CROSS-INFECTION MECHANISMS IN A WARD WITH

.....

CONTROLLED PRACTICES

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by

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SUMMARY

The aim of this study was to examine the relevance of some patient parameters to nasal carriage and wound infection. This was based on cross-sectional surveys made in 38 hospitals between 1967 and 1973, a small continuous survey in two hospitals in 1977, and a continuous survey in one ward made 10 years previously. An attempt was made to formulate a mathematical model measuring the significance of patient parameters on the nasal acquisition of multiple-resistant <u>Staph.aureus</u>. A comparison of the two types of survey was also made.

The primary analysis showed that age and sex were related to the probability of a wound becoming infected. In addition to age and sex, antibiotic usage and length of stay in hospital affected the extent of nasal colonization with <u>Staph.aureus</u>. Multiple-resistant, penicillin-resistant and sensitive strains were considered both separately and together.

In the primary analysis, the factors affecting the probability of wound infection and nasal colonization were similar in both the singleward continuous survey and the cross-sectional surveys. The more recent continuous survey showed a reduction in multiple-resistant <u>Staph.aureus</u> in the patients noses when compared with the previous surveys, but, the carriage of penicillin-resistant only strains still increased with length of stay.

The multiple-regression analysis of the single-ward continuous survey confirmed that age and length of stay were independent significant factors influencing the carriage of multiple-resistant <u>Staph.aureus</u>. However, sex was not significant and antibiotic usage did not influence the carriage rate, as in the large cross-sectional survey. The regression model developed was based on the assumption that nasal carriage of multipleresistant Staph.aureus is a measure of certain aspects of susceptibility to infection.

HOSPITAL INFECTION

CROSS-INFECTION

EPIDEMIOLOGY

STAPHYLOCOCCUS-AUREUS

REGRESSION MODEL

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DEDICATION

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TO

MY DEAR PARENTS

AND

MY DEAR HUSBAND AND SON

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NOMENCLATURE

D.F.	Degrees of Freedom.
x ²	Chi-Squared Statistic.
Р	Probability.
S.S.D.	Sum of Squared Deviations.
R	Correlation Coefficient.
YI	Wound Infection Rate.
YN	Nasal Carriage Rate.
x	Age of Patient (years)
L	Length of Stay in Hospital. (days)
A, B, C	Constants
a, b ₁ , b ₂ ,	Constants
b3, b4	Constants

DEFINITIONS

Nosocomial Infection (Hospital Infection)

Nasal Colonization

Wound Infection

- : Hospital acquired infection.
- : Patient has acquired multiple resistant <u>Staphylococcu⁵aureus</u> in his nose in hospital.
- : Wounds whose severity of infection are listed as more than doubtful or mild are considered to be infected. (apart from excluded wounds)
- <u>Wound Infection Rate</u> : The percentage of patients infected according to the above definition, in a particular group (e.g. Male patient group) under analysis.

Nasal Carriage

- Nasal Carriage Rate
- : The percentage of patients who are Nasal Carriers according to the above definition in a particular group under analysis.

: Patients' whose nose swabs indicated the presence

of Staph.aureus organism. Multiple-resistant,

Penicillin-resistant, sensitive are considered

Staphylococci

: Coagulase-positive staphylococci.

together and separately.

(Staph.aureus)

CHAPTER 1

INTRODUCTION

Florence Nightingale in 1859 said that "It may seem a strange principle to enunciate as the very first requirement in a hospital, that it should do the sick no harm ". Her words are still relevant today in spite of all our improvements in aseptic techniques. Hospitals may still be dangerous places, although much less dangerous than in Miss Nightingale's day. The present rate of hospital infection is between 3.5-15.5 per cent of total patients admitted to hospitals (55, 57), and consists mainly of infections of operation wounds, the urinary and the respiratory tracts (56, 58). The predominant organisms responsible for these infections are gram-negative bacteria and to a less extent coagulasepositive staphylococci (55, 59).

The natural history of the development of nosocomial infections appears to begin with exposure of patients to pathogenic bacteria which have contaminated hospital equipment or colonized the skin and nasopharynx of hospital personnel (60). Gillespie (3) in 1958 states " Cross infection in a hospital does not differ essentially from the crossinfection which goes on all the time in any community such as a household or a school. Microbes, both pathogens and non-pathogens, frequently pass from person to person. Most of this cross-infection is harmless; harm

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comes, however, when the balance between the microbes and the hosts is upset. In hospitals, the balance is often tilted in favour of the microbes, and it is easy to see why. Firstly, the resistance of the patients to infection may be low, for example very young infants, and old people whose tissues are exposed by surgical operations, or whose immunity is lowered by debility. Next, in hospitals, there may be very numbers of pathogenic microbes, produced by patients who themselves are suffering from open infections. Moreover, the patients are often close together and frequently handled by a common staff, so that the microorganisms can spread easily. Finally, the use of antibiotics has upset the balance amongst the microbes themselves, and has favoured the spread and multiplication of strains which have developed resistance to the drugs".

The developments in surgical techniques have increased the length and complexity of many operations, resulting in prolonged anesthesia, extensive tissue damage and more wide spread use of artificial implants. These have increased the number of susceptible patients and moreover, there is an increase in the length of hospitalization of some patients. Under ordinary circumstances, patients are exposed to many different kinds of microbial agents during their hospitalization. Contact spread between a susceptible patient and an infected patient, either directly or through on intermediary, is generally thought to be the commonest and most important route of transmission of hospital organisms.

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Hand transmission by doctors , nurses , and other hospital personnel is accepted as the most common form of contact spread , and handwashing is stressed as means of preventing this.

In the last decade, certain organisms have gained prominence while others have become less prevalent on a percentage basis. The gramnegative, such as klebsiella and pseudomonas were the cause of less than 4 % of septic episodes in wounds in 1960, but increased to about 10 % in 1970, whereas staphylococci having caused 20 % of all septic episodes in 1960, now cause in the neighbourhood of 10 % (Masen, 63). The P.H.L.S. (34) reported that 60 % of all wound infections were due to staphylococcal sepsis in 1959, whereas Ayliffe (61) reported 33 % in 1970. Nevertheless, staphylococcal sepsis is still an important issue in wound infection, due mainly to the complexities of treating multiple resistant strains.

Habits of use of antimicrobial agents are important determinants of the species of organism ultimately causing infection. The use of a given antibiotic in hospitals is frequently followed by the emergence of resistant organisms. Under the continued selective pressure of antimicrobial therapy, resistant organisms have become a frequent cause of infections in some hospitals. Discontinuation of the use of these broad-spectrum and potent antibiotics has usually resulted in re-

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version to a less resistant flora. In the presence of antibiotics, three main changes occur in the micro-organisms. Firstly, previously sensitive strains of staphylococci and many gram-negative bacilli acquire resistance. Secondly, in organisms such as Pseudomonas aerogenesa and bacteroides, strains naturally resistant to antibiotics are selected. Thirdly, some of the resistant strains appear to show an increase in virulence (49).

To reduce the risk of sepsis a considerable amount of research has been carried out. Most of the research has been directed toward reducing the number of micro-organisms in the patient environment. The introduction of improved antiseptics, better nursing practice, mechanical ventilation systems and so forth have reduced the risk of sepsis. Williams et. al. (6) in 1959 and Gillespie et. al. (64) in 1959 were able to obtain a reduction in infection by treating carriage sites and by reducing environmental contamination.

At the conclusion of the International Conference on Nosocomail Infections, Dr. R.E.O. Williams (61) in 1970 opened his summarizing remarks by stating ; "Quite clearly, the first message from this conference is the need for surveillance. It is essential that hospital staffs know what is going on in the hospital, and they should have a mechanism for getting help from outside experts when it is need-

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ed. There seem to be two objectives of surveillance : 1. for better internal control of hospital activities , and 2. to see where one hospital stands in relation to others ". The practical use of surveillance is used as a means of comparing infection rates among different hospitals. Apart from all these approaches discussed above , it is also useful to detect out-breaks of infections as soon as possible, and as well as treatment , and to find out the changes in the area of hospital infections.

Patient parameters are also one of the most important factors in hospital acquired infection. There are many reports that state the significance of patient parameters on nosocomial infection (21, 29, 25, 33, 24, 48). But often environmental factors have become the predominant cause of hospital infection. Bowie et. al. (62) in 1964 states that a patient in hospital may acquire infection in three ways :

(1) By ingestion of contamination food stuffs giving rise to intestinal disturbance.

(2) By aerial infection in which particles of scurf, fibers of clothing and bedding, or other material carry micro-organisms to the skin and other sites of entry to the patient's body.

(3) By direct contact with contaminated hands , tissues .

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instruments , dressings , or other materials.

In this study , only environmental factors have been considered and patient susceptibility and host defences have been ignored. For a study on hospital acquired infection , both patient susceptibility and hospital activities should be taken into account. In other words , when trying to compare the infection rate in two wards , and in determining the significance of environmental factors , the susceptibility of the two patient populations under study must be comparable. In the second objective of surveillance (comparing infection rates in different hospitals) , patient parameters may be biased. The lower infection rate in one hospital when compared with another , may be simply due to differences in patient susceptibility of two different populations , or type of surgery ; as well as different ward and operating theatre practices or facilities.

There is no doubt of the significance of the endogenous source (self - infection) as a route of infection; but there is an argument over the mechanism of exogenous infection; i.e. whether post-operative wound sepsis was due to contamination in the operating theatre or whether it was acquired in the ward. However, the susceptibility index of Goonatilake (49), would indicate that the higher or lower rate of infection is largely due to the patient's

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own physical or clinical condition.

In most reports , the patient parameters are assumed to be unimportant , but environmental factors are considered to be the predominant cause of nosocomial infection. The aim of this study is to consider the significance of patient parameters on nasal colonisation and wound infection. It is assumed that patient parameters are independent of ward parameters. The study is based on three different surveys. A continuous survey carried out between 1968/69 in a surgical ward (B4), Dudley Road Hospital , Birmingham which included about 550 patients (Ayliffe et. al. 17). Another survey was a cross sectional survey (Birmingham Regional Survey) carried out between 1969-72 in the Birmingham region (Ayliffe et. al., 14, 49). The latter survey covered about 12,000 patients in over 500 wards with a multiplicity of ward practices. A further aim of the study, is to compare wound infection rates and nasal carriage rates within these two surveys , taking into account the significance of patient parameters. Also, there is a comparison with another continuous survey that was carried out in 1977 (69), in four surgical wards in two hospitals , covering about 550 patients. Again , the aim is to consider the significance of patient parameters on wound infection and masal carriage in two different decades. However . there are some practical difficulties associated with such surveys ; for

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instance, it takes a long time to collect an adequate sample for analysis, which means there is a bias because of an insufficient number of patients in such short period surveys. The significant patient parameters such as the patient's susceptibility index, will be derived from multiple regression techniques and then, a mathematical model will be postulated on theoretical grounds.

CHAPTER 2

LITERATURE SURVEY

<u>Staphylococcus aureus</u> is one of the most commonly transmitted diseases in hospitals and much of the avialable literature is concerned with such infections. This survey will, therefore, be only concerned with these micro-organisms. Certain strains of <u>Staph.aureus</u> have a propensity for spreading and causing sepsis in a ward and are known as epidemic strains. These are usually multiple resistant and for no apparent reasons, tend to appear and disappear, hence making the comparison of nasal carriage and wound infection rates difficult at different times, even in continuous surveys.

This literature survey is divided into six broad areas: i-The nasal carriage of staphylococci; ii- Post-operative wound infection; iii- Comparison of cross-sectional and continuous surveys; iv-Patient parameters related to nasal carriage and wound infection; v-Porphylaxis and antibiotic treatment; vi- Application of multiple regression analysis to factors associated with nasal carriage.

But only those concerned directly with this current work have been included here and other environmental aspects such as the effect of ventilation have not been included.

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2-1 NASAL CARRIAGE OF STAPHYLOCOCCUS

The principle site where <u>Staph.aureus</u> can multiply is the skin lining the anterior part of the nostrils, Mc Farlen (1938) said " It is still widely believed that its dispersal from the nose is mainly achieved by explusion into the atomsphere in the droplets produced during speaking, coughing and sneezing ". Some people are sometimes found to be carriers and sometimes not and it is not known why one person is a carrier and another is not, or why one person is sometimes a carrier and sometimes is not.

Nasal carriers of <u>Staph.aureus</u> have been found more likely to develop post-operative wound sepsis than non-carriers, and such infection will often be by the strain carried in the nose (Williams et.al., 1959). It has also been found that the infection rate in the carrier group was almost twice the infection rate in the non-carrier group. The difference between the rates is not quite statistically significant at the 5% level of significance (5). Also, it has been shown that antibiotic prophylaxis after operation was effective in both the carrier and non-carrier groups of patients (5), where Ketcham et.al. stated " In the carrier group, the patients recieving placebo treatment had an infection rate of 71.4% which was reduced to 20% in the antibiotic group. In the non-carrier group, staphylococcal wound infection was reduced from 42.9% to 10.7% by the use of antibiotics ".

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Any person touching the skin or clothing of the carrier may acquire the organism directly. But the organism may also reach inaminate objects such as the wash basin, scrubbing brush, pillow or bedding and etc. (1). As long as the carrier remains motionless, dissemination of his staphylococci into the atomsphere is not likely to occur, but any form of activity entailing friction on the skin or agitation of the clothing will suffice to cause dissemination (2). Very little is known about the extent to which this occurs. Carriers vary greatly in the number of organisms they disperse, indeed some disperse little more than do non-carriers (1). To reduce the number of bacteria in the nose, and dispersal of bacteria in the environment, different kinds of antibiotic nasal spray, or ointment, have been applied. Gillespie (3) in 1958 found that there was a marked reduction of nasal cross-infection on using nasal prophylaxis.

There are many different strains of Staphylococci, mostly they are identified by their antibiotic sensitivity pattern and phage types. Over the last fifteen years or so, the staphylococci have become resistant, hence they are now one of the chief organisms of sepsis. Gillespie (3) in 1959 states " The curious thing is that no staphylococci have become resistant to penicillin, because of exposure to it. The explanation of this apparent paradox is that even before penicillin was introduced, about 5% of staphylococci were naturally resistant, beca-

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use they produced the enzyme penicillinase, which destroys penicillin. These strains have multiplied in hospitals, where penicillin is most commonly used , and now are about eighty per cent of the staphylococci isolated from in-patients and staff ".

About 20-30% of people outside of hospital carry staphylococci in their nose, and in this group most of the strains are fully sensitive or just penicillin-resistant. People who have not been in hospital environments are found to have the lowest nasal carriage rate. Harris (4) compared the nasal carriage of a group of casualty patients and a group of in-patients and found that the great majority of strains in the casualty patients were fully sensitive to the antibiotics or resistant to penicillin only, while strains in the in-patient group were multiple resistant. Again , Davidson et.al. (9) has found that the incidence of staphylococcal wound infection among carriers was 12.5 % and the comparable figure for non-carriers was 7.2%. The results suggest a posibility of a relationship between the two factors , there being a higher incidence such a relationship, hence the considerable interest shown in the detection and treatment of nasal carriage as a means of reducing staphylococci infection (7, 6, 8, Hawe and Marston, 1962, Porter, McNeill, Miller, Green, 1963).

A change in antibiotic sensitivity of strains acquired in

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noses of patients in hospital, has occured in the last fifteen years. The persistent trend toward indiscriminate antibiotic " Prophylaxis " in patients undergoing on operative procedure has also contributed to the development or emergence of a wide variety of resistant strains in the hospital environment. Due to the routine use of prophylactic antibiotics there was until recently a high incidence of multiple resistant staphylococci in hospitals. In many published papers between 1964 and 1973, it has been found that the antibiotic resistance of strains of Staph.aureus isolated from the noses of patients in hospital and staff. that most of the strains were resistant to penicillin and tetracycline (10, 12, 13, 11, 14, 17, Shooter, R.A., 1958). Also Lidwell et.al. (15) found in surveys of staphylococci wound infection (1966), that the total carrier rate increased with the duration of stay in hospital. and the percentage of patients carrying staphylococci resistant both to penicillin and to tetracycline increased at least sevenfold in six weeks.

