

ANALYSIS OF CROSS - INFECTION MECHANISMS

IN A HOSPITAL SYSTEM

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S U M M A R Y

The aim of this work was to examine the relevance of factors related to cross-infection in hospitals, based on a large cross-sectional survey, and to formulate a mathematical model depicting the significance of patient parameters, which will be used to standardise future experimental studies.

The analysis showed that age, sex, wound drainage and wound contamination are related to wound infection; and age, sex, antibiotic use and length of hospitalization are related to the nasal carriage of antibiotic-resistant Staphylococci. The significance of the parameters age and length of stay were quantified. Correlation and multiple-regression analyses confirmed the validity of these observations.

Models developed were based on the assumption that nasal carriage of antibiotic-resistant Staphylococci is a measure of certain aspects of susceptibility to infection. From multiple-regression analysis, a carriage-rate profile representing the relationship between age, length of hospitalization and nasal carriage rate was derived. That the surface shifts its origin depending on the state of the parameters sex, antibiotic use and environmental (ward) conditions is shown.

A model for the relationship between age and nasal carriage was developed from theoretical concepts of ageing and acquisition of resistance applied to the total patient population. A deterministic model based on epidemiological principles was developed to represent the relationship between length of hospitalization and nasal carriage.

During the development of the final comprehensive model, the significance of a further variable, the distribution of the number of patients in age and length of stay groups was established. This is a major parameter previously ignored by other researchers and particularly important in comparing infection and nasal carriage rates among different patient populations. The distribution of the number of patients was included as a variable together with age and length of hospitalization in this final model.

HOSPITAL INFECTION
CROSS-INFECTION
STAPHYLOCOCCUS-AUREUS
EPIDEMIOLOGY
MATHEMATICAL MODEL

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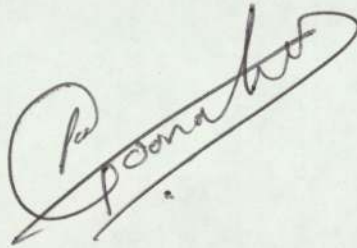
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DECLARATION

No part of the work described in this thesis has been submitted in support of an application for another degree or qualification of this or any other University or other institute of learning.

No part of the work described in this thesis has been done in collaboration with any other person.

A handwritten signature in black ink, appearing to read "P. Poonacha", is written diagonally across the page. The signature is enclosed within a large, hand-drawn oval.

DEDICATION

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N O M E N C L A T U R E

S	Sample Size.
D.F.	Degrees of Freedom.
x^2	Chi- Squared Statistic.
P	Probability.
S.S.D.	Sum of Squared Deviations.
R	Correlation Coefficient.
Y	Wound Infection Rate.
X	Age of Patient (years)
YN	Nasal Carriage Rate (Resistant Strains only)
T	Length of Stay in Hospital (days)
z	Number of Infected Patients at Time 'T'
YX	Incidence Rate at Age 'X'
N	Total Number of Patients.
r	Rate of Interaction Between Carriers and Non-Carriers.
c	Proportion of Susceptibles.
I	Number of carriers at time 'T' = 0
n_i	Number of carriers at any time 'T'
W	Constant of Intergration.
No	Intercept of the Numbers Surface
l,m,n	Constants.
q,u,k	Constants.
V, B_i , B_2	Constants.

DEFINITIONS

- Wound Infection : Wounds (apart from those excluded) whose severity of infection are listed as more than doubtful or mild are considered to be infected. (also see Page 57)
- Wound Infection Rate : The percentage of patients infected according to the above definition, in a particular group (e.g. male patient group) under analysis.
- Nasal Carriage : Patients' whose nose swabs indicated the presence of a Staph aureus organism resistant to one or more antibiotic other than Penicillin are termed nasal carriers.
- Nasal Carriage Rate : The percentage of patients who are Nasal Carriers according to the above definition in a particular group under analysis.
- Staphylococci
(Staph. aureus) : Coagulase positive Staphylococci
- Nosocomial Infection
(Hospital Infection) : Hospital acquired infections.
- Wound Colonization : Evidence of growth of bacteria, but not necessarily evidence of infection or tissue damage.

Remote Infection

: The presence of an infection
other than a wound infection.
(e.g. urinary tract infections,
infected skin disease)

CHAPTER I

INTRODUCTION

In spite of the obvious benefits patients derive from hospitalisation, they face the risk of acquiring infections during their stay in hospital (i.e. nosocomial infections). The medical and nursing professions have been concerned about this major obstacle to hospitalisation for some time. As far back as 1859, her experience with infections among war casualties prompted Florence Nightingale to state 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". The advent of antiseptics as promoted by Lister and Semmelweis, together with the discovery of sulfonamides and antibiotics, have now reduced the mortality of hospital infections. The present rate of hospital infections is about 3 - 5 per cent of total patients admitted to hospitals, and consists mainly of infections of post-operative wounds, the urinary and the respiratory tracts.

