P value
<b>Clinical parameters</b>			
Respiratory rate (/min)	$37,2 \pm 1,7$	$27 \pm 1,3$	$< 0,001$
Confusion	10	3	$< 0,03$
Blood pressure (mmHg)	$94,2 \pm 5,5$	$95,3 \pm 0,3$	NS
Clinical septicemia	9	1	$< 0,01$
Lobes involved	$3,5 \pm 0,4$	$1,5 \pm 0,3$	$< 0,009$
<b>Laboratory parameters</b>			
$P_{aO_2}$ (kPa)	$5,7 \pm 0,3$	$8,2 \pm 0,6$	$< 0,001$
$HCO_3^-$ (mmol/l)	$20,5 \pm 0,9$	$23,2 \pm 0,9$	$< 0,03$
P (A-a) $O_2$ (kPa)	$24,1 \pm 1,7$	$12 \pm 2,4$	$< 0,003$
White cell count $\times 10^9/l$	$15,1 \pm 2,5$	$12,9 \pm 1,9$	NS
Abnormal renal function	14	3	$< 0,006$
Abnormal liver functions and/or serum albumin	17	3	$< 0,01$
<b>Bacteriological data</b>			
Lobar pneumonia	10 (4 d)	13	NS
Bronchopneumonia	7 (4 d)	4 (1 d)	NS
Positive blood culture	8 (4 d)	3	NS
<b>Definite bacteriological diagnosis</b>			
Streptococcal pneumonia	4 (3 d)	2	NS
<i>Klebsiella pneumoniae</i>	4 (1 d)	0	NS
<i>Staphylococcus aureus</i>	2 (1 d)	1 (d)	NS
<i>Haemophilus influenzae</i>	2	1	NS

P (A-a) $O_2$  = alveolar-arterial oxygen gradient.

Clinical septicemia, abnormal renal and liver function — see text.

mens (50% of all negative cultures). *Streptococcus pneumoniae* (6) and *Klebsiella pneumoniae* (4) were the most prevalent pathogens cultured. A high mortality rate was recorded in patients with proven pneumococcal pneumonia requiring ICU care (3 out of 4 patients died) in contrast to *Klebsiella pneumoniae* (1 out of 4 patients).

Relevant clinical, laboratory parameters and complications are shown in Tables II and III. Patients in group I were significantly more tachypnoeic ( $37,2 \pm 1,7/min$ ) than their counterparts in group II ( $27 \pm 1,3/min$ ) ( $P < 0,001$ ). There was a near-linear relationship between respiration rate on admission and mortality (Fig. 1). The other clinical manifestations on presentation that correlate with admission to the ICU were confusion ( $P < 0,03$ ) and clinical evidence of septicemia (9 in group I). In 7 of these 9 patients haemodynamic studies supported the clinical diagnosis of septicemia (low blood pressure with a high cardiac index and low systemic vascular resistance). In 4 other patients in whom septicemia had not been suspected on admission, haemodynamic studies suggested septicemia.

The  $P_{aO_2}$  was significantly lower in group I ( $5,7 \pm 0,3$  kPa) than in group II ( $8,2 \pm 0,6$  kPa) ( $P < 0,001$ ). There was, however, no difference in the admission  $P_{aO_2}$  between survivors and non-survivors (Fig. 2). The  $P_{aCO_2}$  was low to normal in all patients, even those with underlying lung disease such as bronchiectasis and chronic bronchitis. The admission pH remained within normal range in all patients irrespective of changes in  $P_{aCO_2}$  and a low  $HCO_3^-$  in group I patients ( $20,5 \pm 0,9$  mmol/l). The white cell count was not significantly different in the two groups and only 3 patients were leucopenic on admission, 1 in group II ( $3,2 \times 10^9/l$ ) and 2 in group I ( $1,7$  and  $0,9 \times 10^9/l$ ). Two of these 3 leucopenic patients died, 1 being the only patient in the control group who died.

TABLE III. COMPLICATIONS AND OUTCOME IN PATIENTS WITH CAP

	Group I				Group II
	Total	Died	Survived	P value	
Stress diabetes mellitus	9	6	3	< 0,01	2
DIC	11	5	6	NS	0
ARDS	14	7	7	NS	0
Delirium tremens	3	3	0	< 0,04	1
Renal failure	6	5	1	< 0,001	0
Multi-organ failure	5	4	1	< 0,02	0
Ventilated (d)	10,5 ± 2,4	6,2 ± 4,2	14,4 ± 1,6	< 0,05	
Time in hospital (d)	19,1 ± 4,9				4,5 ± 0,9
Mortality	47%				5%
Apache II score (mean)	13,7				< 5

DIC = diffuse intravascular coagulation.