In view of the high rate of administration of antibiotics, and the often-repeated observation that multiple-resistant staphylococci are more rapidly acquired by those who receive antibiotics than by those who do not (15), Edmunds (16) in 1970 has found that the incidence of sensitive strains in patients previously admitted to hospital was 6.6%, that of penicillin-resistant strains was 8.6%, that of tet-

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racycline-resistant strains was 3.4 % . Perhaps , it shows that since 1970, the sensitivity of nasal staphylococci has changed . because Williams et.al. (36) in their survey between 1961 and 1972 found that from 1964 onwards there was a decline in the number of infecions due to multiple-resistant staphylococci. Little change in the frequency of infection due to sensitive strains or strains resistant only to penicillin was found. In part the decline in multipleresistant strains is attributable to the decrease in the number of strains of epidemic type, but there was also a decrease in the proportion of multiple-resistant strains in all phage groups. No one knows why the number of multiple-resistant strains have decreased. In a survey done during 1967 - 68, out of 65 strains, 50 per cent were resistant to penicillin , one fifth of the penicillin-resistant strains were resistant to methicillin and 11.5 per cent of the strains showed resistance to two drugs. Again , the penicillin-resistant strains were a high percentage. Recent paper shows reduction in tetracycline-resistant Staph.aureus since 1968 (74).

It is important to note at this stage that the term " Nasal carriage " has several interpretations. In some studies , it is not clear whether nasal carriage refers to the carriage of particular antibiotic-resistant strains or to all strains of staphylococci.

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It is more relevant to define the carriers of multiple or tetracycline-resistant strains as nasal carriers , because these strains are mainly asociated with hospital environments. But now the situation has changed with the changing nature of staphylococci , and nasal carriers will be defined in this work as the carriers of any strain of staphylococci. Therefore , in comparing nasal carriage rates obtained from different sources , the definition of the term nasal carriage should be first established.

2-2 POST-OPERATIVE WOUND INFECTION AND ASSOCIATION WITH NASAL CARRIAGE

Many factors are shown to be associated with a risk of post-operative wound infection. Most of the wound infections are found following dirty operations (e.g. the lower gastro-intestinal tract). Many workers have shown that the risk of wound infection has been affected by the type of operation (clean - dirty), length of incision, duration of operation, type of drain, wound dressing, etc.

Certain other factors may also be associated with postoperative wound infection because, approximately, 7.5 per cent of patients contract a post-operative wound infection of varying severity (19). It seems that the roles of local and systemic host defen-

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se factors on some patients are such that they may prevent the contaminating bacteria from establishing themselves and producing infection in the tissues. The N.R.C. report (24) states "28.6% of the dirty cases progressed to infection. Thus, in every operation wound there exists a complex interplay between the forces of bacterial invaders and the host's defenses. As a result of these multiple factors a few clean wounds become infected, and some massively contaminated wounds heal primarily ".

One of the many other factors which influence the incidence of wound infection is bacterial contamination of the wound. Inasmuch as bacterial contamination is a "necessary ", but not the only reason for wound infection, its role in the fate of a given wound may be obscured by other factors, e.g. when a grossly contaminated wound heals primarily. But, McNeill et.al. (8) in 1961 isolated staphylococci from the skin of the patient in the region of the operation field in twelve of some forty-three patients and of these, six developed staphylococcal infections of the same phage type. They concluded that contamination of the skin of the operation field may be an important contributing cause of infection. Cohen et. al. (21) states that when the type of suture material, the type of anaesthesia, and the type of skin preparation were

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studied, no differences related to the occurence of infection were detected. These results, it is felt, were not reliable because of small numbers and the great variety of regimes employed.

Douglas (22) studied the association of the position of the operation on the list with the incidence of sepsis in clean cases, and found that there was a significant difference between operations at the begining of the list and at the end of the list. Also, it was found that patients whose operations were at the begining of the list had a lower rate of infection than those on the end of the list (23, 28). This is perhaps, because of gradual contamination in the operating theatre with the increase in the number of operations. In the N.R.C. study (24), infection rates were related to the particular types of operations performed at different time of day. The majority of operations performed late in the day were dirty operations, and therefore have a higher risk of infection, than clean operations at the begining of the list.

The Public Health Laboratory Survey (34) indicated that duration, length of incision, drainage of wound and age of patient were related to sepsis, as well as the order of the operation on the list. Douglas (22), divided clean operations into long, medium and short duration, and found that with the ' first ' cases there was

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a higher incidence of ' long ' cases, which ought to have a greater incidence of sepsis , but did not. The ' first ' cases in his study were those operations given a priority on the operation list. But. on the other hand, Cohen et. al. (21) in their study, found that the operations of patients who acquired infection lasted, on the average. 50 % longer than those of the 8,811 patients who did not become infected, and that the infection rate increased with increasing duration of operation. The correlation is highly significant (r = 0.985). Whether this time-risk association is more related to the nature of operation procedures with increased exposure to bacteria, or to the multiplication of the organism during operation, or other factors, requires further study. By applying multiple regression analysis to extensive material published in a P.H.L.S. report (34) in 1960 , Lidwell (29) in 1961 demonstrated that " Certain variables, such as duration of operation, length of incision, and insertion of drain into a wound, were associated with an increased risk of sepsis. The first two factors increased the exposure to micro-organisms in the operating theatre , while the third factor , drainage , mainly augmented the risk of wound contamination in the wards.

The patient susceptibility to infection is another factor that influences the wound infection rate, and patients who were treated with prophylactic antibiotics prior to the operation, demonstrated

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a higher infection rate (24, 25). Since long term use of prophylactic antibiotics clearly increase risk , and are administered to patients of high risk of post-operative infection, then perhaps it is unwise to treat the patients prophylactically. Recent reports (Keighly, 1978,20) suggest that short term antibiotic prophylaxis is effective in reducing post-operative infection in certain types of wound. Patients who are treated with immuno-suppressive drugs or are otherwise particularly susceptible, are also more likely to develop infection. This is supported by the N.R.C. study (24) in which a higher wound infection rate was found in association with diabetes, obesity and steroid therapy. In patients with remote infections (infection other than in the area of the operation incision), there is an indication of a higher risk of acquiring wound infection (24, 20). Apparently, patients with remote infection such as urinary tract infection, lung infection, etc ..., are more susceptible to wound infection, and in general, remote infection is an indication of lower resistance of the patient.

In some reports, a good correlation is found between ward air and wound infection, which indicates that ward air might be a source of staphylococcal infection (26,27). But, the report from the committee of the N.R.C. (24) in 1964 concludes that though ultraviolet radiation reduced the number of bacteria-carrying particles in the air in the operating theatre to a low level, post - operative wound inf-

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ection was not significantly reduced. Hambraeus and Gillquist (1967) also reduced the air contamination in the operating theatre without effecting any change in wound infection rate.

A great number of patients admitted to hospital are operated on the same day, the day after admission or just a few days after admission, and only a small number of patients stay in hospital for a long period of time before operation for tests or other treatment. A higher risk of post - operative wound infection is associated with this last group, where the length of pre-operative stay in hospital is related to the risk of wound infection (24 , 25). Patients with a long pre-operative stay in hospital are often treated with prophylactic antibiotics as previously discussed , thus giving a higher risk of wound infection probably by reducing the patients' resistance to resistant organisms. Since long stay pstients are more likely to be masal carriers of hospital strains of staphylococci , this may put the patient at a higher risk of wound infection caused by resistant strains. As Linbom (30) in 1963 states, two factors have been emphasized as important determinants of post-operative wound sepsis, the acquisition of nasal staphylococci of hospital origin (Williams et. al. 1962, 31), and the duration of hospitalisation. Also, McEwin (32) Showed using the X^2 test that infection rate increases with the pre-operative length of stay. This test gave a value of 6.86 with two

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degrees of freedom, which is significant at better than the five percent level.

Age and sex of patient are also associated with a risk of wound infection. Many workers have found that these two patient parameters have very close relationship with wound sepsis. It seems that the risk of infection is higher in older patients, and thus increases with age (25, 21, 24, 14, 33, 34), and there are two main reasons for this : i- The resistance of old patients to various infections is in general much lower than it is in the young patients (21, 24). ii- Young patients more often have clean operations than old patients and this results in the lower infection rates (N.R.C. study, 24). This is not surprising, because other factors (e.g. dirty operations, etc.) which are associated with higher infection rates are also associated with older patients.

In considering other patient parameters such as race and sex , Cohen et. al. (21) states that these bear no relation to infection , and Whyte et. al. (35) also states in the results of a study on a mechanically ventilated ward and two open wards, that the results failed to show any significant difference between males and females in the two units. There are, however, many other reports that shows a higher infection rate in males than in females (14, 25, 24, 27, 34). In a further explanation, the N.R.C. study (24) states that a greater

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number of non-clean wounds occuring in males may account for the higher infection rate. When only clean wounds were considered, the wound infection rate was slightly lower in males than in females; but for nonclean wound the infection rate was higher in males than in females. In the end, they concluded that , when all types of wound infection rates were used the sex of patient was not a primary determinant of wound sepsis risk.

Lindbom (30) in 1958 showed that auto-infection, defined as wound sepsis caused by staphylococcal strains carried in the nasopharvnx before the operation, was probably an important factor in approximately 1/3 of all septic cases. Also, Williams et.al. (6) in 1959 demonstrated a significant association between nasal carriage of Staph. aureus and post-operative wound infection. Again, Williams et. al. (31) in 1962 with a greater number of patients confirmed their finding. Their results showed that " patients who aquired staphylococci in their nose during hospitalisation, developed staphylococcal sepsis more than five times as often as others who did not. In most cases nasal colonization preceded the sepsis. The P.H.L.S. survey (34) in 1960 also observed a similar relation between nasal carriage and wound sepsis, in which the difference was not statistically significant. Also, McNeill et: al (8) in 1961 states that the acquisition of nasal staphylococci of hospital type by patients admitted to surgical wards , has been

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singled out as an important determinant of post-operative wound infection. An alternative view, as expressed by Rountee et. al. (1960) would deem it equally likely that, where patients acquire ward strains of staphylococci at about the same time in their nose and their wounds, then both nose and wound have been infected from some another source. Moore and Gardner (37) in 1963 in their study found that post-operative wound sepsis had occured a less frequently in patients who were staphylococcal nasal carriers on admission to hospital than in non-carriers.

Gillespie (3) in 1958 noted that where " nasal prohyplaxis " was applied in two surgical wards, as a sole precaution, there had been a marked fall in the nasal carriagerate, but at the same time a far smaller effect on the incidence of wound was observed. He suggested that, to control cross-infection in surgical patients, it might be necessary to deal with both carriers and the infected operative wound, while at the same time blocking some of the more obvious routes of ward cross-infection, such as contaminated blankets or baths. On the other side, Bruum (25), reported a significant reduction in nasal carriage rate and wound infection rate, following nasal prophylaxis.

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2-3 COMPARISON OF CROSS-SECTIONAL AND CONTINUOUS SURVEY

Williams in a report concerning ' hospital infection ' said, an historical survey of attempts to control hospital infection could begin with Florence Nightingale's campaign for better design of hospital wards and improved standards of nursing; with Joseph Lister's introduction of antiseptic surgery; or with Oliver Wendall Halmes's or Ignas Semmelweis's work on puerperal sepsis. Continuous survey are carried out over a long period of time in one hospital with no break during this period. A cross-sectional or prevalence survey includes all patients in a hospital or ward at one time. This may be repeated in different hospitals. Most of the repeated survey's are continuous surveys. In continuous surveys, the ward and hospital practices are more likely to remain constant as long as time intervals are not too long and therefore there should be fewer problems of different practices than in cross-sectional surveys. Cross-sectional surveys are preferable when large quantities of data are required in a short time. and if carried out in different hospitals are less likely to be biased by individual parameters.

The surveys of PH.L.S. (34) in 11 hospitals between 1957 to 1959 found the age of patient, length of pre-operative stay in hospital, length of incision, and duration of operation were all assocaited with

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increased sepsis rate, as was the use of a drainage tube. Lindbom (30) in a continuous study in 1958-59 found that duration of operation, duration of hospitalisation and nasal staphylococci of hospital origin were associated with an increased risk of sepsis. In both reports, <u>Staph.aureus</u> was the most common pathogen. Also, in cross-sectional surveys in Danish hospitals during the year 1957-66, Jessen et. al. (38) found a higher infection rate in males than in females, and the risk of infection in older patients was higher. Jepsen et. al. (39) in 1965-66 found a higher but not sinificant rate of purulent infection among the men. He introduced a theory that this difference is probably due to a predominance of " bad risk" operations in men.

There are three reports, two cross-sectional and one continuous reporting survey made between 1966 and 1973. They state similar results, namely, age, type of drain, duration of operation, length of incision tends to increase the infection rate. The results were confirmed by Berbee et.al. (40) between 1971 and 1973 from their continuous survey. In the other cross-sectional survey made in 38 hospitals between 1967 and 1973, Ayliffe et. al. (14) showed a high correlation between infection rate and age. The infection rate was higher in males than in females, and there was a high correlation between nasal carriage rate and age, and nasal carriage rate and length

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of stay. Again males had a higher risk of infection than females. In comparison, Noble (10) in his continuous survey between 1966 and 1968 showed a higher infection rate in males than in females.

2-4 PATIENT PARAMETERS

Patient's age and sex are parameters unique to the individual, independent of other factors such as type of operation, type of drain, and duration of operation, etc. There is another parameter, length of stay in hospital which is a measure of degree of exposure to the hospital environment and can be considered as an independent parameter of each individual patient, because it depends on the patient's condition which may be a function of his own susceptibility. The effect of these patient's parameters may determine the nasal carriage rate and wound infection rate. In other words, these patient parameters probably have a close association with a measure of a patient's susceptibility.

2-4-1 AGE OF PATIENT

There are a few reports that show a relationship with increasing age of patient and nasal carriage rate. Lidwell et. al. (41) showed that where was a predominance of elderly patients (about 61 % of the group were over 60 years of age), there was a higher rate of

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nasal colonization and acquisition among them. Bruun (25) also reported an increase in nasal carriage rate of all strains of staphylococci (as well as multi-resistant strains) with increasing patients age , and Ayliffe et. al. (14) shows a higher nasal carriage rate with increasing age of the patient , in age groups between one and seventy years.

The age is also closely associated with wound infection itself, because Ayliffe et. al (14) reports a high correlation coefficient between age and wound infection rate. In the P.H.L.S. study (34) and Jessen et. al. (38) infection rate also increased with age. Berbee et. al. (40) states age and some other factors increase the likelihood of clinically apparent infection. Again, Ayliffe and Collins (42) in a study on post-operative infection state that the host factors such as age and sex have a major influence on the occurence of wound infection. There is one report that has failed to establish the significance of age on wound infection (Cohen et. al. (21)). As an explanation they say that, since the nature of the operations performed varies with age, the data does not necessarily indicate that increasing age is associated with decreased resistance to post-operative infection. Bruke (43) found the lowest infection occuring in the 15 to 24 years age group and increasing up to twice that rate in the

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65 to 74 years age group, and Bruun (25), indicated that the rate of wound infection is higher as the age increases. Cowling (33) reported a significantly higher wound infection rate with older patients, indicating that a total infection rate for patients below the age of 40 years was 8.8 % and for patients above that age, the infection rate was 14.1 %. In conclusion, the N.R.C. study (24) in their controlled study showed the incidence of infection is influenced frequently by such other factors as the hospital in which the operation was performed, the duration of operation, nutritional and metabolic factors of patients, and the duration of the patient's pre-operative hospitalisation. However, even after adjusting the data for all these factors, increasing age is still associated with an increasing incidence of wound infection.