Although the major threat of post-operative wound infections has been greatly reduced, about 5 per cent of post-operative wounds become infected. This inevitability of infection may partly be due to changes in certain factors that relate to the development of infections. The main factors are, (1) susceptibility of the host, (2) the presence of potentially pathogenic organisms in the wound or other susceptible site and (3) the environment (e.g. air contamination). It is perhaps surprising that the incidence of wound infection has not been obviously reduced over the last 20 - 30 years, but the susceptibility of the hospital population

has tended to increase. The following factors associated with the susceptibility of the patient population, have changed with the advancement of medical science in the last two or three decades:

(a) Type of Patient Hospitalised

The advances in surgery and resuscitation techniques have resulted in an increase in the number of premature infants and elderly patients in hospitals. Further, this has meant an increase in the length of hospitalisation in these groups, which results in a greater degree of exposure to micro-organisms. Owing to the benefits that can be derived from the National Health Service (and similar health insurance schemes in other countries), a greater proportion of the elderly are now hospitalised. This increase in the number of neonates and elderly patients in hospitals, has increased the susceptibility (to infection) of the total patient population. Developments in therapeutic measures to combat long term diseases such as leukaemia, tumors and severe diabetes have also increased the number of susceptible patients hospitalised.

(b) Diagnostic and Therapeutic Procedures

The developments in surgical techniques have increased the length and complexity of operations, resulting in prolonged ^aanesthesia, extensive tissue damage and more wide-spread use of artificial implants. The increase in intravenous infusions and other types of instrumentation in recent years, have further increased the number of susceptible patients. The use of the immuno-suppressive drugs and steroids in the treatment of leukaemia and

other conditions has impaired the defense mechanism of susceptible patients. Use of antibiotics has resulted in the displacement of the normal flora of the bowel causing an increase in the acquisition of antibiotic-resistant gram-negative bacilli and overgrowth by yeasts.

The indiscriminate use of antibiotics in prophylaxis and therapy during the last three decades has changed the micro-organisms. In the fifties and mid-sixties antibiotic-resistant staphylococcus aureus emerged as a problem of post-operative wound infection. Since penicillin was the most extensively used antibiotic, most staphylococci now have the ability to produce the enzyme penicillinase, and are resistant to benzyl penicillin. Now staphylococci resistant to tetracycline, erythromycin, methicillin and many other antibiotics are common in hospital environments. Although a large proportion of healthy individuals outside hospitals carry staphylococci in their noses (nasal carriers), almost all of these strains are sensitive to all antibiotics or resistant to penicillin only. Multi-resistant strains are common only in hospital environments. Particularly, strains of the phage types 80/81, 6/7/47/54/75, 83A, 84/85, (WILLIAMS, 1) and 29/77 and 94/96 (AYLIFFE, 2) have been recognised as causing epidemic or epidemic infections in hospitals in many parts of the world over the years.

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 Aeruginosa* and *bacteroides*, the strains naturally resistant to antibiotics get selected. Thirdly, some of the resistant strains appear to show an increase in virulence.

Since the emergence of penicillinase-resistant penicillins, Staph.aureus has been of less importance and replaced by gram-negative bacilli. For instance, staphylococci sepsis has reduced from 60 per cent of all septic episodes in 1959 (P.H.L.S.,3) to about 33 per cent in 1970 (AYLIFFE,4), whereas gram-negative bacilli sepsis has increased from 30 per cent to 55 per cent during this period. Nevertheless, staphylococci sepsis is still a major issue of wound infection, due mainly to the complexities of treating the still present multiple resistant strains.

Apart from complicating the clinical conditions of patients, infections have many cost implications. At present 5 - 10 per cent of patients acquire some clinical infection during their hospitalisation. Earlier reports (Mc LEOD, 1965, 5; FARRER and CLUFF 1961, 6) have stated that about ten per cent of patients with post-operative infection died as a direct result of the infection. This may reflect a mortality rate of about one in two hundred for the whole patient population. However, with the advances in medical science, the risk of death associated with post-operative infections, is being reduced.

A major inconvenience associated with infection is prolonged hospitalisation. An extra mean duration of hospitalisation of between eight to fifteen days due to infection, has been reported (CLARK 7, Mc LEOD 5, COHEN et al., 8). The Public Health Laboratory Service (P.H.L.S.,3) survey in 1961 estimated the total excess stay in hospital due to sepsis may be about 1,000,000 days per year, or about three per cent of the total bed occupancy of acute hospitals, which in monetary terms is equivalent to about 0.5 per cent of the total

cost of the National Health Service. A similar American study(9) covering about a quarter of all hospitals in the U.S.A. in 1967, estimated that the cost of post-operative infection in U.S.A. to be about \$ 3.2 Billion. Apart from these obvious financial costs, there are other costs associated with prolonged hospital stay such as the cost of sickness insurance, temporary or permanent disability, loss of wages and so forth. It is rather ironic that if it was possible to reduce the extent and the degree of infection, much of the current shortage of hospital beds in the National Health Service could possibly be resolved without having to resort to further funds.