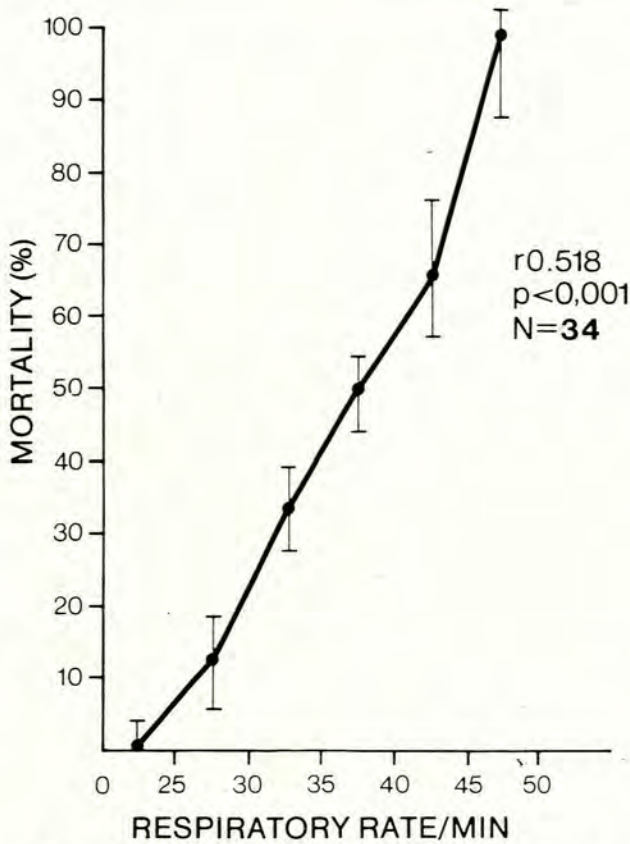


Fig. 1. Influence of respiratory rate on mortality in patients with CAP.

Abnormal liver function and/or low serum albumin was present on admission in all ICU-treated patients and in 42% of the control group. The most significant abnormality was the low serum albumin level in 82% of the ICU-treated patients in contrast with the 30% of the control patients ( $P < 0,001$ ). However, no correlation was found between abnormal liver function or a low serum albumin and mortality. On admission renal functions were abnormal (mainly pre-renal uraemia) in 82% of the ICU-treated patients and only 17% in the control group ( $P < 0,006$ ). Of the 14 patients in group I with abnormal renal function, the condition of 6 eventually deteriorated to such an extent that dialysis was required.

ICU-treated patients needed hospitalisation for  $19,1 \pm 4,9$  days in contrast with the control patients ( $4,5 \pm 0,9$  days). The mortality rate for the patients who needed mechanical ventilation (group I) was 47% in contrast with 5% in group II. Factors

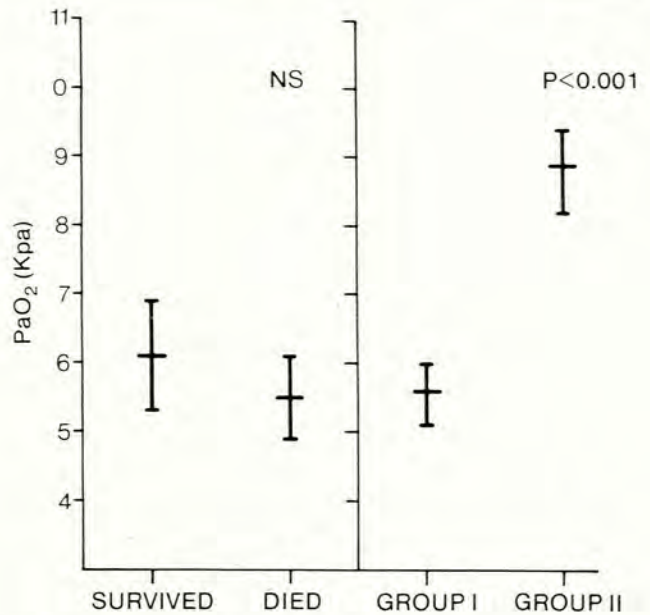


Fig. 2. Admission Pao<sub>2</sub> in patients with CAP.

associated with a fatal outcome were respiration rate on admission ( $P < 0,01$ ) and certain complications which developed during the patient's stay in the ICU such as stress diabetes ( $P < 0,01$ ), delirium tremens ( $P < 0,04$ ), multi-organ failure ( $P < 0,02$ ) and renal failure ( $P < 0,001$ ).