2-4-2 SEX OF PATIENT

In the N.R.C. study (25) a lower infection rate among females is reported, but in explanation they indicate the increased incidence of wound infection in males is due to more contaminated procedures in men. In making adjustments to correct infection rates for wound classification, the infection rates in males and females become essentially the same. Cohen et. al. (21) also found similar results showing that sex has no relation to infection. But, in com-

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parison, Ayliffe et. al. (14) in the cases of nasal carriage rate and age , masal carriage rate and length of stay , and wound infection rate and age found a significantly lower infection rate and carriage rate in females. Lidwell et. al. (15) found that staphylococcal sepsis and wound colonisation were both more frequent in male than female patients. Also Jepsen et. al. (27) have a similar explanation to higher risk of infection in males and they introduce a theory that the higher infection in males is due to a predominance of ' bad risk ' operations in males. Fekety and Murphy (45) found even in new born babies a greater susceptibility to staphylococcal skin infection in males, and Bethune (46) found that dispersal of all aerobic bacteria was more profuse in men than in women. Futher supportive evident was given by Ayliffe et. al. (17) who experienced a significantly lower mean settle-plate count when a ward was occupied by female patients. These last three reports may indicate a lower carriage rate in females than in males, but some doubt still persist about whether the infection rate may be due to differences in operations in males.

2-4-3 LENGTH OF STAY IN HOSPITAL

The length of hospitalisation directly relates to the patients exposure to micro-orgnisms in the ward environment. This obviously effects the risk of infection in open wounds, as well as nasal carriage

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rate. As Berbee et. al (40) say, the mean stay for the infected group was 19.2 days and for the uninfected 15.5 days. The distribution of duration of stay is statistically significant (x^2 =17.4, d.f. = 8, $1 \% \rangle P \rangle 0.1 \%$). The PH.L.S. study (34) states that the length of pre-operative stay in hospital is associated with increased sepsis rates and again Lindbom (30) points to the duration of hospitalisation as an important determinant of post-operative wound sepsis. In other reports, there was found to be a steady increase in the proportion carrying tetracycline-resistant strains of staphylococci with length of stay in hospital (41, 47, 48), and that the number of sensitive strains of staphylococcus or penicillin-resistant strains of staphylococcus decreased with length of stay in hospital (47, 48).

2-5 ANTIBIOTIC PROPHYLAXIS AND TREATMENT

Many of the patients in hospitals are treated with antibiotics, especially those who undergo a surgical operation. This particular group may receive pre or post-operative antibiotics or both. The antibiotics may be administered topically, orally, or parenterally. The effect of a topical application is to destroy infecting organisms in the wound, oral non-absorbable antibiotics reduce the bacterial flora in the colon, and systemic antibiotics kill the bacteria during operation.

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Although the introduction of antibiotics and other chemotherapeutic agents has revolutionised the treatment of bacterial infections, many bacteria have responded to this threat to their existence by acquiring resistance to a varying number of useful antimicrobial agents (Ayliffe, 1972). The widespread prophylactic use of antibiotics is undoubtedly hazardous, and may select resistant strains present in small number. Ayliffe in a report in 1972 and Lindbom (30) state that most of the antibiotic-resistant bacteria are found in hospitals and in particular Staph.aureus, a common cause of operation wound infection, has demonstrated its ability to acquire resistance to every nontoxic effective antibiotic introduced. Lidwell et. al. (15) found carriers of multiple-resistant strains disseminated more heavily than did the carriers of sensitive organisms; many were undoubtedly receiving antibiotics to which their nasal strains were resistant. Also, Cohen et. al. (21) says " In our survey when antibiotics were given, the staphylococci causing infection were usually more resistant to antibiotics than when prophylaxis was not given ". Anderson et. al. (50) states patients giving a history of penicillin therapy had the same resistance rate of nasal carriage as patients without a history of such therapy. Ayliffe et. al. (14) found patients receiving antibiotics had a significantly higher carriage rate of resistant strains than those not receiving antibiotics. Parker et. al. (48) reported that patients who

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received antibiotics acquired multiple-resistant strains in the nose. An antibiotic policy to control their use is essential according to Speller et. al. (51), in order to preserve their value in lifethreatening infections by bacteria resistant to other agents.

Ignoring the influence of antibiotics on nasal carriage. there is still a high risk of wound infection with resistant stapylococci associated with the administration of antibiotics. The use of prophylactic antibiotics does not necessarily change the overall infection rate following general surgery, although the spectrum of organisms may be shifted, Fekety (45). Cowling et. al. (33) found two per cent of clean wounds become infected in the absence of antibiotic cover, but in cases in which antibiotics were used prophylactically, this figure was 7.1 %. Berbee et. al. (40) also reported that only 33% of patients given prophylactic antibiotics become infected compared with 18% of those not given antibiotics, this is statistically significant ($X^2 = 9.1$, P (1%). But because of insufficient number of patients, the analysis was carried out on all operation classifications and no sub-division into clean and dirty operations was possible. The P.H.L.S. study (34) states despite the demonstrably biased selection of patients for antibiotic prophylaxis, an attempt to correct for the bias did not alter the fact that treated patients have a much higher infection rate than untreated patients. Also, Ketcham et. al. (5)

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comments on the effectiveness of post-operative antibiotic prophylaxis in both the carrier and non-carrier groups of patients, and says that for the carrier group, the patients receiving placebo treatment have staphylococcal wound infection rate of 71.4% which reduces to 20.0 % in the antibiotic treated group. In the non-carrier group, the staphylococcal wound infection rate was reduced from 42.9 %^{to} 10.7 \% by the use of antibiotic.

With the introduction of new antibiotics almost every decade, the use of antibiotics is changing. Altermeier (53) said in 1958 " As a result of the tremendous impact of antibiotic therapy and the everyday miracles following its use, the evolution of the belief among surgeons that there were no longer any important problems in the prevention or control of surgical infection was probably inevitable. This concept has led to the general and indiscriminate use of many antibiotic agents during the past ten years and has now brought into sharp focus the obvious limitations of chemotherapy as well as some of the factors which have contributed to the present problem of wound infection ". A list of antibiotics used in 1962-63 produced by Parker et. al. (48) showed the main agents to be tetracycline, penicillin, streptomycin, neomycin, and chloramphenicol. The antibiotics used between 1964 and 1967 (Barrett (52)) were similar except for a decrease in that of kanamycin and some newer antibiotics in 1967. The most commonly

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used antibiotics in these years (1964-67) were apparently penicillin, tetracycline, erythromycin, and streptomycin. Two years later in 1969, Ayliffe et. al. (12) reported that the most used antibiotics were ampicillin, tetracycline, benzyl-penicillin, and less commonly streptomycin and cloxacillin. Again, Ayliffe et. al. (11) in between 1967 and 1975 found topical antibioitcs, especially neomycin widely used. Recently in 1974-75 many of the patients have been receiving gentamicin, tobramycin, lincomycin, or a mixture of tobramycin and lincomycin (51).

2-6 APPLICATION OF MULTIPLE-REGRESSION

The simple analysis contained in previous studies suggests that wound sepsis and nasal carriage are influenced by a number of factors, so it seems desirable to explore some form of analysis which would given estimates of the independent effect of the several variables. Multiple-regression analysis would evaluate the relative importance of an independent variable (e.g. length of stay, type of operation, duration of operation) on the dependent variable (e.g. infection rate or nasal carriage rate). The availability of electronic high-spead computers now makes possible methods of analysis which were previously quite impracticable because of the excessive labour involved in hand computation.

Since these methods have not yet been widely used in problems

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of this kind, there are very few reports available. The incidence of post-operative wound infection and sepsis in some 3000 patients in twelve hospitals has been the subject of a report of the Public Health Laboratory Survey (34) and Lidwell (29) applied multiple-regression analysis to the results of this P.H.L.S. study and he established the significance of various operative procedures and patient factors on the risk of post-operative wound infection. The predominant factors considered: age over 60, male sex, long duration of operation, incision over 6 inches long, and the insertion of a drain in the wound were all found to be associated with increased risk of post-operation sepsis. Bruun (25) also applied a multiple-regression analysis on some of his results and found the type of operation, wound contamination, insertion of drain, nasal carrier state of resistant strains, duration of operation and pre-operative hospitalisation to be factors associated with wound infection.

CHAPTER 3

IMPLICATIONS OF LITERATURE SURVEY

3-1 GENERAL CONCLUSIONS OF THE LITERATURE SURVEY

The literature survey suggests certain general conclusions. Hospitalised patients aquire antibiotic resistant strains of staphylococci in their noses. The reason why some people become carriers, and some do not, under similar environmental conditions is still not clear. The rate of nasal carriage in old patients is higher than in young patients. Also at the present time, the number of resistant strains of staphylococci in the nose is reduced and nasal strains of staphylococci tends to be penicillin-resistant or fully sensitive.

Whether there is a significant association between nasal carriage of resistant strains and wound infection, is difficult to reject or accept from the literature cited. Nasal carriage of resistant staphylococci is a measure of the patient's exposure to the ward environment and possibly an indication of the patient's susceptibility. Therefore, nasal carriage of resistant staphylococci can be used as a measure of post-operative staphylococcal cross-infection.

The factors associated with the risk of post-operative sepsis such as type of operation, length of incision, duration of operation, drainage and some other procedures are more apparent. Patient parameters

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such as age and sex are also cosely associated with the risk of wound infection.

The actiology of staphylococcal wound infection can be studied either using a continuous or a coss-sectional survey. A cross-sectional survey is a method of surveillance which is very useful for inter-hospital comparisons. By the use of the same criteria for judging infections , a meaningful comparison of nasal carriage rates and infection rates between hospitals is possible. Continuous surveys are carried out in over a longer period of time, with no breaks during this period. and are useful for demonstrating the occurence of infection in an individual hospital under similar ward conditions. The literature cited appears to show that there is similarity between the results of cross-sectional surveys and continuous surveys, particularly in patient parameters and in this work it is intended to measure patient parameters in a continuous survey in hospitals where cross-sectional results are known. Obviously interaction due to differing ward practices are reduced under these conditions.

The significance of patient parameters on wound infection and nasal carriage has been well documented. The age of patients is most important; older patients are more likely to acquire infection because they undergo more complicated survey and this can be considered as a

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function of patient's age as well as susceptibility to infection. The relationship between age and nasal carriage of resistant staphylococci is well known; i.e., there is a higher nasal carriage rate in older patients. The wound infection rate and nasal carriage rate is lower in females than in males. As explanation for lower wound infection rate, the female patients may undergo less complicated surgery, but the reason for lower nasal carriage rate is unknown. The length of stay in hospital is closely related to the nasal carriage rate, which can be used as a measure of exposure and to the patient's susceptibility to infection.

The significance of antibiotic therapy on nasal carriage and wound infection is doubtful. It is difficult to say in most studies, whether it was administered to patients with a higher risk of infection, or whether the antibiotic treatment resulted in a higher infection rate. But there is no bias in the relationship between antibiotic use and nasal carriage, and probably, the sensitive strains of staphylococci are suppressed by the use of antibiotics resulting in a higher carriage rate of resistant strains. Multiple-regression analysis is useful in determining the relative significance of various factors on nasal carriage and wound infection.

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3-2 THE PRESENT WORK

The aim of present work is to consider the significance of patient parameters on nasal colonization and wound infection. The significant patient parameters determined in the different survey data, will be represented as a patient's susceptibility index, then a mathematical model will be fomulated. A further aim of this study is a comparison between cross-sectional surveys and continuous surveys. This comparison is based on the significance of age on wound and nasal carriage, and length of stay on nasal carriage. The sex and antibiotic treatment are also considered. But there is a bias in the results because of small size of samples in the more recent study.

3-3-1 DUDLEY ROAD (B4) CONTINUOUS SURVEY

Studies were carried out by the Infection Research Laboratory, Dudley Road Hospital, Birmingham (17), in a modified ward (B4), containing nineteen beds; fourteen of them were in the open ward, one in a window-ventilated side-room, two in cubicles with recirculation and two in self-contained isolation suites with plenum ventilation, ultra-violet (uv) barriers at doorways and airlocks (Fig. 1). The ward was studied from October 1965 to December 1969, apart from several periods during which it was either closed or used for patients who were not included in the series. The ward was mainly used as an

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Fig. 1. Plan of ward B4, Dudley Road Hospital.

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ordinary surgical ward; patients in the self-contained plenum-ventilated unity remained in them throughout their stay in hospital, but patients in the recirculation and window-ventilated rooms walked through the open ward to the bathroom and toilet.

3-3-2 TECHNIQUE OF SURVEY

In addition to personal details such as age, sex, and date of admission, the information included days in hospital, diagnosis, operation, wound and other sepsis, antibiotics given and bacteriological results. Information on sepsis was obtained daily from the ward sister by the laboratory staff. Wounds were classified as septic if there was any evidence of clinical infection irrespective of presence or absence of pus. Swabs were taken daily for 6 days a week from patients' noses and weekly from the staff. Swabs were taken from drained or moist wounds at the first dressing and at subsequent dressings whenever possible, also from any other infected lesions. All the information on all patients was transferred to specially designed forms (Appendix A) suitable for transfer to punch cards. In this work, only the last two years has been studied. The data validation and analysis was carried out using the University of Aston Computer ICL 1904s.

3-3-3 BACTERIOLOGICAL METHODS

Nasal swabs were cultured on nutrient agar containing 1 %

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serum and phenol phthalein diphosphate (Barber & Kuper, 1951, 44). Wound swabs were cultured aerobically on blood agar, McConkey medium and in cooked meat broth, which was subcultured aerobically and anaerobically. Tests of antibiotic sensitivity on <u>Staph.aureus</u> were made by a ditch-plate (Topley, Lowbury & Hurst, 1951) or disc diffusion method. Antibiotic sensitivity tests were made on strains grown from the nose and wound. Most strains of <u>Staph.aureus</u> isolated from wounds, lesions and noses were phage typed (Blair & Williams, 54).

3-3-4 DEFINITIONS

WOUND INFECTION.

Operation wounds were divided into three categories modified from those described in a survey made in the U.S.A. (National Research Council, 1964, 24) as follows:

Clean Wounds

An operation not transecting gastro-intestinal, genito-urinary or tracheo-bronchial systems and not performed in the vicinity of any apparent inflammatory reaction.

Clean-Contaminated

An operation transecting one of the above systems, where bacterial contamination could occur but evidence of contamination was uncertain, e.g. operation on the stomach, gull-bladder and bladder.

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Contaminated

An operation transecting systems where bacteria are known to be present (and usually abundent), or in the vicinity of apparent inflammatory reactions, e.g. operations on colon, perforated appendix, mouth.

Severity of infection was defined as follows:

Mild. A small or superficial area of inflammation with minimal discharge.

<u>Moderate</u>. Superficial inflammation of whole wound (or over one-third) with a serious exudate or small amount of purulent discharge; or a deeper infection involving a small area (one-third or less) usually with purulent discharge.

Severe. A deep purulent infection with or without sinuses or fistula or wide spread cellulitis, or wound breakdown with an obvious inflammatory reaction and pus.

3-4-1 D.R. (D15 & 21) AND G.H. (8 & 9) CONTINUOUS SURVEY

The survey was made from first of November until the end of December 1977 by the Infection Research Laboratory, Dudley Road Hospital, Birmingham (69). The survey were carried weekly on patients in four surgical wards, in an old (Dudley Road) and a new district (Good Hope) general hospital. The wards in Dudley Road hospital consisted of two open surgical wards (1 male, 1 female) with between 25-30 beds; and

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a side room with one or two beds (Fig. 2a). The wards in Good Hope hosptial consisted of 30 beds (mixed male and female); in rooms with one, two, or four beds (Fig. 2b). The wards had one separate dressing room which was used for the routine dressing of wounds.