The adverse effects of hospital infection have been recognised for quite some time, and a considerable amount of research has been carried out to find out ways of reducing the risk of sepsis. Probably inspired²³ by the tremendous reduction of infection achieved by the application of LISTER'S antiseptic methods and the aseptic methods, most of the research has been directed towards reducing the number of micro-organisms in the patient environment. The introduction of improved antiseptics, better nursing practice, design of ventilation systems, cubicalisation of some types of patients and so forth have reduced the risk of sepsis. The recognition by WILLIAMS (10) in 1959 of a correlation between nasal carriage and wound sepsis, led to the investigation of contaminated ward sites, and the development of methods to reduce nasal carriage.

In further investigating this correlation, GILLESPIE et al.(11) were able to obtain a reduction in infection by treating carriage sites and by reducing environmental

contamination. There have been quite a large number of studies carried out since then, reporting the significance of many ward sites as reservoirs of staphylococci organisms. Laundry chutes (I2, I3), bedding (I4), walls (I5, I6), blankets (I7, I8), ward floor (I9, 20), ward surfaces (2I), stethoscopes (22, 23) have all been investigated as possible reservoirs with varying conclusions. The effect of certain structural features such as sub-division of wards and isolation (24, 25) and ventilation (26) has also been reported.

With the experience and knowledge gathered from the above studies, many ward practices were instigated to combat staphylococci contamination, but the corresponding effect on the reduction of wound infection was often slight (although the nasal carriage rate has been somewhat reduced). This is partly due to the lack of understanding of the relationship between airborne staphylococci, nasal carriage and wound infection. The prime objective has been to reduce the amount of aerial contamination as much as possible, without having any regard to the amount of benefit to be gained by such action. Often, the cost implications of introducing new systems were not considered, let alone a proper cost-benefit analysis. LIDWELL (24) has pointed out that the risk of nasal acquisition is less than proportionately reduced to a reduction in the aerial contamination. The failure in obtaining a reduction in wound infection by reducing the level of environmental contamination, may reflect some doubt on the correlation between nasal carriage and wound infection demonstrated by WILLIAMS. Equally strong literature can be quoted for supporting WILLIAMS (27, 28, 29, 30, 31, 32), as well as contradicting him (33, 34, 35, 36). However, because of its respiratory function, the nose is an effective sampler of

the ward contamination, and hence the importance of nasal carriage rate as a measure of the ward cross-infection, cannot be neglected. Further, the nose readily acquires new strains of staphylococci and it can be easily sampled.

The source of hospital acquired infections may broadly be classified as endogenous or exogenous. There is no doubt over the significance of the endogenous source (self-infection) as a route of infection. However, there is a controversy surrounding the mechanism of exogenous infection; whether the post-operative infection was due to contamination that occurred in the operating theatre or whether it was acquired in the ward. SHOOTER et al.(37), and ROUNTREE et al.(38) have stated that ward cross infection plays a larger part in wound sepsis than theatre infection. Whereas AYLIFFE and COLLINS (39), and WALTER et al.(40) have demonstrated the incidence of sepsis associated with disseminating carriers in the operating room. A comprehensive study carried out by the National Research Council (41) on the relationship between the bacterial flora found in the operating theatre and in the patient during operation and the infecting bacteria in post-operative wound infection, concluded that there was no correlation. THOMSEN et al. (42) have also concluded that post-operative wound infections by Staph.aureus originate mainly from the wards. Due to these contradictory findings, attempts have been made to reduce the risk of infection both at theatre level as well as the ward level. Although it is likely that the importance of the source of infection may vary from hospital to hospital, it would have been more fruitful had there been objective studies aimed at ascertaining the precise significance of either factor, before embarking on devising

measures to counteract a perceived threat. However, there are many practical difficulties in undertaking such a study.

Lately, emphasis has been laid on the importance of surveillance as one of the means of combating hospital acquired infections. In summarising the inferences of the International Conference on Nosocomial Infections (1970), WILLIAMS (43) stated that "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 needed. There seem to be two objectives of surveillance: one, for better internal control of hospital activities and, the other, to see where one hospital stands in relation to the others". Apart from these broad functions of surveillance, it is also useful in detecting outbreaks of infections as early as possible and giving some indication of the long term changes occurring in the area of hospital infection. The practicality of using surveillance as a means of comparing infection rates among different hospitals is however, somewhat doubtful.