## Discussion

Across the world pneumonia is still a major cause of morbidity and mortality.<sup>18-20</sup> During 1979/80 respiratory tract infections ranked third after cardiovascular/cerebrovascular diseases and malignant diseases as a cause of death world-wide.<sup>18</sup> The role of ICU management of the very sick patient with pneumonia was recently questioned by Hook *et al.*,<sup>3</sup> who recorded a mortality rate in patients with bacteraemic pneumococcal pneumonia very similar to the figures reported 20 years earlier by Austrian and Gold.<sup>6</sup> The reason for the high mortality rate in patients with pneumonia who require mechanical ventilation<sup>3-5</sup> is still unclear. In a retrospective study of 593 patients with bacteraemic pneumococcal pneumonia Austrian and Gold<sup>6</sup> in 1964 philosophically suggested that patients who die 'have passed the physiological point of no return' and that data 'suggest that antimicrobial therapy has no effect on the outcome

of infection among those destined, at the onset of illness, to die'. Twenty years later Hook *et al.*,<sup>3</sup> who reviewed 154 bacteraemic pneumococcal pneumonia cases, shared this view and concluded that the physiological consequences of pneumococcal bacteraemia may have been delayed or modified by ICU care, but that the ultimate outcome was probably determined by events occurring early in the course of infection. This point of view has led physicians to believe that if patients with pneumonia do not improve on appropriate antibiotics and an oxygen mask, little more can be done to improve the ultimate outcome. Patients are consequently only referred for ICU care after cardiopulmonary resuscitation or in a moribund condition, and this may explain the high mortality rate in patients with pneumonia who eventually require mechanical ventilation.

Studies with the emphasis on early recognition of clinical features which indicate a potentially unfavourable outcome in the extremely ill patient with pneumonia are not available. This study identifies clinical and laboratory parameters in patients with CAP who, once admitted to hospital, require more aggressive ICU management. The factors identified as important danger signals include simple clinical and first-line laboratory observations such as respiratory rate, confusion, signs of septicaemia, clinical and radiological signs of bronchopneumonia or multiple lobe involvement, a low  $P_{aO_2}$ , abnormal liver and renal function, a low serum albumin level and metabolic acidosis. A scoring system for severity of pneumonia is suggested, based on the danger signs identified on admission in this study. This can be a valuable aid to the primary care physician in deciding which patients to refer for early ICU management (Table IV). A comparable severity of disease scoring system, for example the Apache II system (acute physiology and chronic health evaluation),<sup>21</sup> was designed for evaluation of all critically ill patients, including post-trauma and postoperative cases and does not include important prognostic factors for patients with pneumonia. The main aim of the above system is to predict mortality and not to guide management approach.

**TABLE IV. SEVERITY-OF-DISEASE SCORING SYSTEM FOR CAP**

Sign	Score
<b>Bronchopneumonia or <math>\geq 2</math>-lobe lobar pneumonia</b>	<b>10</b>
<b>Respiration rate <math>&gt; 30</math>/min</b>	<b>10</b>
<b><math>P_{aO_2} \leq 7,5</math> kPa on <math>F_{iO_2} 0,4</math></b>	<b>10</b>
<b>Abnormal liver function test (including serum albumin <math>&lt; 30</math> g/l)</b>	<b>5</b>
<b>Clinical septicaemia*</b>	<b>5</b>
<b>Pre-existing factors <math>\geq 2</math> for poor prognosis in pneumonia</b>	<b>5</b>

Patients scoring over 20 points require immediate ICU management.

\*Clinical septicaemia = combination of 3 or more of: blood pressure  $\leq 75$  mmHg, central venous pressure  $\leq 3$  cm  $H_2O$ , confusion, pre-renal uraemia,  $HCO_3^- \leq 20$  mmol/l.

All patients who required ICU admission presented with a respiratory rate  $> 30$ /min. Respiratory rate was also the only clinical parameter which on admission correlated with mortality ( $P < 0,01$ ) with a near-linear relationship between respiratory rate on admission and mortality. All patients who presented on admission with a respiratory rate  $> 45$ /min died. This may relate in these patients to either the degree of desaturation or low compliance of the lungs or to both factors. The two additional factors present on admission in all ICU-treated

patients that were of equal importance were the extent of lung parenchymal involvement and a low  $P_{aO_2}$  ( $< 7,5$  kPa in all patients). Individually neither of the last two factors correlated with a fatal outcome. Other points of difference of lesser importance between the two groups that have also been included in the scoring system are confusion with other clinical signs of septicaemia (e.g. low blood pressure and central venous pressure, low urine output with pre-renal uraemia and metabolic acidosis) and abnormal liver function and/or low serum albumin values.

In patients with pneumonia certain risk factors have repeatedly been associated with a poor prognosis. These include: age  $> 50$  years; alcoholism; multiple lobe involvement; heart, lung, renal and liver disease; and any factor compromising the immune system such as diabetes mellitus, malnutrition and malignant disease.<sup>5-10</sup> These factors, however, were not found more frequently in the ICU-treated patients than in controls in this study. However, the present study is hampered by small numbers and the significance of these factors, specifically alcoholism, has been well proven in other studies.<sup>6,10</sup> The importance of alcoholism can be illustrated by the fact that all the patients in this study who developed delirium tremens in the ICU died. No significant difference in the leucocyte count between the two groups was recorded, but 2 of the 3 patients who presented with leucopenia (white cell count  $< 4 \times 10^9/l$ ) died; they were both alcohol abusers which emphasises the gravity of prognosis in alcoholics who present with pneumonia and leucopenia.<sup>10,11</sup> We consider the incorporation of these factors in a scoring system of severity for pneumonia essential.