3-4-2 TECHNIQUE OF SURVEY

The collected data were entered on specially designed forms (Appendix B). Information about patient's age and sex, date of admission, date of operation, movement, diagnosis, duration of operation, surgeon, operating theatre, length of incision, wound sepsis or other infection, and some more procedures were obtained from the kardex or patient's notes and recorded on one form. Information about antibiotic usage was entered on another form. Wounds were sampled using cotton wool swabs, which were moistened in saline; the presence or absence of sepsis was recorded according to the definitions previously described. Swabs were taken from the noses of all the patients in the ward, and from most operation wounds or other lesions. The data validation and analysis was carried out using the University of Aston Computer (ICL 1904s). The bacteriological methods and definitions for wound infection were the same as in the previously described.

3-5 THE BIRMINGHAM REGIONAL SURVEY (CROSS-SECTIONAL)

This survey was carried out between 1967 and 1973 by the In-

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Sluice	Bathroom
13	/2
14	11
15	10
16	9
17	8
18	7
19	6
20	5
21	4
22	3
23	2
24	1
Clerk	Staff
Kitchen	25

0

Fig. 2a. Plan of ward D15 & D21, Dudley Road Hospital.

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Fig. 2b. Plan of ward 8 & 9, Good Hope Hospital.

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fection Research Laboratory, Dudley Road Hospital, Birmingham (14). The survey consisted of hospitals in the Birmingham region, where 38 hospitals were visited, and repeated surveys were made in 12 hospitals. Over 12,000 patient records were collected from over 500 wards with a multiplicity of ward practices. This represented a large number of patients when compared with most other surveys (both types), where the patient numbers was rarely greater than 550. Goonatilake (49) applied multiple regression analysis to the results of this survey, and formulated a mathematical model on the significant patient parameters. Because there are similarities for patient parameters between continuous and cross-sectional surveys, it is intended to use the work of Goonatilake (49) as a basis for comparison with the continuous surveys for Dudley Road hospital that will be used in this thesis.

PART I

PRIMARY ANALYSIS

CHAPTER 4

SIGNIFICANCE OF PATIENT PARAMETERS ON WOUND INFECTION

4-1 INTRODUCTION

In chapter 2, the association of hospitalisation with a higher incidence of nasal carriage of tetracycline <u>Staph.aureus</u> and the association of carriage with a higher risk of the wound infection was observed using carriage of resistant staphylococci as convenient method of measuring cross infection transmitted on dry equipment or in the hospital air. Patient parameters such as age and sex are unique to every individual patient, irrespective of his clinical or operative condition, and while the association of increasing age with a high risk of acquiring post-operative wound infection is stated in previous studies, the significance of the sex of patient has been somewhat inconclusive.

In this chapter, the rate of wound infection in relation to nasal carriage before and after operation, and also the significance of age of patient on wound infection rate is quantified using a curve fitting approach. The association of sex of the patient is also investigated. Any bias arising from associated factors such as type of wound, presence of drains and type of operation is also included. However, before analysis, it is necessary to define wound infection.

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4-2 DEFINITION OF WOUND INFECTIONS

In the two continuous surveys considered for this work (Dudley Road (B4) 1968/69, and Dudley Road (D15 & 21) & G.H. (8 & 9) 1977), the wounds were described as having: i- no infection; ii- redness of edges and serious discharge; iii- pus; iv- cellulitis. The presence of haematoma, sinuses or fistula, wound breakdown, slough, or deep abcess was recorded. The presence or absence of a drain was also recorded.

Wounds described as clinically infected were graded as mild, moderate or severe. Doubtful infections, mild infection of drainage wounds and wounds previously infected but healed at the time of the survey, were also recorded.

Severity of infection was defined as follows: <u>Mild</u>. A small or superficial area of inflammation with minimal discharge. <u>Moderate</u>. Superficial inflammation of whole wound (or over one-third) with a serious exudate or small amount of purulent discharge or a deeper infection involving a small area (one-third or less) usually with a purulent discharge.

Severe. A deep purulent infection with or without sinuses or fistula or widespread cellulitis or wound breakdown with an obvious inflammatory reaction and pus.

The grade of severity, although based on the above definitions, was examined and assessed by one or the other of two abservers.

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In the analysis, doubtful infections and certain categories of operations, e.g. vaginal, rectal, traumatic, and drainage of absecesses, have been excluded.

4-3 NASAL CARRIAGE AND WOUND INFECTION RATE

Out of 533 patients in dudley Road (B4) continuous survey (1968/69), 283 patients had operations and the corresponding total wound infection rate was 14.13%. Table 1 shows the wound infection rate and nasal carriage of tetracycline resistant <u>Staph.aureus</u>. As the literature survey led us to expect, the infection rate was lower in patients that were not colonized (11.87 %) than in patients that were colonized (40.90 %). The difference between these two categories is statistically significant (X^2 = 14.07, 1 D.F., P(0.005). The patients were further classified to sex. Table 2 shows that the wound infection rate in males was 12.26% and in females 16.66%. The difference between infection rates is not statistically significant (X^2 = 3.56, 1.D.F., P(0.1), but the number of females with infection was very small.

Table 1. Nasal Colonization and Wound Infection Rate.

	No. in group	Percentage Infected	
Colonized	22	40.90	
Not-colonized	261	11.87	
Total	283	14.13	

Colonized = Patient has acquired tetracycline resistant <u>Staph.</u> <u>aureus</u> in his nose in hospital.

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Table 2.	Nasal Colonizat	ion, Sex and	Wound Infection Rat	e.
	Fema	les	Maj	es
	No. in Group	infection (%)	No. in Group	Infection (%)
Colonized	4	50.00	18	38.88
Not-colonized	116	15.51	145	8.96
Total	120	16.66	163	12.26

Out of 22 infected patients, 7 were colonized before operation and 15 were colonized after operation. Table 3 shows infection rate is statistically significant in patients that have become colonized after operation ($\chi^2 = 767.19$, 1 D.F., P(0.001).

Table 3. Wound infection rate and nasal colonization before and after operation.

	Colonized Patients	Percentage Infected
Before operation	7	42.85
After operation	15	40.00
Total	22	40.90

4-4 EFFECT OF AGE AND SEX OF PATIENT ON WOUND INFECTIONS

4-4-1 DUDLEY ROAD (B4) CONTINUOUS SURVEY (1968/69)

Patient ages were classified in seven groups for convenience, and to provide an adequate number in each group, 10 years was taken as the interval. The wound infection rates for these age groups are shown in Table 4. Wounds in patients under ten years of age were excluded for

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the purpose of analysis, because of a very small number of patients.

Age Group	No. of Patients	Infection Rate	
11-20	22	9.09	
21-30	33	6.06	
31-40	39	17.94	
41-50	64	7.81	
51-60	61	11.47	
61-70	30	30.00	
71 & over	25	32.00	
Total	283	14.13	

Table 4. Wound Infection Rate and Age of Ptient.

The differences in infection rates in these seven age group were statistically significant ($\chi^2 = 42.58$, 6 D.F., P(0.005). The relationship between wound infection rate and age can however, be well represented by a quadratic equation, YI = A - BX + CX², where YI is the infection rate, X is the age and A, B and C are constants. For the data in Table 4 the following quadratic equation gave the best fit with a sum of squared deviation (SSD) of 167.85 which absorbs 82 per cent of the variance about the mean:

 $YI = 15.27 = 0.527 X + 0.01 X^2$

differentiating to obtain the minimum value for Y,

$$\frac{dy}{dx} = 0, x = 26,$$

This fitted curve together with the 95 per cent confidence limit

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(Fig. 3) therefore suggests a minimum infection rate about the age of 26, with the infection rate increasing for younger or older age.

The patients in the some age groups were further classified according to sex (Table 5). The total infection rate was slightly higher in female patients (16.67%) than in male patients (12.27%). This difference is not statistically significant ($X^2 = 1.09$, 1 D.F., $P \langle 0.500 \rangle$). The relationship between age and wound infection rate for both groups can be represented by quadratic equations. The equation for the female patients is:

 $YI = 6.86 - 0.215 X + 0.008 X^2$, SSD = 309.18

which absorbs 82 per cent of the variance about the mean and has a minimum infection rate at 13 years (Fig. 4). For male patients: $YI = 23.9 - 0.81 X + 0.01 X^2$, SSD = 402.05

which absorbs 41 per cent of the variance about the mean and has a minimum infection rate at 40.5 years (Fig. 4).

Table 5. Age	, Sex and Wound	I Infection Rate	<u>e.</u>		
Age Group	Ma	Males		Females	
	patients	% infected	patients	% infected	
11-20	11	18.18	11	0.00	
21-30	22	4.55	11	9.09	
31-40	15	13.33	24	20.83	
41-50	32	3.12	32	12.50	
51-60	43	11.63	18	11.11	
61-70	21	33.33	9	22.22	

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71 & over	11	18.18	14	42.86
Total	163	12.27	120	16.67

4-4-2 D.R. (D15 & 21) AND G.H. (8 & 9) CONTINUOUS SURVEY (1977)

Out of 559 patients, 164 patients had operations. Patient ages were classified in three groups (50 - over 70) for convenience, 10 years was taken as the interval . Wounds under 50 years are excluded for the purpose of analysis because , there was no infected patients under this age group. The wound infected rates for these groups are shown in Table 6.

Table 6	5.	Age	of	Patient	and	Wound	Infection	Rate

Age group	No. of Patients	Infection Rate
51 - 60	24	25.00
61 - 70	45	22.22
71 & over	43	23.25
Total	112	23.21

The differences in infection rates in these three age groups (50 - over 70) were not statistically significant $(X^2 = 5.44, 2 \text{ D.F.}, P \langle 0.10 \rangle)$. The relationship between wound infection rate and age can best represented by a quadratic equation of the form YI = A- BX + CX^2 , where YI is the infection rate , X is the age and A , B and C are constants . For the data in Table 6, the following quadratic equation

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gave the best fit, with a sum of squared deviation (SSD) of 0.00 which absorbs 100 percent of the variance about the mean:

$$YI = 108.34 - 2.5 X + 0.019 X^2$$

and has a minimum infection rate at 67 years, with the infection rate increasing for younger or older patients. (Fig. 5)

The patients in the same age groups were further classified according to sex (Table. 7). The total infection rate was the same in males (23.33%) females (23.07%). Quadratic equations were the best fit in the both groups . For female patients the equation is :

$$YI = 704.87 - 20.07 X + 0.145 X^2$$
, SSD = 0.00

which absorbs 100 percent of the variance about the mean and has a minimum infection rate at 69 years. For males patients:

$$xI = -419.95 + 12.8 x = 0.091 x^2$$
, $SSD = 0.00$

which absorbs 100 per cent of the variance about the mean and has a minimum infection rate at 70 years. Both curves are shown in Fig. 5.

Table 7. Age, Sex and Wound Infection Rate.

	Fen	ales	Males		
Age Group	Number	% Infected	Number	% Infected	
51-60	12	41.66	12	8.33	
61-70	19	15.78	26	26.92	
71 & over	21	19.04	22	27.27	
Total	52	23.07	60	23.33	

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CHAPTER 5

SIGNIFICANCE OF PATIENT PARAMETERS ON NASAL CARRIAGE

5-1 INTRODUCTION

In chapter 4, patient parameters related to post-operative wound infection were examined. Staphylococcal cross-infection, however, is largely dependent on the level of ward contamination (64, 70, 67), which could be different in different parts of the ward. It has been more practical to define the carriers of multiple or tetracycline-resistant strains of staphylococci as nasal carriers, because these strains were mainly associated with hospital environments. But the current situation is somewhat different with the changing nature of staphylococci, nasal carriers therefore, will be defined in this chapter as the carriers of any strain of staphylococci; with explanation in brackets.

Age, sex length of stay in hospital and exposure to antibiotic can be classified as patient parameters, because these are independent of patients' clinical or operative conditions. The significance of age and length of stay on nasal carriage will be quantified using curve fitting techniques and the association of sex of patient and chemotherapy with nasal carriage is also investigated in this chapter.

5-2 AGE AND SEX OF PATIENT

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5-2-1 DUDLEY ROAD (B4) CONTINUOUS SURVEY (1968/69)

Patient ages were classified in seven groups, ten years was taken as the class interval. The analysis was carried out for four types of strain of Staphylococcus aureus: i- resistant strains, ii- penicillin resistant strains, iii- sensitive strains, iv- all strains.

i- RESISTANT STRAINS

The masal carriage rate of tetracycline-resistant staphylococci for different patient age groups are shown in Table 8.

Table 8.	Age of Patient	and Nasal Carriage Rate.	
Age group		No. of patient	Nasal carriage rate
11-20		34	8.82
21-30		56	5.35
31-40		69	4.34
41-50		107	5.60
51-60		113	9.73
61-70		74	7.89
71& over		64	10.93
Total		533	7.50

The relationship between masal carriage rate and age can however, be represented by a quadratic equation, $YN = A - B X + C X^2$, where YN is the masal carriage rate, X is the age and A, B and C are constants. For the data in Table 8, the following quadratic equation gave the best fit; with a sum of squared deviation (SSD) of 12.89 which absorbs 77 per cent of the variance about the mean;

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$YN = 11.42 - 0.305 X + 0.004 X^2$

This curve with the 95 per cent confidence limits are illustrated in Fig. 6. The minimum carriage rate is at 38 years.

The patients in the same age groups were further classified according to sex. As Table 9 shows, the total nasal carriage rate is higher in males (11.85%) than in females (3.04%). This difference is statistically significant ($x^2 = 14.88, 1 \text{ D.F.}, P\left(0.005\right)$). A quadratic equation were the best fit in both instances. For female patients the equation is: $YN = 1.48 - 0.055 X + 0.0013 X^2$, SSD = 47.35 with 42 per cent of the variance about the mean absorbed and a minimum carriage rate at 21 years. For male patients the equation is: $YN = 29.74 - 0.926 X + 0.01 X^2$, SSD = 114.42

with 64 per cent of the variance about the mean absorbed and a minimum carriage rate at 46 years. These curves are illustrated in Fig. 7.

Table 9. As	e and Sex of Pa	tient and Nas	al Carriage Rat	<u>e</u> .
	Femal	85	Male	5
Age group	Number	×	Number	ж
11-20	20	0.00	• 14	21.42
21-30	29	0.00	27	11.11
31-40	42	4.76	27	3.70
41-50	55	3.64	52	7.69
51-60	46	0.00	67	16.41
61-70	31	0.00	43	13.95
71& over	37	8.11	27	13.79
Total	263	3.04	270	11.85





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11- PENICILLIN-RESISTANT STRAINS

Table 10. Age of Patient and Nasal Carriage Rate.

The nasal carriage rate of penicillin-resistant staphylococci for different age groups are shown in Table 10.

Age group	No. of patients	Nasal carriage rate
11-20	34	32.35
21-30	56	28.57
31-40	69	27.53
41-50	107	21.49
51-60	113	25.66
61-70	74	18.91
71& over	64	25.00
Total	533	24.39

A quadratic of the type $YN = A - BX + CX^2$ was the best fit for the relationship between nasal carriage rate and age of the patient, where YN is the nasal carriage rate, X is the age and A, B and C are constants. The equation for all patients is:

 $YN = 40.56 = 0.59 X + 0.0049 X^2$, SSD = 33.104

which absorbs about 82 per cent of the variance about the mean. This curve together with the 95 per cent confidence limits are illustrated in Fig. 8. The minimum carriage rate is at 60 years.