All these approaches discussed above have one major weakness in common. Most of them have more or less assumed that patient parameters (susceptibility) are unimportant or are a constant; and hence the emphasis on environmental factors as the predominant cause of hospital infection. Even the few who recognised the significance of some of the patient parameters (44,45,46,8,9,41,47,48), it has nearly always been viewed as a qualitative concept as opposed to a quantitative concept. If this assumption is wrong, then the conclusions made by many, on the significance of certain environmental

factors may be biased, if not totally invalid. In other words when trying to determine the significance of some environmental factor, by comparing infection rates in two wards, the susceptibilities of the two patient populations under study must be compatible. Some of the controversy surrounding the significance of nasal carriage on wound infection, and the source of infection (theatre or ward) could well be attributed to the non-compatibility in the patient populations studied by some researchers. Recognising this somewhat obvious phenomenon, WILLIAMS (43) in his final note to the International Conference on Nosocomial Infections (1970), emphasised the need to conduct proper clinically controlled studies to combat the difficulty of obtaining statistically convincing evidence. However, even if such studies were carried out, it would only increase the experimental quality of the studies, and the bias arising from the differing susceptibilities of patients would still persist.

If it were possible to quantify the susceptibility of a patient (related to patient parameters), preventive measures could be directed towards those most likely to acquire an infection. Also some kind of a susceptibility index can be used to correct any bias introduced into experiments, due to the heterogenic nature of the patient population being studied. Such an index can also be used as an effective tool in surveillance. The second objective of surveillance (comparing infection rates between hospitals) can only be achieved with the aid of such an index. A crude comparison of infection rates between two hospitals may indicate that the infection rate in one hospital is lower than in the other; but this difference may simply be due to the differences in patient

susceptibilities or type of surgery in the two hospitals, and nothing whatsoever to do with differences in ward and operating theatre practices or facilities.

A susceptibility index can also be effectively used as an independent adjudicator in the ever growing threat of hospital litigation, particularly in the U.S.A. HOYT (49) discusses the hospital's legal liability as a result of some alleged failure to use proper hygienic or sterilisation techniques. Helman Vs. Sacred Heart Hospital (50) is a typical example where damages were awarded to a patient who acquired an infection in hospital. In litigations of this nature, it is extremely difficult to ascertain whether the infection was caused by the negligence on the part of the hospital, or whether it was entirely due to the higher susceptibility of the patient. A susceptibility index, would in the least, indicate whether an infected patient had a higher or a lower risk of acquiring the infection, due to his own physical or clinical condition.

The aim of this study is to investigate the significance of patient parameters on nasal colonisation and wound infection, based on a large cross-sectional survey carried out between 1969 - 1972 in the Birmingham region (AYLIFFE et al. 51). Since the survey was a cross-sectional one, certain assumptions were made before the analysis. The survey covered about 12000 patients in over 500 wards with a multiplicity of ward practices; hence it was assumed that the patient parameters are independent of ward parameters for the purpose of this study. Ideally, a continuous study in a smaller number of hospitals where ward practices are less varied, would possibly have been more useful.

However, there are many practical difficulties associated with such surveys, for instance, it would take a longer period of time to collect an adequate sample for analysis, and even then, any bias due to the changes in the infecting micro-organisms over the years must be accounted for before the analysis. A smaller number of hospitals would be insufficient to allow for variability between hospitals.

Once the significant patient parameters are isolated from this cross-sectional survey, they will be represented as a quantitative index defining the susceptibility of the patient population. Initially, the index will be derived from multiple regression techniques and then, a mathematical model postulated on theoretical grounds. Although the model is based on a patient population in the Birmingham region, a method of applying the model on a national or an international patient population, is discussed.

When the survey was originally planned, information regarding ward practices, structures and facilities were all collected with the intention of isolating the significance of some of the environmental factors on infection. For the reasons described previously, a crude comparison of infection or nasal carriage rates associated with each of these ward factors might show spurious associations. However, after the concept of the susceptibility index is accurately defined, that index will be used to correct the bias resulting from the diversity of patient parameters in the data. Then the corrected data will be used to validate the significance of ward factors.

CHAPTER 2

LITERATURE SURVEY

Before the literature survey proper, certain features of the staphylococcal organism which may influence the interpretation of the literature, must first be discussed. Resistant strains of certain types of staphylococci (e.g. 80/81) appear to be more virulent and possess a greater propensity to spread than other types. These strains tend to appear and disappear for no apparent reasons, and hence make the comparison of nasal carriage and wound infection rates difficult at different times (even in continuous surveys in a single ward). For instance, when a particular strain is used as a measure of hospital infection, assessment will be difficult if epidemic strains appear and disappear periodically.

The literature survey is divided into seven broad areas for convenience. These are literature related to (1) The nasal carriage of staphylococci, (2) Post-operative wound infection, (3) The association between nasal carriage and sepsis, (4) The source of post-operative wound infection (ward or theatre), (5) The influence of environmental factors, (6) Patient parameters related to nasal carriage and wound infection, and (7) Application of multiple-regression analysis to factors associated with wound infection and nasal carriage. It was necessary to carry out an extensive literature survey, in order to look at the many controversies in proper perspective.