The mortality rate in the ICU patients was 47%, a figure that compares favourably with other similar series.<sup>2,5,6</sup> Other factors, apart from respiratory rate, that were associated with a fatal outcome in our patients with CAP were stress diabetes, renal failure and multi-organ failure. These factors were not included in our scoring system because its principal aim is to assist the physician in identifying on admission the patient with pneumonia who needs more active management. When our patients were scored on admission according to the Apache II system<sup>21</sup> the predicted mortality rate in the ICU group should have been 10 - 20%. This discrepancy suggests that the Apache II system is not a reliable prognostic index in pneumonia patients. An independent scoring system for critically ill pneumonia cases is therefore justified. It is evident from our data (Tables II and III) that patients who presented with 1 major and 1 minor or 3 minor prognostic features (15 points) required ICU observation. Patients who scored more than 20 points should be admitted for ICU management.

CAP remains a disease with a significant morbidity and mortality rate. Notwithstanding remarkable advances in the last 20 years in the medical profession's ability to support failing vital organs during an acute illness, patients with pneumonia who need ventilatory support to maintain adequate oxygenation still have a mortality rate in excess of 50%. As CAP is a potentially curable disease, an aggressive approach in managing these patients is justified. Our study identified factors which, when present on admission in patients with CAP, were associated with an unfavourable course and a high mortality rate. Therefore we feel that the early recognition of these factors is an important aspect in the successful management of these patients. We postulate that the early recognition of the critically ill patient with pneumonia, using a scoring system coupled with an aggressive approach to management, may change the outcome. This hypothesis is at present being tested prospectively.

We wish to thank the Medical Superintendent of Tygerberg Hospital for permission to publish, and Jacomine Rossouw of the Department of Anaesthetics, for preparing the manuscript for publication.

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# Die mikrobiologiese etiologie van akute bekken- infektiewe siekte in Pelonomi-hospitaal, Bloemfontein

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## Summary

In 40 women with acute pelvic inflammatory disease (APID) specimens for microbiological study were obtained from the rectum, urethra, vagina, cervix and peritoneal cavity. In most patients (83%) the aetiology of the infection was polymicrobial. *Chlamydia trachomatis* was the most common invader (73,3%), followed by anaerobic organisms (46,6%), *Neisseria gonorrhoeae* (40%) and aerobic organisms (26,6%). Only 1 patient had a positive peritoneal culture for *N. gonorrhoeae*. All the other positive *Chlam. trachomatis* and *N. gonorrhoeae* cultures were obtained from rectal, urethral and cervical specimens. The positive anaerobic and aerobic cultures were all from peritoneal cavity specimens.

*S Afr Med J* 1988; **73**: 81-82.

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Aanvaar 1 Sept 1986.

Alhoewel daar groot omstredenheid bestaan oor die patogene van akute bekken- infektiewe siekte (ABIS), word die rol van nie-kommensale organismes soos *Neisseria gonorrhoeae* en *Chlamydia trachomatis* as die primêre bron van infeksie oor die algemeen aanvaar.

Hierdie nie-kommensale organismes koloniseer gewoonlik die endoserviks. Die normale vaginale flora (meestal aërobiese en anaërobiese organismes) kry dan 'n sekondêre toegang tot die boonste genitale traktus. Dit is dan veral d.m.v. 'n anaërobiese progressie dat die Fallopius-buis uiteindelik beskadig word.

Dit is nie altyd moontlik om alle pasiënte met ABIS toe te laat nie en antibiotika word dus ook meestal lukraak aan buitepasiënte toegedien. Om dit te regverdig is 'n omvattende studie noodsaaklik, sodat veral die mikrobiologiese etiologie vir 'n spesifieke omgewing en populasie bepaal kan word.

## Pasiënte en metodes

Die seleksie van 40 pasiënte volgens vasgestelde kriteria is deur dieselfde klinikus gedoen, na die versekering dat geen vaginale lokale antiseptika of orale antibiotika binne 14 dae van toelating gebruik is nie.

Die volgende mikrobiologiese deppers is vir kulture geneem: endoservikaal — *N. gonorrhoeae*, *Chlam. trachomatis*; hoog vaginaal — *Mycoplasma hominis*, *Ureaplasma urealyticum*; uretraal — *N. gonorrhoeae*; *Chlam. trachomatis*; rektaal — *N. gonorrhoeae*; vanaf die fimbriële eindes van die Fallopius-buise