Examination of Table 11 shows that the total masal carriage rate in males (25.55%) is similar to females (23.19%), where the difference is not statistically significant (χ^2 = 0.39, 1 D.F., P (0.750).

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Table 11.	Age and Sex	of Patient an	d Nasal Carriage	Rate.
	F	emales	Male	8
Age group	NO.	%	No.	%
11-20	20	20.00	14	50.00
21-30	29	20.69	27	37.03
31-40	42	30.95	27	22.22
41-50	55	25.45	52	17.30
51-60	46	15.22	67	32.83
61-70	31	19.35	43	18.60
71& over	37	27.03	27	22.22
Total	263	23.19	270	25.55

A quadratic equation was the best fit in both groups. For female patients the equation is: $YN = 21.24 + 0.06 X = 0.0006 X^2$, SSD = 172.29

which absorbs 5 per cent of the variance about the mean and a minimum carriage rate is at 53.3 years. For male patients the equation is: $YN = 70.73 - 1.749 + 0.015 X^2$, SSD = 235.83

which absorbs 86 per cent of the variance about the mean and a mimimum carriage rate is at 58.5 years. Fig. 9 shows these curves.

iii- SENSITIVE STRAINS

The masal carriage of sensitive staphylococci for the different age groups are shown in Table 12. A quadratic of the type $YN = A - B X + C X^2$, where the best fit for the relationship between masal carriage rate and age of the patient. The equation for all patients is: $YN = 23.08 - 0.688 + 0.009 X^2$, SSD = 5.725

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with 91 per cent of the variance about the mean absorbed and a minimum carriage rate at 38 years. This curve with 95 per cent confidence limits are illustrated in Fig. 10.

Table 12	Age of	Patient and	Nasal Carriage	Rate.	
Age group		No.	of patients	Nasal	carriage rate
11-20			34		14.70
21-30			56		12.50
31-40			69		8.69
41-50			107		11.21
51-60			113		14.15
61-70			74		16.21
71& over			64		23.43
Total			533		14.07

Examination of Table 13 shows that the total nasal carriage rate in males (12.22%) is slightly lower than in females (15.97%), where the difference is not statistically significant (χ^2 = 1.53, 1 D.F., P $\langle 0.250$).

Table 13 Ag	e and Sex of p	atient and Nas	sal Carriage Ra	te.
	Fema	les	Ma	les
Age group	Number	%	Number	%
11-20	20	20.00	14	7.14
21-30	29	13.79	27	11.12
31-40	42	9.52	27	7.40
41-50	55	12.73	52	9.6
51-60	46	19.57	67	10.44
61-70	31	22.58	43	11.62



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71& over	37	18.92	27	29.62
Total	263	15.97	270	12.22

A quadratic equation was the best fit in both groups. For females patients the equation is: $YN = 23.72 - 0.517 + 0.0067 X^2$, SSD = 75.27

which absorbs 65 per cent of the variance about the mean and a minimum carriage rate is at 38.5 years. For male patients the equation is: $NN = 18.69 - 0.728 X + 0.0109 X^2$, SSD = 80.099

which absorbs 83 per cent of the variance about the mean and a minimum carriage rate is at 33 years. Fig. 11 shows these curves.

iv- ALL STRAINS

The masal carriage rate of all staphylococci for the different age groups are shown in Table 14.

Table 14 Age of Patient and Nasal Carriage Rate.

Age group	No. of patient	Nasal carriage rate
11-20	34	47.05
21-30	56	41.07
31-40	69	36.23
41-50	107	38.31
51-60	113	26.54
61-70	74	35.13
71& over	64	48.43
Total	533	38.46

A quadratic of the type $YN = A - B X + C X^2$, where YN is the masal carriage rate, X is the age and A, B, and C are constants, was the



best fit for the relationship between nasal carriage rate and age of the patient. The equation for all patients is: $YN = 68.04 - 1.517 X + 0.016 X^2$, SSD = 105.82

which absorbs 82 per cent of the variance about the mean and a minimum carriage rate is at 47 years. This curve with 95 per cent confidence limits are illustrated in Fig. 12.

As Table 15 shows, the total nasal carriage rate is slightly lower in males (37.77%) than in females (39.16%), where the difference is not statistically significant ($\chi^2 = 0.1$, 1 D.F., P $\langle 0.900 \rangle$).

Table 15	Age and Sex of	Patient and	Nasal Carriage	Rate.
	Fe	emales	M	ales
Age group	Number	%	Number	×
11-20	20	40.00	14	57.14
21-30	29	34.48	27	48.14
31-40	42	40.47	27	29.62
41-50	55	38.18	52	26.92
51-60	46	34.78	67	43.28
61-7 0	31	41.93	43	30.23
71 over	37	45.94	27	51.85
Total	263	34.16	270	37.77

A quadratic equation was the best fit in both groups . For female patients the equation is:

 $Y N = 44.96 - 0.45 X + 0.006 X^2$, SSD = 40.37



with 73 per cent of the variance about the mean absorbed and a minimum carriage rate at 37.5 years. For male patients the equation is:

 $YN = 89.41 - 2.477 X + 0.026 X^2$, SSD = 257.66

with 84 per cent of the variance about the mean absorbed and a minimum carriage rate at 47.5 years. These curves are illustrated in Fig. 13.

5-2-2 D.R. (D15 & 21) & G.H. (8 & 9) CONTINUOUS SURVEY (1977)

Since_there was not any tetracycline-resistant strains of staphylococci, then the analysis was carried out for penicillin-resistant strains. The nasal carriage rate of penicillin-resistant staphylococci for the different age groups are shown in Table 16.

Table 16	Age of Pat	cient and Nasal Carriage Rate	
Age group		No. of Patients	Nasal Carriage Rate
11-20		50	18.00
21-30	· .	44	20.45
31-40		40	5.00
41-50		53	18.86
51-60		84	17.85
61-70		125	13.60
71& over		163	14.72
Total		559	15.38

A quadratic of the type $YN = A - B X + C X^2$ was the best fit for the relationship between nasal carriage rate and age of the patient, where YN is the nasal carriage rate, X is the age and A, B and C are constants. The equation for all patients is:

 $YN = 21 - 0.248 X + 0.002 X^2$, SSD = 153.37

with 31 per cent of the variance absorbed about the mean and a minimum

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carriage rate at 62 years. This curve together with 95 per cent confidence limits are illustrated in Fig. 14.

Examination of Table 17 shows that the total nasal carriage rate in males (18.36%) is higher than in females (12.07%), where the difference is statistically significant ($\chi^2 = 4.22$, 1 D.F., P $\langle 0.05 \rangle$).

Table 17	Age and Sex of I	Patient and Nas	al Carriage R	ate.
	Fen	ales	M	ales
Age group	Number	ж	Number	%
11-20	30	13.33	20	25.00
21-30	21	23.80	23	17.39
31-40	24	0.00	16	12.50
41-50	23	17.39	30	20.00
51-60	35	14.28	49	20.40
61-70	51	7.84	74	17.56
71& over	81	12.34	82	17.07
Total	265	12.07	294	18.36

A quadratic equation was the best fit in both groups. For female patients the equation is:

 $YN = 19.1 - 0.24 X + 0.0018 X^{2}, SSD = 314.93$ with 22 per cent of the variance about the mean absorbed and a minimum carriage rate at 75 years. For male patients the equation is: $YN = 27.18 - 0.39 X + 0.0037 X^{2}, SSD = 67.68$ with 47 per cent of the variance about the mean absorbed and a minimum carriage rate at 53 years. These curves are shown in Fig. 15.

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5-3 CHEMOTHERAPY

Patients receiving one or more antibiotic at the time of the survey, were included in the antibiotic group. The analysis has been done for both Dudley Road (B4) continuous survey (1968/69) and D.R. (D15 & 21) and G.H. (8 & 9) continuous survey (1977).

5-3-1 DUDLEY ROAD (B4) CONTINUOUS SURVEY (1968/69)

Tetracycline, penicillin and ampicillin were the most commonly used antibiotics, which together accounted for more than half the total antibiotics being administered. The analysis has been carried out for four types of strain of <u>Staph.aureus</u>:

i- Resistant strains

The nasal carriage rate of tetracycline resistant staphylococci of patients who received antibiotics (13.67%) was significantly higher than that of the patients who did not receive antibiotics (3.42%), (χ^2 = 19.32, 1 D.F., P $\langle 0.005 \rangle$). The effect of the administration of individual antibiotic is shown in Table 18., and the related histogram is illustrated in Fig. 16. The statistical significance of each agent was tested against the no-antibiotic group for the difference in carriage rate. This difference was significant for patients treated with all antibiotics listed in Table 18, expect for nitrofuratoin which showed a lower carriage rate than the untreated group. Patients treated with penicillin showed the highest carriage rate. Some other antibiotics

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such as neomycin and kanamycin were not included, as their use was too infrequent. A higher nasal carriage rate for treated patients was found in males (24.24%) than in females (4.42%), the difference is statistically significant (χ^2 = 17.47, 1 D.F., P (0.005).

Table 18 Nasal	Carriage in rela-	tion to type of Ant	ibiotic.	
Antibiotic	No. in group	Carriage rate	x ²	Significance
None	321	3.42		
Penicillin	51	21.56	26.23	Sig(P (0.005)
Ampicillin	48	10.41	4.80	Sig(p (0.050)
Sulphanamide	15	13.33	3.56	NS(p 0.100)
Tetracycline	86	10.46	7.29	Sig(p 0.010)
Nitrofurantoin	8	0.00	0.27	NS(p 0.750)

Sig = Significant

NS = Not-significant

ii- Penicillin resistant strains

The nasal carriage rate of penicillin resistant staphylococci in patients who received antibiotics (31.13%) was significantly higher than that of patients who did not receive antibiotics (19.93%) (x^2 = 8.67, 1 D.F., P $\langle 0.005 \rangle$). The statistical significance of each antibiotic was tested against the non-antibiotic group for the difference in nasal carriage rate (Table 19). This difference was significant for patients treated with penicillin and tetracycline, but for Amplicitin, the nasal carriage rate was lower than in untreated groups. Patients treated with penicillin showed the highest carriage rate. A lower carriage rate in treated patients was found in males (27.43%) compared with females (35.35%), but the difference was not significant ($X^2 = 1.55$, 1D.F., P $\langle 0.250 \rangle$). The related histogram for all patients is illustrated in Fig. 17.

2	-
Antibiotic No.in group Carriage rate X Si. (%) 1D.F.	guilleance
None 321 19.93	
Penicillin 51 39.21 9.38 Si	g(p (0.005)
Ampicillin 48 16.66 0.29 NS	(P(0.750)
Sulphanamide 15 33.33 1.73 NS	(p (0.250)
Tetracycline 86 33.72 7.25 Si	g(p(0.010)
Nitrofurantoin 8 25.00 0.12 NS	(P (0.750)

iii- Sensitive strains

The masal carriage rate of sensitive staphylococci in patients who received antibiotics (10.37%) was significantly lower than that of patients who did not receive antibiotics (16.51%) ($\chi^2 = 3.95$, 1D.F., $p \langle 0.050 \rangle$. The effect of the administration of individual antibiotic is shown in Table 20, and the related histogram is illustrated in Fig. 18. The statistical significance of each agent was tested against the nonantibiotic group for the difference in the masal carriage rate. In sensitive strains, patients treated with nitrofurantoin showed the highest carriage rate, and the masal carriage rate for males (10.10%) and females

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(10.61%) was similar.

Table 20 Nasal	Carriage in r	elation to type of A	ntibiotic.	
Antibiotic None	No.in group 321	Carriage rate (%) 16.51	x ² lD.F.	Significance
Penicillin	51	9.80	1.53	NS(p (0.250)
Ampicillin	48	10.41	1.16	NS(p (0.500)
Sulphanamide	15	20.00	0.12	NS(p 0.750)
Tetracycline	86	8.13	3.78	NS(p 0.100)
Nitrofurantoin	8	25.00	0.77	NS(p 0.750)

iv- All strains

The nasal carriage rate of all staphylococci for patients who received antibiotics(41.50%) was similar to patients who did not receive antibiotic (36.44%). The effect of the administration of individual antibiotics is shown in Table 21, the related histogram is illustrated in Fig. 19. Patients treated with sulphamanide showed the highest carriage rate. The nasal carriage rate between male patients (45.45%) and female patients (38.00%) was similar.

Table 21 Nasa	1 Carriage in rei	lation to type of	Antobiot:	ic.
Antibiótics	No. in group	Carriage rate	x ² 1D.F.	Significance
None	321	36.44		
Penicillin	51	49.01	1.91	NS (p(0.250)
Ampicillin	48	27.08	1.59	NS (p (0.250)

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Sulphanomide	15	53.33	1.68	NS (p (0.250)
Tetracycline	86	41.86	0.43	NS (p (0.750)
Nitrofurantoin	8	50.00	0.36	NS (p (0.750)

5-3-2 D.R. (D15 & 21) AND G.H. (8 & 9) CONTINUOUS SURVEY (1977).

Ampicillin was the most commonly used antibiotic, but to a lesser extent co-trimaxazole was used, which together accounted for more than half the total antibiotics administered. The masal carriage rate of penicillin resistant staphylococci in patients who received antibiotics (15.58%) was the same as patients who did not receive antibiotics (15.92%). The effect of the administration of individual antibiotics is shown in Table 22, and the related histogram is illustarted in Fig.20.

Table 22 Nasal	Carriage in	relation to Type	of Antibi	otic.
Antibiotic	No.in group	Carriage rate (%)	x ² 1D.F.	Significance
None	314	15.92		
Penicillin	6	0.00	1.22	NS (p (0.500)
Ampicillin	101	13.86	0.25	NS (p (0.750)
Amoxycillin	6	16.67	0.002	NS (p <0.975)
Cloxacillin	4	25.00	0.21	NS (p < 0.750)
Flucloxacillin	7	28.57	0.87	NS ($p \langle 0.900 \rangle$
Tetracycline	8	12.50	0.08	NS ($p < 0.900$)
Co-trimoxazole	26	11.54	0.31	NS (p <0.750)
Sulphadimidine	7	28.57	0.88	NS (p (0.500)
Erythromycin	2	0.00	0.36	NS (p (0.750)
Lincomycin	1	0.00	0.25	NS (p (0.750)
Nitrofurantoin	3	33.33	0.66	NS (p (0.500)

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Metronidazole	16	12.50	0.55	NS (p (0.500)
Cephaloridine	3	33.33	0.66	NS (p<0.500)
Cephalexin	7	28.57	0.88	NS (p (0.500)
Cephazolin	11	9.09	0.43	NS (p < 0.750)
Chloramphenicol	5	20.00	0.06	NS (p (0.900)
Gentamicin	4	25.00	0.21	NS (p(0.750)
Neomycin	14	21.42	0.35	NS (p < 0.750)

The statistical significance of each agent was tested against the nonantibiotic group for the difference in carriage rate. The difference was not significant for patients treated, with all antibiotics. Other antibiotics such as fusidic acid and streptomycin were not included, as their use was too infrequent.

5-4 LENGTH OF STAY IN HOSPITAL AND SEX OF PATIENT

The length of stay in hospital of patients was considered for the analysis to be the number of days spent in hospital the day the nose swab was taken. The analysis was carried out for the two continuous surveys.

5-4-1 DUDLEY ROAD (B4) CONTINUOUS SURVEY (1968/69)

The length of stay was divided into 6 groups varying in size from 3.4 days to over 30 days. Varying time intervals were taken for the first 10 days, and then 10 days interval was taken to give the reasonable group sizes for analysis. Patients with 1=2 days of stay in hospital are not included, because of the small and variable numbers. The analysis Was carried out for four types of staphylococci.