There were many publications indicating apparent significant solutions to the problem of hospital infection, some of

which are not included in the literature survey due to their small sample size and the statistically uncontrolled nature of their experiments. Therefore, as an indication of the representativeness of the experiments, the size of the sample (S) is given when possible with the quoted literature. Further, in the quoted literature where statistical tests have not been carried out, independent tests have been made by the author based on these data. These are denoted by asterisks (*) in the text. However, it must be recognised at this stage that although it is best to carry out proper statistically controlled experiments, there may be many practical problems associated in designing such tests. Multiplicity of factors associated with infections, difficulties of collecting information (e.g. inadequate records, transfer of patients elsewhere), lack of suitable bacteriological samples, are examples of these difficulties.

2.I Nasal Carriage Of Staphylococci

The nasal carriage of staphylococci is a normal phenomenon and usually not associated with clinical infections. The nose can be considered as the major reservoir of the organism. About half or more of the patients and staff in hospital are likely to carry staphylococci in their noses. "The normal carrier rate for adults lies between 35 and 50 per cent. Some 10 per cent of the population rarely harbour staphylococci in their noses and about 20 per cent carry them regularly, the remainder are found sometimes to be carriers and sometimes not" (WILLIAMS et al.52). It is not known why one person is a carrier and another is not. There are many strains of staphylococci,

most of which could be identified by their antibiotic sensitivity pattern and the phage type. Due to the excessive use of antibiotics many strains of staphylococci have now acquired resistance to many antibiotics. Penicillin resistance is due to the inherent ability of staphylococcal strains to produce the enzyme penicillinase. Therefore, the use of penicillins results in the selection of resistant strains.

Although many healthy individuals outside hospital environments carry staphylococci in their noses, most of these strains are either sensitive or resistant to penicillin only. Patients who have had no contact with hospital environments are known to have the lowest nasal carriage rate (52,53). HARRIS (54,S=1200), in comparing the nasal carriage of a group of casualty patients and a group of in-patients, found that about 92 per cent of the strains in the casualty patients were completely sensitive or resistant to penicillin only, whereas in the in-patient group, the figure was only 46 per cent (* significant, $P < 0.01$). A study by EDMUNDS (55, S=2863) did not find a difference in the nasal carriage of penicillin-resistant strains between patients who had previous hospital admissions and those not previously admitted. However, the previously admitted group (3.4%) had a higher rate of tetracycline-resistant strains than those not previously admitted (1.3%), and this difference persisted only for 2 weeks.

Carriers disseminate staphylococci into the air when they speak, cough, sneeze or snort. Also, any form of activity entailing friction on the skin or agitation of the clothing, will increase the dissemination (56).

The carriers vary greatly in the number of organisms they disperse, and in some cases carriers disperse no more than non-carriers do (57). This dispersal by the carriers increases the level of environmental contamination, resulting in new acquisitions by non-carriers; this creates a vicious circle, making the problem of staphylococci nasal carriage endemic in hospital environments. It is possible to reduce the number of bacteria in the nose, and the dispersal to the environment, by treating the carriers with antibiotic nasal spray or ointment (58,59,60,61). However, this practice does not necessarily reduce the subsequent nasal carriage rate in the particular environment where it was applied. This may be due to the complexity of the relationship between the risk of acquisition of nasal staphylococci and the extent of environmental contamination (i.e. exposure). It is possible to reduce more than four-fifths of the bacteria in air by the use of a combined air-and-formite system of bactericidal conditioning (62); but even then the effect on the level of nasal carriage of staphylococci is minimal. LIDWELL et al. (63,64,25) have pointed out that the overall risk of nasal acquisition increases much less than proportionally to the increase in exposure, and is considerably greater for a given airborne exposure in the case of the tetracycline-resistant strains. In quantifying this relationship, they have pointed out that the risk of acquisition varies as the one-fifth power of the exposure. For example, "an average dose of 10 airborne staphylococcal particles of a single strain corresponded to a probable risk of nasal acquisition of about 1 in 800 or 1 in 300 for tetracycline-resistant staphylococci". This relationship somewhat explains the apparent lack of

significant reductions in nasal carriage, resulting from the introduction of new ventilation systems in hospital wards. LIDWELL et al.(63,64,25) further pointed out that the chance and rate of nasal acquisition are related to both the airborne counts and to the number of possible sources.

It is worth noting at this stage that a great deal of confusion has been caused by the indiscriminate use of the term nasal carrier. In some literature it is not clear whether nasal carriage refers to the carriage of a particular antibiotic-resistant strain, or all strains of staphylococci. It is more practical to define the carriers of multiple or tetracycline-resistant strains as nasal carriers, because these strains are mainly associated with hospital environments. A further aspect of this theme has been highlighted by MOORE and GARDNER (65). They point out the importance of stating the day the nasal swab was taken, whether on the day of admission or on a later day. For reasons described in Section 2.5, a sample of patients swabbed on the day of admission would generally have a lower carriage rate than a sample at a later date. Therefore, in comparing nasal carriage rates obtained from different sources, the definitions of the term nasal carriage must be established first.

2.2. Wound Infections

Many factors are shown to be associated with the risk of post-operative wound infection. The variation of the risk of infection has been well reported (3,8,41,66). Most of the wound infections are found following operations in the gastro-intestinal tract. The presence of a post-operative drain (which is somewhat related to the type of

operation) also increases the risk of post-operative wound infection (3,41,45,67,115); and different infection rates are attributed to different types of drains (3,41,45). The duration of operation has been reported to be associated with the risk of infection (8,41,45,46,67). COHEN et al. (8,S= 8900) pointed out that the incidence of wound infection increases more or less linearly with the duration of operation. Others stated that lengthy operations are generally associated with a higher risk of infection compared with short operations. The other variable at operations, the length of incision is also reported to be a determinant of the risk of infection. BRUUN (45, S=2557) reported that long incisions increase the risk of post-operative infection. It must also be understood at this stage that some of the above factors are inter-related. For instance, the presence of a drain, lengthy operations and ^{long} incisions may all indicate dirty wounds, which on their own are regarded to be operations with a high risk of infection.

Certain other factors not directly linked to the type of operation may also be responsible for post-operative wound infection. For instance, the operation list-position has been pointed out as a determinant of the risk of infection. Patients whose operations were first on the list had a lower rate of infection than those who were on the bottom of the list (41,68,69). This may be due to the gradual build up of contamination in the operating theatre with the increase in the number of operations performed. Surgeon fatigue may also influence this factor. The N.R.C. study (41, S=15000) attributes the difference in the risk of infection to the particular types of operations performed

at different times of the day. Their explanation was that, since the majority of operations performed late in the day were dirty operations, these would obviously have a higher risk of infection, compared with the cleaner operations which were given priority on the operation list.

Although the N.R.C. study concluded that the time of day at which an operation begins cannot be considered as a primary determinant of wound infection, their results even after adjusting for differences in wound classification and urgency of operation, showed a lower infection rate for operations performed between 07.30 and 09.30 in the morning. A similar study by DOUGLAS (68, S=584) based only on clean wounds, reported that patients who were first on the operation list had a significantly lower infection rate. Apparently, the 'first' cases in his study had more drains and longer operations than 'other' cases (age distribution similar in both groups), and hence, should have had a higher infection rate. This somewhat contradicts the conclusions made by the N.R.C. study. In both these studies the infection rates appear to be increasing linearly, with the increasing operation list-position.

The majority of patients admitted to hospital for operations are operated on the day of admission or on the following day, whereas some patients are required to spend a considerable amount of time in hospital prior to the operation, undergoing tests and treatment linked to the operation to be performed. A higher risk of post-operative wound infection is associated with this second group, where the extent of the pre-operative stay in hospital is related to the risk of infection(41,45,70,115).

Since long stay patients are more likely to be nasal carriers of hospital strains of staphylococci, this may explain the higher risk of wound infection attributed to patients with long pre-operative stay in hospital. On the contrary, the long pre-operative stay patients may materially differ from the other patients. The patients who are kept in hospital for a length of time before operation, normally undergo a course of therapeutic treatment to prepare them for surgery. These treatments may lower the resistance of the patient, thus increasing the risk of post-operative wound infection. It is more likely that both these factors- the lowered resistance and the increased exposure, together contribute to a higher risk of infection in longer pre-operative stay patients.

It has also been reported that another class of patients, those who undergo urgent or emergency operations, are associated with a high risk of infection. The N.R.C. study (41) explains that this is caused by the greater amount of contaminated wounds found in urgent and emergency operations. After they corrected their figures for this bias arising from contaminated wounds, the difference between the urgent or emergency operations and other operations was not apparent. COHEN et al.(8) also did not find any significant increase in wound infections in emergency operations.

The patient's medical or clinical condition may also influence the infection rate. The significance of many host-factors on wound infection is well documented. COHEN et al.(8) experienced a higher risk of infection associated with obesity, hypotension, need for blood transfusion during operation, congestive heart failure and cancer surgery. In explaining this association, they suggest that impairment

of local circulation may be of great importance in predisposing to surgical wound infection. The higher risk in cancer surgery may be due to the complex operative procedure and the administration of immuno-suppressive drugs. The N.R.C. study (4I) reported higher wound infection rates associated with diabetes, steroid therapy, severe obesity and severe malnutrition. Although these host-factors are significant, these factors are only present in about 5 per cent of the patients undergoing surgery.

The presence of remote infections, other than wound infection, are also indications of higher risk of acquiring infections (4I). This is not surprising because the presence of remote infections are indications of low resistance and further, the presence of other remote infections lower the overall resistance of the patient, making the patient more susceptible to wound infection. The type of operative closure is another factor associated with infected wounds. Higher infection rates were found in wounds closed secondarily, and unclosed or partially closed than in wounds primarily closed. Further, the technique of the surgeon is also probably an important factor, but there is very little evidence to evaluate its significance. Even the significance of seasonal changes on wound infection have been studied (8,4I) and concluded that seasonal changes do not have any significance on wound infection.