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i- Resistant strains

Table 23 gives the nasal carriage rate of tetracycline-resistant staphylococci in relation to length of stay in hospital. From the table it is evident that the maximum rate of carriage was reached after 30 days.

Table 23	length of Stay and Nasal Carriage	Hate.
Days in hospital	No. in group	Nasal carriage rate (%)
3-4	60	3.33
5-6	41	2.43
7-10	165	5.45
11-20	175	8.57
21-30	37	8.10
31& over	28	21.42
Total	506	7.11

A linear relation between carriage rate and length of stay fits the data, with a correlation coefficient of 0.916. The best fit is given by the equation: YN = 0.3 + 0.51 L, where YN is the nasal carriage rate and L is the length of stay. Table 24 shows the relationship between nasal carriage rate and length of stay for male and female patients. Both groups had a maximum carraige rate at over 30 days. The linear equation for female patients was: YN = 0.54 + 0.19 Lwith a correlation coefficient of 0.592. The linear equation foe male patients was: YN = 1.41 + 0.7 L

For all patients, the male and female linear carriage rates are represen-

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ted in Fig. 21. This figure shows that the carriage rate for males was higher than for females for all lengths of stay.

Idulto 24	Delig the of body, be	The callos How det	ourrange marte.	
Days in		Female	1	Male
hospital	Number	%	Number	%
3-4	35	2.86	25	4.00
5-6	15	0.00	26	3.84
7-10	65	4.62	100	6.00
11-20	105	2.86	70	17.14
21-30	19	0.00	18	16.66
31& over	9	11.11	19	26.31
Total	248	3.22	258	10.85

Table 24 Length of Stay, Sex and Nasal Carriage Rate.

ii- Penicillin-resistant strains

Table 25 gives the masal carriage rate of penicillin resistant staphylococci for all patients in relation to length of stay in hospital. From the table it is evident that the maximum carriage rate was reached after 30 days.

Table 25 Length of Stay and Nasal Carriage Rate.

Days in hospital	No. in group	Nasal carriage rate
3-4	60	20.00
5-6	41	24.39
7-10	165	21.21
11-20	175	26.28
21-30	37	29.72
31& over	28	42.85
Total	506	24.90

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A linear relationship between carriage rate and length of stay fits the data, with a correlation coefficient of 0.949. The best fit is given by the equation: YN = 16.5 + 0.68 LTable 26 shows the relationship between nasal carriage rate and length of stay for males and females. Both groups had a maximum carriage rate

at over 30 days. The linear equation for female patients was:

$$YN = 16.79 + 0.54 L$$

with correlation coefficient of 0.793. The linear equation for male pat-

ients was: YN = 19.08 + 0.63 L

with a correlation coefficient of 0.850.

For all patients, the female and male linear carriage rate are represented in Fig. 22.

Table 26	Length of Stay,	Sex and Nasal	Carriage Rate.	
Days in		Female	М	ale
hospital	Number	%	Number	- %
3-4	35	17.14	25	24.00
5-6	15	33.33	26	19.23
7-10	65	21.54	100	21.00
11-20	105	24.76	70	28.57
21-30	19	31.58	18	27.27
31& over	9	33.33	19	47.36
Total	-248	24.19	258	25.58

Fig. 22 shows that the carriage rate for males was higher than that for females for all length of stay.



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iii- Sensitive strains

Table 27 gives the nasal carriage rate of sensitive staphylococci of all patients in relation to length of stay in hospital. From the table it is evident that the maximum rate of carriage was reached by over 30 days.

Table 27 Length of Stay an	a Nasal Carriage Rate.	
Days in hospital	No. in group	Nasal carriage rate
3-4	60	16.66
5-6	41	12.19
7-10	165	16.36
11-20	175	11.42
21-30	37	16.21
31å over	28	17.85
Total	506	14.42

A linear relationship between carriage rate and length of stay fits the data, with a correlation coefficient of 0.756. The best fit is giving by the equation: YN = 11.70 + 0.17 L

Table 28 shows the relationship between nasal carriage rate and length of stay for male and female patients. A quadratic of type $YN = A - B L + C L^2$ was the best fit for the female patients, where YN is the nasal carriage rate, L is the length of stay and A, B and C are constants. The equation for female patients is:

$$YN = 19.3 - 0.74 L + 0.02 L^2$$
, $SSD = 103.32$

Which absorbs about 45 percent of the variance about the mean.

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The linear equation for male patients was:

$$IN = 6.3 + 0.39L$$

with correlation coefficient of 0.711 .

For patient, the female and male patients linear carriage rates are represented in Fig. 23. This shows that carriage rate for male was lower than that for females for the first 18 days, and carriage rate for males is higher than that for females for after 30 days.

Table. 28 Length of Stay, Sex and Nasal Carriage Rate

Days in	Fem	Female		e
hospital	Number	%	Number	%
3-4	35	22.86	25	8.00
5-6	15	13.33	26	11.53
7-10	65	18.46	100	15.00
11-20	105	13.33	70	8.50
21-30	19	10.53	18	22.22
over 30	9	22.22	19	15.78
Total	248	16.12	258	12.79

iv- All strains

Table 29 gives the nasal carriage rate of all staphylococci of all patients in relation to length of stay in hospital. From the table it is evident that the maximum rate of carriage was reached by over 30 days, a linear relationship between carriage rate and length

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of stay fits the data, with a correlation coefficient of 0.915. The best fit is given by the equation: YN = 28.31 + 0.84 L

Days in hospital	No. in group	Nasal carriage rate
3-4	60 -	36.66
5-6	41	36.58
7-10	165	37.77
11-20	175	37.71
21-30	37	45.94
over 30 .	28	60.71
Total	506	39.32

Table 29 Length of Stay and Nasal Carriage Rate

Table 30 shows the relationship between nasal carriage rate and length of stay for male and female patients. Both groups had a maximum carriage rate after 30 days. The linear equation for female patients was: YN = 32.5 + 0.98 Lwith a correlation coefficient of 0.683. The linear equation for male patients was: YN = 25.4 + 1.02 Lwith a correlation coefficient of 0.860. For all patients, the female and male patients linear carriage rates are represented in Fig. 24.

This shows that the carriage rate for males was lower before 15 days of stay, then higher than that for females for greater length of stays.

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Table 30	Length of Stay, Sex and	Nasal Carriage	Rate.	
Days in	Female		Male	
hospital	Number	ъ	Number	%
3-4	35	40.00	25	32.00
5-6	15	46.66	26	30.76
7-10	65	40.00	100	36.00
11-20	105	38.09	70	37.14
21-30	19	42.10	18	50.00
over 30	9	55.55	19	63.15
Total	248	40.32	258	38.37

5-4-2 D.R.(D15 & 21) AND G.H.(8 & 9) CONTINUOUS SURVEY (1977)

The length of stay was divided into 4 groups from 5 - 10 to 20 - 25 days, 5 days of interval taken to give a reasonable group size for analysis. The under 5 days length of stay group is not included, because of the small and variable numbers. Table 31 gives the nasal carriage rate of all patients in relation to length of stay in hospital. From the table it is evident that the maximum rate of carriage was reached by 25 days, a linear relationship between carriage rate and length of stay fits the data, with a correlation coefficient of 0.316. The best fit is given by the equation YN = 12.73 + 0.209 L, where YN is the nasal carriage rate and L is the length of stay.

Table 32 shows the relationship between nasal carriage rate and length of stay for male and female patients. The female patients

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had a maximum carriage rate beyond 25 days . The linear equation for female patients was : IN = 9.99 + 0.295 Lwith a correlation coefficient of 0.934 . The linear equation for male patients was IN = 13.88 + 0.2 Lwith a correlation coefficient of 0.815. All patients , the female and male linear carriage rates are represented in Fig. 25. This shows that the carriage rate for males was higher than that for females for all length of stay.

Table 31. Length of Stay and Nasal Carriage Rate

Days in hospital	No. in group	Nasal carriage rate
5-10	184	14.13
11-15	26	7.69
16-20	18	22.22
21-25	24	16.67
Total	252	14.28

Table 32. Length of Stay, Sex and Nasal Carriage Rate

Days in	Fen	ale	Mal	e
hospital	Number	%	Number	%
5-10	102	12.75	82	15.85
11-15	7	14.29	19	5.26
16-20	7	14.29	11	27.27
21-25	12	16.67	12	16.67
Total	128	14.84	124	16.93



5-5 OTHER FACTORS RELATED TO NASAL CARRIAGE

The plan of ward B4 during the Dudley Road (B4) continuous survey (1968 / 69) is shown in Chapter 3, Fig. 1. Out of 533 patients, 400 patients were in the open ward and the corresponding total carriage rate was 7.50 %. The open ward has been divided into two parts. The lower nasal carraige rate was found in the half nearest to the ward (5.88 %) in comparison to the half nearest the sluice (9.49 %), as shown in Table 34, this difference is not statistically significant ($X^2 = 1.78$, 1 D.F., p $\langle 0.250 \rangle$.

Table 34 Nasal Carriage Rate in Two Parts of The Open Ward.

	Part near to sluice	Part near to entrance	Total
Colonized	17	13	30
Not-colonized	162	208	370
Carriage rate (9	8) 9.49	5.88	7.50

The implication is that the patient requiring minimum supervision and ready for discharge will tend to be moved to the end of the ward (near to sluice). The patients are , therefore , likely to have been in longer than the patients at the other end of the ward. They are, therefore, more likely to have become colonized. The patients were further classified according to sex. Table 35 shows the nasal carriage rate in the open ward is higher in males (14.81 %) than in

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females (3.12 %), and the difference is statistically significant ($x^2 = 8.81$, 1 D.F., P (0.005).

Table 35 The Nasal Carriage Rate According to Sex in The Open Ward.

Male

Colonized	24	Female	Colonized	6
Not-colonized	192		Not-colonized	178
 Carriage rate (%)	11.11		Carriage rate (%)	3.26

CHAPTER 6

COMPARISON OF CROSS-SECTIONAL AND CONTINUOUS SURVEYS ON THE SGINIFICANCE

OF PATIENT PARAMETERS

6-1 INTRODUCTION

The similarities of patient parameters between continuous and cross-sectional surveys were examined in Chapter 2. In continuous surveys, the ward and hospital practices remain constant and there can be no question of interactions between different practices, but in crosssectional surveys where a large quantity of data is required in a short time, there are obviously questions about interactions to be asked. If the patient parameters are independent of ward parameters, then crosssectional surveys are preferable.

The significance of patient parameters such as age and length of stay in hospital between continuous (Dudley Road, B4) and Birmingham Regional (cross-sectional, (49)) surveys is compared in this chapter. Curve fitting techniques are used. This comparison is also investigated between Dudley Road (B4) continuous and D.R.(D15 & 21) & G.H.(8 & 9) continuous surveys in a different decade. The latter continuous survey was carried out in 1977, some ten years after the first two survyes.

6-2 AGE AND WOUND INFECTION RATE

The relationship between age and post-operative wound infection rate can best be represented by quadratic equation of the form

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 $YI = A - B X + C X^2$, where YI is the infection rate, X is the age and A, B, and C are constants. For the data in the Table 36 from the continuous (Dudley Road (B4)) survey carried out in 1968, the quadratic equation is $YI = 15.27 - 0.527 X + 0.01 X^2$, SSD = 167.85, which absorbs about 82 percent variance about the mean, and has a minimum infection rate at 26 years.

Table 36 Ag	e and Wound Infection Rate for D	udley Road (B4) continuous surve
Age	No. in group	Infection rate
11-20	22	9.09
21-30	33	6.06
31-40	39	17.94
41-50	64	7.81
51-60	61	11.47
61-70	30	30.00
Over 70	25	32.00
Total	284	14.08

In comparison, the data in Table 37, from the Birmingham Regional survey (Cross-sectional, Goonatilake,(49)), carried out between 1969 and 1972, the quadratic equation is;

 $YI = 15.35 - 0.34 X + 0.0065 X^2$, SSD = 0.5which absorbs about 99 per cent of variance about the mean and has a minimum infection rate at 26 years. These two fitted curves are shown in Fig. 26 and there is an interesting similarity between these two curves. The infection rate for age under 50 years is slightly lower in the contin-

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Table 3	37 Age	and Wound	Infection Rate	for Birmingham	Regional Survey
Age			No. in group		Infection rate
1-10			177		13.6
11-20			234		12.0
21-30			310		11.3
31-40			316		11.4
41-50			458		13.1
51-60			551		16.2
61-70			614		21.2
Total			2660		15.1

uous survey, but this could be caused by the difference in patient numbers between the two surveys. The total infection rate in the two surveys are very close together.

In the other D.R.(D15 & 21) & G.H.(8 & 9) continuous survey (1977) carried out in the next decade, the number of patients was so small in the early age groups that the analysis is done for age above 50 years (Table 38). The quadratic equation is:

YI = $108.39 - 2.56 \text{ X} + 0.019 \text{ X}^2$, SSD = 0.00 which absorbs 100 per cent of variance about the mean and has a minimum infection rate at 67 years. This curve is also shown in Fig. 26.

Table 38 Age	and Wound Infection Rate	for D.R.(D15&21) & G.H.(8&9) Continuous
Age	No. in group	Infection rate	Survey.
51-60	24	25.00	
61-70	45	22.22	
Over 70	43	23.25	
Total	112	23.21	

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6-3 AGE AND NASAL CARRIAGE RATE

The association between nasal carriage rate and age of patient is compared for the two continuous and the cross-sectional surveys.

6-3-1 DUDLEY ROAD (B4) CONTINUOUS (1968/69) AND BIRMINGHAM REGIONAL SURVEYS

The nasal carriage rate of tetracycline resistant staphylococci for different patient age groups of the two surveys are shown in Table 39.

Table 39 Age and Nasal Carriage Rate.

	Dudley Road(B4) Continuous survey		Birminghan Regional survey	
Age	No.in group	Carriage rate (%)	No.in group	Carriage rate (%)
1-10	-	-	766	6.1
11-20	34	8.82	717	4.5
21-30	56	5.35	1340	5.2
31-40	69	4.34	991	4.6
41-50	107	5.60	1200	6.3
51-60	113	9.73	1622	9.6
61-70	74	7.89	1890	10.9
Over 70	64	10.93	-	-
Total	517	7.54	8526	7.4

The relationship between age and nasal carriage rate can best be represented by a quadratic equation of the form $YN = A - B X + C X^2$, where YN is the carriage rate, X is the age and A, B and C are constants. The quadratic equation for the Dudley Road (B4) continuous survey data is: $YN = 11.42 - 0.30 X + 0.004 X^2$, SSD = 12.89

which absorbs about 77 per cent of the variance about the mean, and has a minimum carriage rate at 38 years. The quadratic equation for the data of the Birmingham Regional survey is:

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$$YN = 6.718 - 0.179 X + 0.0038 X^2$$
, $SSD = 2.08$

which absorbs about 95 per cent of the variance about the mean, and has a minimum carriage rate at 23.5 years. The two fitted curves are shown in Fig. 27 in which there is a high degree of similarity between the two curves.

6-3-2 DUDLEY ROAD (B4) CONTINUOUS (1968/69) AND D.R. (D15&21)& G.H. (8&9) CONTINUOUS (1977) SURVEYS

The masal carriage rate of penicillin resistant staphylococci for different age groups of two surveys are shown in Table 40.

Table 40 Age and Nasal Carriage Rate.

Dudley Road (B4) continuous survey D.R. (D15&21)& G.H. (8&9) contin-

uous survey

Age	No.in group	Carriage rate (%)	No.in group	Carriage rate (%)
11-20	34	32.35	50	18.00
21-30	56	28.57	44	20.45
31-40	69	27.53	40	5.00
41-50	107	21.49	53	18.86
51-60	113	25.66	84	17.85
61-70	74	18.91	125	13.60
Over 70	64	25.00	163	14.72
Total	517	24.75	554	15.38

The quadratic equation for the data of the Dudley Road (B4) continuous survey $YN = 40.56 - 0.59 X + 0.0049 X^2$, SSD = 33.104is: which absorbs about 82 per cent of the variance about the mean, and has a minimum carriage rate at 60 years. The quadratic equation for the data of the D.R.(D15&21)& G.H.(8&9) continuous survey is:

 $YN = 21 - 0.248 X + 0.002 X^2$, SSD = 153.37



which absorbs about 31 per cent of the variance about the mean and has a minimum carriage rate at 62 years. These two similar curves are shown in Fig. 28.

6-4 LENGTH OF STAY IN HOSPITAL AND NASAL CARRIAGE RATE

The relationship between the length of stay in hospital and nasal carriage rate can best be represented by a linear equation in the form of YN = A + B L, where YN is the nasal carriage rate, L is the length of stay and A & B are constants. The association between the nasal carriage rate and length of stay in hospital is compared between two continuous and a cross-sectional surveys.

6-4-1 DUDLEY ROAD (B4) CONTINUOUS (1968/69) AND BIRMINGHAM REGIONAL SURVEYS

Table 41, gives the classification of the nasal carriage rate for tetracycline resistant staphylococci for patients in two surveys into categories depending on their length of stay in hospital.

Table 41 Length of Stay and Nasal Carriage Rate.

-	Dudley Road (H	4) continuous	Birmingham Re	gional
Davis	survey		survey	
hospital	No.in group	Я	No.in group	ħ
3-4	60	3.33	1517	4.0
5-6	41	2.43	1206	4.7
7-10	165	5.45	1800	6.4
11-20	175	8.57	2180	10.5
21-30	37	8.10	916	15.0
Over 30	28	21.42	446	20.0
Total	506	7.11		



The linear equation of best fit for the data from the Dudley Road (B4) continuous survey is: YN = 0.3 + 0.51 L with a correlation coefficient of 0.916. The regression equation for the data from Birmingham Regional survey (cross-sectional) is:

$$YN = 2.52 + 0.507 L$$

with a correlation coefficient of 0.998. The nasal carriage rates for these two surveys are represented graphically in Fig. 29.

6-4-2 DUDLEY ROAD (B4) CONTINUOUS (1968/69) AND D.R.(D15&21)& G.H.(8&9) CONTINUOUS (1977) SURVEYS

Table 42 and 43, gives the classification of the nasal carriage rate for penicillin resistant staphylococci of patients in two surveys, in categories depending on the length of stay in hospital. The linear equation of best fit for the data from the Dudley Road (B4) continuous survey

is:
$$YN = 16.5 + 0.68 L$$

with a correlation coefficient of 0.949. The regression equation for the data from the D.R.(D15&21)& G.H.(8&9) continuous survey is:

$$YN = 12.73 + 0.209 L$$

with a correlation coefficient of 0.316. The nasal carriage rates of two surveys are represented graphically in Fig. 30.

Table 42 Length of Stay and Nasal Carriage Rate.

D.R.(D15&21)& G.H.(8&9) continuous survey

Days in hospital	No. in group	Carriage rate (%)
1-4	297	15.49
5-9	184	14.13
10-14	26	7.69
15-19	18	22.22

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Days in h	nospital	No.in group	Carriage rate (%)
20-24		24	16.67
Total		554	14.80
Table 43	Length of st	ay and Nasal Carris	age Rate.

Dudley Road (B4) continuous survey

Days in hospital	No.in group	Carriage rate (%)
1-2	27	14.81
3-4	60	20.00
5-6	41	24.39
7-10	165	21.21
11-20	175	26.28
21-30	37	29.72
Over 31	28	42.85
Total	533	24.39





PART II

MULTIPLE REGRESSION MODEL

CHAPTER 7

MULTIPLE REGRESSION ANALYSIS

7-1 INTRODUCTION

The significance of patient parameters to nasal carriage of multiple-resistant strains of <u>Staph.aureus</u> on Dudley Road (B4) continuous survey is evident from the primary analysis carried out in Part I, but this analysis does not give the relative significance of each individual patient parameter. However, multiple regression analysis can be used for determining the relationship between any number of independent variables. To reduce bias due to correlations between parameters, a correlation matrix may be introduced.

The multiple regression analysis was applied to the Dudley Road (B4) continuous survey, and in the data, the carriage rates are defined as categorical (non-metric) variables, having one of two values, the value 1 when the patient is a carrier and the value 0 when the patient is a non-carrier. Although, multiple regression is ideally suited for canonical (metric) type of variables, to transfer this categorical dependent variable to a canonical variable, patients were categorized into groups containing combinations of patient parameters. The carriage rates were calculated for individual groups and the number of patients in each group was used as weighting factor in the regression analysis, this should counteract any bias arising from unrepresentative data derived from small sample sizes.

7-2 MULTIPLE REGRESSION APPLIED TO NASAL CARRIAGE

The primary analysis on Dudley Road (B4) continuous survey data indicated that age, sex, length of stay in hospital and exposure to antibiotics, are associated with the nasal carriage of multipleresistant strains of Staph.aureus. The multiple regression analysis was now applied to the Dudley Road (B4) continuous survey, considering only the latter four parameters. Since, age and length of stay are linear variables, age was classified into 7 groups and each of these groups was classified into 6 length of stay groups, making a total of 42 groups, and these groups were further classifed into sex and antibiotic groups, making a final total of 168 groups for analysis. The carriage rates in each group were calculated and the number of patients in each group was used as a weighting factor in the regression analysis to counteract any bias arising from unrepresentative data derived from small sample sizes. The multiple regression model can be stated in the following form:

$$YN = a + b_1 X_1 + b_2 X_2 + b_3 X_3 + b_4 X_4$$

in which X_1 is age and X_2 length of stay, both of which are linear variables. The variable X_3 was assigned the value 1 for male sex and 0 for female sex; and the variable X_4 assigned the value 1 for patients treated with antibiotics and the value 0 for other patients. The constant 'a' as the hypothetical value of YN when patient parameters are

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equal to zero, may account for the significance of other parameters on nasal carriage (e.g. ward parameters). The correlation matrix is shown in Table 44, and it shown no correlation between the four patient parameters. The results of the multiple regression analysis is shown in Table 45. All the regression coefficients except the coefficient for sex are statistically significant as the 't' statistics are greater than 1.96. The multiple correlation of 0.656 is not very high; suggesting a sample size effect due to the small number of patients in each group.

Table 44	Correlation Matrix	- Nasal Car	riage.	
	Age	Days	Sex	Antibiotic
Age	1.00	0.00	0.00	0.00
Days	0.00	1.00	0.00	0.00
Sex	0.00	0.00	1.00	0.00
Antibiotic	0.00	0.00	0.00	1.00
Carriage H	ate 0.13	0.10	0.02	-0.14
Table 45	Multiple Regression	n Analysis o	n Nasal Carria	ge I

Variable	Regression	't'	Partial
Name	Coefficient	Statistic	Correlation
Constant	3.258		
Age	0.024	3.24	0.12
Days	0.125	1.98	0.10
Sex	0.142	0.07	0.02
Antibiotics	-1.047	3.77	-0.14

Multiple Correlation = 0.656

Model:

YN = 3.258 + 0.024 X Age + 0.125 X Days + 0.142 X Sex - 1.047 X Antibiotics.

From the regression model, it is evident that the length of stay generally of carrage contributes a higher risk of nasal of multiple resistant <u>Staph.aureus</u> than age. But for ages over 5 years, age is as important as length of stay. Since the primary analysis in Part I, indicated that the age curves are quadratic, then the age-term and the age-square term are applied jointly with nasal carriage in this analysis. Hence, by introducing this agesquare term to the regression model, the multiple correlation was slightly increased (0.666). As before, the regression coefficients except the coefficient for sex, are statistically significant. The result of the multiple regression is shown in Table 46.

Table 46	Multiple Regression Analysis on	Nasal Carriage	<u> </u>
Variable	Regression	't'	Partial
Name	Coefficient	Statistic	Correlation
Constant	1.655		
Age	0.169	9.69	0.12
Age-square	-0.001	8.25	-0.05
Days	0.125	1.69	0.10
Sex	0.119	0.05	0.02
Antibiotics	-1.261	6.03	-0.18

Multiple Correlation = 0.666

Model:

 $YN = 1.655 + 0.169 X Age - 0.001 X Age^2 + 0.125 X Days +$

0.119 X Sex - 1.261 X Antibiotics.

From the regression model, when the constant, age and agesquare terms are taken together, nasal carriage increases until 80 years of age, and does not follow exactly the same quadratic function as in the primary analysis of Part I. Treatment with antibiotics shows no effect on nasal carriage in the regression model but that again does not follow the results of the primary analysis of Part I. Also, the multiple correlation of 0.666 is not high enough to confirm a high degree of fit. The implication from all this is that the number of patients (530) arranged in 168 groups is too small for a multiple regression analysis, and consequently patients are scattered irregularly in the groups.

7-3 GRAPHICAL REPRESENTATION OF THE REGRESSION MODEL

The regression model of:

YN = 1.655 + 0.169 X Age - 0.001 X Age² + 0.125 X Days + 0.119 X Sex - 1.261 X Antibiotics.

can be represented graphically in a three dimensional system. A three dimensional surface can be generated from the age and length of stay components of the regression analysis on the nasal carriage rate. The X-axis represents nasal carriage (Fig. 31). On the age plane, a quadratic function represents the age effect, and on the length of stay plane, a linear function represents the length of stay effect. The intercept of the age surface on the nasal carriage rate axis (Y-axis) represents the constant in the regression. The other two categorical (non-metric) variables, sex and antibiotics have been taken as 0 in the surface. Fig. 32 shows the modified graphical model taking account of sex and antibiotics. In the presence two of these other parameters the surface would be moved upwards or downwards. This also changes the value of the constant by the coefficient of these variables. The result is four surfaces for the four combinations of sex and antibiotic, female antibiotic, male no-antibiotic, female antibiotic, female antibiotic) and which are similar in nature but separated by a constant from each other.

7-4 APPLICATION OF REGRESSION MODEL AND COMPARISON WITH BRIMINGHAM REGIONAL SURVEY

The multiple regression analysis has been applied to the patient parameters related to nasal carriage in this chapter and the model can be used to determine the relative significance of patient parameters on nasal carriage. For example, if a study was carried out to determine the significance of two particular age groups on nasal carriage, the model must first be used to find the expected carriage rates in these two age groups. Using the patient characteristics such as age, sex, length of stay and antibiotic treatment, the expected carriage

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rate for individual patients would be determined. The expected carriage rate for a particular age group is calculated by summing the expected carriage rates of all patients in the group and then dividing this total by the number of patients. Using the observed and expected carriage rates in these two particular age groups the significance of two age groups could be determined statistically for nasal carriage. Also, from this regression model, the significance of the ward parameters on nasal carriage can be compared for two wards using different ward practices.

The similar regression model produced from the Birmingham Regional Survey (14, 49) on the basis of patient parameters for about 12,000 patients in more than 500 wards is:

> YN = 0.642 - 0.0015 X Age + 0.0011 X Age² + 0.185 X Days + 2.217 X Sex + 3.127 X Antibiotics.

In comparison, the regression model derived from the Dudley Road (B4) continuous survey in this chapter:

YN = 1.655 + 0.169 X Age - 0.001 X Age² + 0.125 X Days + 0:119 X Sex - 1.261 X Antibiotics.

Considering age, the quadratic equation in the Birmingham Regional Survey increased linearly, and in the case of the Dudley Road (B4) continuoussurvey the quadratic equation has a linear function until about 85 years of age. The difference between the two regression models is in

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exposure to antibiotics; in Dudley Road (B4) continuous survey, it appears that the patients treated with antibiotics have a lower risk of becoming a masal carrier. Although, the multiple regression analysis of the Dudley Road (B4) continuous survey is biased by the small patient numbers, the difference appears to be true. For the other patient parameters, the regression models from continuous and cross-sectional surveys follow the same trend, and the difference in the constant is because the variety of ward practices in the Birminghan Regional Survey (14, 49) has become smaller.

CHAPTER 8

DISCUSSION

8-1 DISCUSSION ON THE IMPLICATIONS OF THE PRIMARY ANALYSIS IN PART I 8-1-1 PATIENT PARAMETERS AND WOUND INFECTION

The significance of age on wound infection was confirmed in this study, supporting work carried out by others (49, 24, 25, 14, 71). The quadratic equation of the form $YI = A - BX + CX^2$ fits very well the data of Dudley Road (B4) continuous survey. Using this equation, it is possible to estimate the infection rate at any age. The constants B & C relate to age, but the constant 'A' could be considered as a measure of factors other than patient parameters (e.g.ward parameters), and in this case, the constant 'A' would vary from hospital to hospital, as ward and other parameters differ. The quadratic equation for age and wound infection rate was confirmed by the N.R.C. (24) survey, Ayliffe et.al. (14), and Goonatilake (49) in their cross-sectional surveys, and a similar quadratic equation was also found to fit closely above 50 years age for the D.R. (D15 & 21) and G.H. (8 & 9) continuous survey data with a high constant 'A'. However, the number of infected patients in age groups under 50 years was so small that the analysis has only been carried out for patients above 50 years of age.

In the literature cited, there is no significant difference between males & females in their influence on the wound infection rate (21, 25, 35, 24, 27, 34) and this is true for the two continuous surveys

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in this study. The quadratic equation was in the form of : $YI = A + BX - CX^2$ for male patients (thus inverting the curve) in D.R.(D15 & 21) and G.H.(8 & 9) continuous survey, this could be due to the small number of patients.

8-1-2 NASAL CARRIAGE AND WOUND INFECTION

The significance of nasal carriage on post-operative wound infection rate as reported by others (6, 30, 31, 8, 70) was confirmed in this study. Also, patients that were colonized after operation showed a significant difference when compared with patients that were colonized before operation, that could be due to association of nasal carriage and length of stay or due to spread from wound to nose.

8-1-3 PATIENT PARAMETERS AND NASAL CARRIAGE

The quadratic equation for age and nasal carriage rate in the form of $YN = A - BX + CX^2$ fitted the data for the two continuous surveys (D.R.(B4) and D.R.(D15&21) & G.H.(8&9)) i.e., the same form of equation for age and wound infection rate which reflects the closeness of the two relationships. In Dudley Road (B4) continuous survey, the analysis has been carried out for four antibiotic sensitivity patterns of staphylococcus strains in order to examine the effect of each type on nasal carriage rate. The minimum carriage rate for resistant and all strains as was expected, because the very young and the elderly are more suscepti-

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ble to nasal colonization with antibiotic resistant <u>Staph.aureus</u> (49), while as Harris (4) found the great majority of nasal strains in the casualty patients were fully sensitive or penicillin-resistant only strains, also, in D.R.(D15& 21) & G.H.(8 & 9) continuous survey the minimum carriage rate for penicillin-resistant strains (62 years) was high. The minimum carriage rate for sensitive strains in Dudley Road (B4) continuous survey was at 38 years, that is somewhat unexpected. The relationship between sex and nasal carriage rate was significant only for resistant strains of staphylococci in Dudley Road (B4) continuous survey and for penicillin-resistant strains of staphylococci in D.R.(D15 & 21) & G.H.(8 & 9) continuous surveys.

In the Dudley Road (B4) continuous survey, a significant increase in nasal carriage rate was observed in the group of patients who received antibiotics. The nasal carriage rate of patients who received antibiotics was similar to patients who did not receive antibiotics in D.R.(D15&21) & G.H.(8&9) continuous survey, that was carried out almost on decade after the first. Perhaps, this difference is because of a change in the nature of staphylococi, a reduction in cross-infection, and the introduction of new antibiotics over the decade. The nasal carriage rate is higher for male patients but is only significant for multiple-resistant strains of staphylococci in the Dudley Road (B4) continuous survey.