Certain parameters not directly linked to the clinical condition or the operative procedure, may determine the risk of infection. Patients who were treated with prophylactic antibiotics prior to the operation, demonstrated a higher infection rate (4I,45). Before making any firm conclusions

on the effect of antibiotics, one must examine the possibility that prophylactic antibiotics are in the majority administered to patients who have a high risk of acquiring a post-operative infection. If this is generally true, then the significance of antibiotic therapy is purely spurious. In the N.R.C. study (41), even after adjusting the figures for factors known to cause high infection rates, the significance of antibiotic therapy on wound infection still prevailed. However, recent reports (KEIGHLEY, 1978,71) suggest that short term antibiotic prophylaxis is effective in reducing post-operative infection in certain types of wounds.

Two other parameters, the age and sex of patient, which are unique to every individual patient, are also associated with the risk of infection. BRUUN (45) and the N.R.C. (41) study report a higher infection rate among male patients. COHEN et al.(8) states that sex and race bore no relation to infection, but they have not quoted any figures which could be used to analyse this concept further. In trying to explain the higher infection rate among males, the N.R.C. study introduces the hypothesis that the high proportion of contaminated wounds among male patients resulted in a higher infection rate. When only clean wounds were considered, the male patients had a lower infection rate than females. Their final conclusion is that sex of patient is not a significant determinant of wound infection.

Increasing age is associated with a high risk of acquiring infection (3,8,41,45,67,115). Here too, any bias arising from types of operations related to different age groups, must be considered. In the N.R.C.(41) study they hypothesised that young patients have a greater degree of

clean operations which result in lower infection rates. However, when only the clean wounds were considered the effect of age was still apparent. Even after adjusting the figures for other factors associated with high infection rates, the higher rate of infection among older patients still persisted.

2.3 Association Between Nasal Carriage and Wound Infection

WILLIAMS et al.(10, S=700) in 1959 demonstrated the association between the nasal carriage of Staph. aureus and post-operative wound infection. They stated that the incidence of post-operative wound sepsis was 2 per cent in 342 patients who were never nasal carriers of staphylococci and 7.1 per cent in 380 patients who carried a strain of Staph. aureus at some time (* difference significant, $P < 0.01$). They further stated that in about half the infected cases the sepsis was due to a staphylococci of the same phage type as was found in the nose. The P.H.L.S. survey (3,S=3276) in 1960 also observed a similar association between nasal carriage and wound infection; 8.9 per cent of the carriers showed wound sepsis, compared with 7.1 per cent of the non-carriers. However, this difference was not statistically significant. Subsequent studies by WILLIAMS et al.(28, S=2555) in 1962 confirmed their original finding. They further reported that "patients who acquired staphylococci in their nose during their stay in hospital, developed staphylococci sepsis more than five times as often than those who did not. In most cases nasal colonisation preceded the sepsis. The patients who acquired staphylococci also had a higher incidence of non-staphylococci sepsis, but this

appeared to be associated with prolonged stay in hospital".

A similar study by CALIA et al.(72, S=269) in 1969 also supports this concept. In their study, wound colonisation occurred more than twice as often in skin and nasal carriers (37%) as in non-carriers (16%) and the difference was statistically significant ($P < 0.001$). When the actual wound infection rates were compared, carriers (17%) had twice as many infections as non-carriers (9%), but this difference was not significant. Further, skin carriers of staphylococci had a higher rate (56%) of wound colonisation compared with nasal carriers (22%), (* Significant, $P < 0.005$). Also skin carriers had a wound sepsis rate of 22 per cent which was significantly higher than in non-carriers ($P < 0.04$). Since 1959, many other researchers (27,29,30,31,32) were able to demonstrate the association between nasal carriage and wound infection.

However, this association has been challenged by many who carried out similar studies (33,34,35,36,65). MOORE and GARDNER (65, S=538) in their study at Torbay Hospital experienced a lower wound infection rate among nasal carriers (5.9%) and a higher infection rate among non-carriers (9.4%) (* not significant, $P < 0.1$). This study is somewhat different to the studies reported by WILLIAMS et al.(10,28). At Torbay Hospital, the interval between the patient's admission to hospital and the operation was so brief that the likelihood of acquiring a hospital strain was very remote. This implies that a majority of the carriers at Torbay carried penicillin-resistant strains. This may well be the reason why they failed to demonstrate an association between nasal carriage and wound sepsis. In WILLIAMS'S study at the