The linear increase in carriage rate was clearly evident in all

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studies reporting the association between nasal carriage and length of stay in hospital (25, 31, 48, 4, 47, 15). As the majority of these studies showed the highest carriage rates for any type of staphylococci was observed around the fifth or sixth week of stay in hospital. As an increases explanation, the exposure to the micro-organisms with increasing the length of stay in hospital. A linear regression equation fitted closely most of the observed carriage rates in both continuous surveys. The male patients had a higher carriage rate in all categories under study, except that the nasal carriage rate for sensitive strains in male patients was lower than in female patients and for all strains of staphylococci in Dudley Road (B4) continuous survey. This perhaps was, because the nasal carriage rate was higher in the early age groups in female patients. The significance of sex on nasal carriage rate is somewhat uncertain. however, lower carriage rate for female patients has been reported before (24, 14, 49). There are some explanations, such as new-born males being more susceptible to staphylococci skin infections (45), higher settle plate counts when a ward was occupied by male patients (17), and men disseminating more staphylococci than women (46).

8-1-4 COMPARISON OF CONTINUOUS AND CROSS SECTIONAL SURVEYS

In comparing the Dudley Road (B4) continuous survey having 533 patients and Birmingham Regional Survey (cross-sectional) with 12,000

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patients, the quadratic equation for the relationship between age and infection rate was of the type $YI = A - B X + C X^2$, and the constant 'A' was the same in both surveys. Furthermore, the point of minimum infection rate (26 years) was the same, which reflects the closeness of the two relationship. The quadratic nature of the relationship between age and nasal carriage rate for tetracycline-resistant strains of staphylococci followed the same trend in both surveys. The lower value of minimum carriage rate in the Birmingham Regional survey (14, 49) could be well explanied by the great number of very young patients in this survey, although there was no patient under 10 years age in the Dudley Road (B4) continuous survey. Considering length of stay, the linear regression equation fitted the data of both surveys closely and the highest carriage rate reached at 35 days in both. The linear increase of the nasal carriage rate of tetracycline-resistant strains of staphylococci in the Dudley Road (B4) continuous survey was similar to the Birmingham Regional survey (cross-sectional, 49, 14), but of smaller magnitude, this obviously is because of the difference in patient numbers. These similar results from either continuous and cross-sectional surveys on the association of patient parameters on nasal carriage rate and infection rate has also been reported by others (30, 34, 38, 40, 14, 49).

8-1-5 COMPARISON OF TWO CONTINUOUS SURVEYS OF DIFFERENT DECADE

When comparing the Dudley Road (B4) continuous survey in 1968/

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69 and D.R. (D15 & 21)& G.H. (8 & 9) continuous survey in 1977 with similar number of pateints, it was found that same quadratic equation for the relationship between age and infection rate held. The constant 'A' being a measure of the parameters other than patient in the equation of the type YI = A - BX + AX² is higher in D.R.(D15&21)& G.H.(8&9)continuous survey , that is somewhat unexpected with the introduction of new disinfectant, and detergents, and attempts to improve the ward environments almost any time (24, 17, 72, 73). As expected, the number of patients in age groups under 50 years was so small that analysis has been carried out only in those above 50 years of age. The quadratic nature of the relationship between age and nasal carriage rate for penicillin resistant strains of staphylococci followed a similar trend in both Dudley Road (B4) continuous and D.R. (D15 & 21) and G.H. (8 & 9) continuous surveys; the minimum carriage rate was similar. The nasal carriage rate was lower in D.R.(D15 & 21) and G.H.(8 & 9) continuous survey (1977) for all age groups. As reported by others (17, 18, 16), a change in the nature of staphylococci from multiple-resistant to penicillin-resistant or sensitive strains over the last decade was associated with a decrease in the nasal carriage rate. This is generally true, even for the relationship between length of stay in hospital and nasal carriage rate. Because the overall nasal carriage rate in D.R. (D15 & 21) and G.H. (8 &9) continuous survey was lower for all lengths of stay.

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A further explanation for this is , as the results show in the latter survey, the majority of patients stayed in hospital for less than 10 days, showing that duration of hospitalisation had changed and higher carriage rates will not be observed consequently.

8-2 DISCUSSION OF THE IMPLICATIONS OF THE MULTIPLE REGRESSION ANALYSIS. II

The regression model can be used to measure the susceptibility of a patient or a patient population to masal colonization; and masal colonization can also be used as a measure of ward cross-infection. Three main results were achieved from the multiple regression analysis of the Dudley Road (B4) continuous survey. Firstly, the correlation analysis on parameters related to nasal carriage confirmed no correlation between age, sex, length of stay in hospital and exposure to antibiotics. therefore, there is not any bias arising from the interactions between these parameters. Secondly, the relative significance of each parameter on the nasal carriage rates was established. The multiple regression coefficients for age, length of stay and exposure to antibiotics were statistically significant. The regression coefficient for sex of patient was not statistically significant; as discussed before in this chapter, the significance of sex on nasal carriage rate is somewhat uncertain, although a higher carriage rate for male patients has been reported before (24, 14, 49). The regression model showed a lower carriage rate for patients treated with antibiotics, but this may be biased due to the small

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size of sample (530) especially as 168 groups were included the multiple regression analysis. For this reason, the multiple correlation of 0.666 was not very high. It is also probable that strains of staphylococci were not acquiring resistance to antibiotics used. The regression model can also be used to determine the relative significance of ward parameters by the introduction of the constant to the regression analysis. The constant in the continuous surveys relates to one single ward with specified ward practices and in comparing, the constant in cross-sectional surveys will introduce a bias into observations due to the correlation between parameters of different wards in hospitals.

In comparing the regression models of two surveys, Dudley Road (B4) continuous and Birmingham Regional (cross-sectional, 14, 49), age, sex, and length of stay showed similar effects on nasal carriage except the regression coefficient for sex in Dudley Road (B4) continuous survey was not significant. In the case of antibiotics, in the Birmingham Regional survey, the contribution of exposure to antibiotics with the high risk of carriage is explained by high age and extreme length of stay, as well as the emergence of tetracycline-resistant strains follows the use of tetracycline (49). The difference in the size of constant is due to the different ward and hospital practices in the Birmingham Regional survey (14, 49).

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The graphical representation of the regression model is useful because it reflects the significance of both the patient and the ward parameters. The constant which relates to ward parameters is independent of any patient parameters and would change from ward to ward , is well represented graphically. The surface derived from the significance of age and length of stay being shifted up or down depending on the presence of sex and antibiotics on nasal carriage, represents the relative significance of patient parameters.

CHAPTER 9

CONCLUSIONS

The literature survey indicated the significance of certain parameters on wound infection and nasal carriage. The primary analysis of the data from the Dudley Road (B4) continuous and D.R.(D15& 21)& G.H. (8& 9) continuous surveys established that age, and nasal carriage is associated with wound infection. The association was not significant for sex.

Considering nasal carriage of multiple-resistant <u>Staph.aureus</u>, patient parameters such as age, sex, length of stay and exposure to antibiotics appeared to be significant in the Dudley Road (B4) continuous survey. The same factors were significant in the D.R.(D15 & 21) & G.H. (8 & 9) continuous survey, apart from exposure to antibiotics, but the relationship was with penicillin-resistant and not multiple-resistant strains.

The correlation analysis on Dudley Road (B4) continuous survey confirmed that patient parameters are not correlated, there is not any bias arising from interactions of these parameters. The multiple regression indicated that age and length of stay are both related to nasal carriage, but the regression coefficient for sex was not significant. Nasal acquisition was lower in patients who were treated with antibiotics.

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The major objective of this study was to establish whether similarity existed between results of continuous and cross-sectional surveys. The curves derived from the patient parameters such as the age and length of stay in the Dudley Road (B4) continuous survey was similar to curve derived from the Birmingham Regional survey (crosssectional ,14, 49). Also, the regression model of these two surveys were similar, and the results of the Dudley Road (B4) continuous survey and the Birmingham Regional survey (cross-sectional) follow each other closely.

The lower carriage rate of multiple-resistant strains of <u>Staph.aureus</u> in the Dudley Road (\mathbb{B}^4) continuous survey, indicates that less cross-infection occured than in hospitals in the region as shown in the regional cross-sectional survey. This difference may well have been due to the small number of patients and the absence of overcrowding and the availability of islation cubicles. The most recent survey D.R.(D15 & 21) & G.H.(8 & 9) continuous survey was of particular interest. Tetracycline-resistant strains had almost disappeared in both hospitals, one of which was old large open wards (D.R., D15_& 21) and the other was a new hospital (G.H., 8 & 9). This is part of a general trend in many hospitals and could be related to a general reduction in the use of tetracycline (Ayliffe, 74). The results also showed the

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lack of a relationship between staghylococcal resistance and antibiotic usage, which was apparent in the Birmingham Regional survey. It That the relationship is also of interest of length of stay with penicillin-resistant only strains was still present indicating that patients were still acquiring staphylococci during their hospital stay. However, phage-typing showed little evidence of cross-infection with these strains.

A cross-sectional survey is therefore a valid technique for measuring wound infection or staphylococcal cross-infection in a hospital. However, large samples are necessary and several surveys may be required in a year. The cross-sectional survey may miss short outlines of infection and a continuous survey is preferable in an individual hospital. The cross-sectional survey is particularly suitable for obtaining data on a number of hospitals over a short time period and can be used to investigate the relevance of other factors which might be associated with infection.

The multiple regression model developed from the Dudley Road (B4) continuous survey's data was useful in determining the significance of patient and environmental (ward) parameters on nasal carriage. These parameters were well demonstrated by the graphical representation. Therefore, this confirmed that the continuous surveys mimic the cross-sectional surveys and demonstrate the useful-

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ness of multiple regression model in determining the significance of patient and environmental (ward) parameters on nasal carriage of staphylococci.

APPENDIX A

PATIENT'S INFORMATION RECORD		
OSPITAL 2 4	1	1
B 4		4
onth and year		7
of admission		11
d number P/L (for regional leave blank)		
a number - by (for regionar leave blank)		13
ndition - B4		15
x 1. Male 2. Female		17
re		18
spital Unit number		20
te of discharge (B4) or date of survey		
v in hospital		26
		28
		22
2,		. 32
peration		36
DateDays after admission		. 39
0. No wound 1. Clean - not drained 2. Clean - drained 3. Contaminated not drained 4. Contaminated drained 5. Not known 6. Excluded 7. Clean - contaminated - not drained 8. Clean - contaminated - drained		41
1. Dressed before onset of infection 2. Dressed after onset	-	
SCRIPTION		40
 Not infected 1. Margin red with serious discharge Purulent 3. Sinuses or fistulas 4. Wound break down Deep abscess 6. Cellulltis 7. Previously infected (now clean or healed) 8. Haematoma 9. Slough 		45 44 45 46
EVERITY OF INFECTION		
1. Doubtful 2. Mild 3. Moderate 4. Severe 5. Drain wound only mild		47
DURCE OF INFECTION	-	48
REXIA O. No 1. Yes > 100° F 2. Not known	=	40
nset of infection (days after operation)		50
-7/47		0
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THER INFECTION	
· ·····	52
· ·····	54
	56
CQUIRED IN HOSPITAL	
0. No acquired infection 1. A. 2. B. 3. C. 4. A + B. 5. B + C. 6. A + C. 7. A + B + C.	58
ACTERIOLOGY	
1. Site	59
Organisms	60
2. Site	62
Organisms	63
ntibiotic sensitivity of staph. sureus.	
0. Not applicable 1. Sensitive 2. Resistant to penicillin only Site 1 3. Resistant to 1 antibiotic other than penicillin 4. Resistant	65
TUENOTUERADY	00
CHEMOTHERAFI	1-
6. Tetra 7. Neo 8. Nitrofurantoin 9. Meth	68
A. Eryth B. Novo C. Poly D. Kana E. Ceph F. Fuc G. Linco H. Topical Antibiotic K. Chloramphanicol L. Gentamycin M. Carbenicillin	69 . 70
SSOCIATED FACTORS	
1. Immuno-suppressive drugs 2. Irradiation, 3. Steroids	
4. Diabetes 5. Uraemia 6. Obesity 7. Malnutritiod	71
8. Agammagiobuliinaemia 9. Others specify	72
aemoglobin	73
rocedures	74
	75
solation (Regional survey) 0. Nil 1. Side-ward 2. Ventilated	76
side-ward 3. Barrier-nursing in main ward	10
ther information	77
Record No.	79

APPENDIX B

CROSS-INFECTION SURVEY-REGIONAL SURVEY

PATIENT'S INFORMATION RECORD

Hospital	••,*					. [111
Ward					*		114
Month and Ye	ar)	e odmi ooi uu					6
Day	}	admission					10
Type of pati	ent						12
Bed. No.							14
Sex. 1.	Male.	2. F	emal	e	* •		16
Age							117
Hospital Uni	t Number						19
Date of surv	ey						ورجع والمرجع والمحافظ
Days in Hosp	ital	• .					25
Diagnosis	1		••••				28
	2	•••••				111	32
Position in o	operation	n list				ſ	736
Operation	• •					F	38
Surgeon	1					F	41
	2	•••••				Ī	43
	3					Ĩ	45
Operating the	eatre						47
Duration of o	operation	(minutes)					48
Length of ind	cision (c	m.)				· [51
Date of opera	ation		da	ays after admiss	ion	Ī	53
WOUND							
0. No wound,	. 1.	Clean.	2.	Clean-contamina	ted.		55
3. Contamina	ated. 4.	Not known.	5.	Excluded.			
TYPE OF DRAIN	1						
0. No drain.	. 1.	Redivac.	2.	Corrugated. 2.	Large	tube.	56

4.	Wick. 5. Sma	11 <u>t</u>	ube. 6. More	than one drain (of	
differ	rent type). 7.	Oth	er drain specify		· · · · · · · · · · · · · · · · · · ·
DESCR	IPTION		· · · · · · · · · · · · · · · · · · ·		
0.	Not infected.	1.	Margin red with	serous discharge.	57
2.	Purulent.	3.	Sinuses or fistu	lae.	58
4.	Wound break down.	5.	Deep abscess.	6. Cellulitis.	59
7.	Previously infect	ed (now clean or heal	ed). 8. Haematoma.	60.
9.	Slough.				·
SEVER	TY OF INFECTION				
Т.	Doubtful.	2.	Mild.	3. Moderate.	1 61
4.	Severe.	5.	Drain wound only	- mild.	_
SOURCE	OF INFECTION				
1.	Ward.	2.	Theatre.	3. Ward or theatne	F 62
4.	Self.	5.	Unknown.		<u> </u>
OTHER	ACQUIRED INFECTION				
A				F	T 1 63
В				-	1 65
c					67
MOVEME	INT OF PATTENTS			· · · · · · · · ·	
0.	Unknown 1	Bed	ridden	n-mohile in chair.	1 69
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J.	Restricted mobili	by.	4. MODILE.	d gines enemation?	- 70
nas pa	tient visited anot	ner	lepartment or ward	a since operation:	110
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OTHER	INFORMATION	••••	••••••	Г	73
	Salling State			Record NO.	75

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CROSS INFECTION SURVEY-REGIONAL SURVEY

PATIENT'S INFORMATION RECORD

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CROSS-INFECTION SURVEY-REGIONAL SURVEY

PATIENT'S INFORMATION RECORD

Hospital Unit No.

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10.	Eryth.	11.	Fuc.	12	. L:	in.	13.	Cl	in.	14.	Nit.	
15.	Nal.	16.	Met.	17	. Ce	ephlor.	18.	Ce	phthin.			1997 - 1997 -
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23.	Kana.	24.	Gen.		25.	Tob.	20	6.	Amik.	27.	Carben,	
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