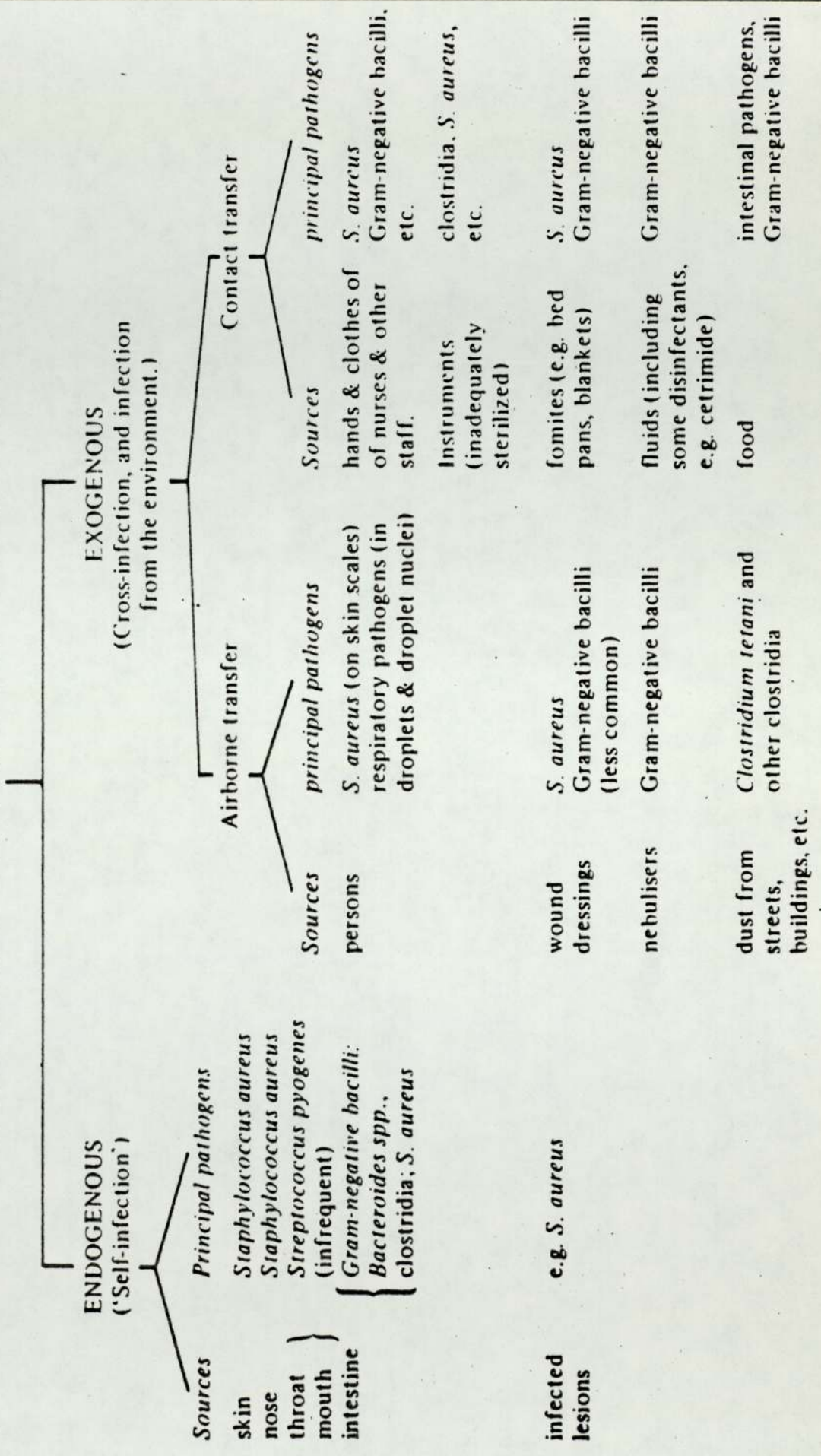
St. Bartholomew Hospital, patients often stayed a considerable amount of time in hospital before operation, giving them adequate opportunities to acquire hospital strains. Even in the Torbay study patients who carried a staphylococci of the 80 group (which are known to cause epidemics) had a higher wound sepsis rate (13.2%) than carriers of other types of staphylococci (2.6%), (* Significant, $P < 0.01$).

Most of the studies covering this concept, failed to recognise the significance of other patient parameters. For instance, factors such as age and type of operation, influence the wound infection rate, and length of stay in hospital influences the nasal carriage rate. Before making conclusions on any association between nasal carriage and wound infection, the influence of these other factors on the two groups in the study, must be considered. Although MOORE and GARDNER (65) considered the influence of these factors in their study, a firm conclusion cannot be drawn, because the patients in their study stayed only a short time in hospital prior to the operation.

This association between nasal carriage and wound infection has been accepted unreservedly by many researchers. The implications were that if the nasal carriage rate of the patient population can be reduced, this will result in a lower post-operative wound infection rate. This led to the introduction of nasal prophylaxis and changes in ward practices, structures and facilities aimed at reducing the nasal carriage (which are discussed in detail in Section 2.5). BRUUN (45, S=2557) reported a significant reduction in nasal carriage rate and wound infection rate, following the introduction of a preventive program, which mainly included nasal prophylaxis.

FIGURE 1

HOSPITAL INFECTION: SOURCES, ROUTES AND PRINCIPAL PATHOGENS



A flurry of studies aimed at reducing nasal carriage rate followed, WILLIAMS et al. (10). Some of these studies produced spurious results, due to their failure in recognising the significance of other factors on nasal carriage. For example, SHOOTER et. al.(73) reported that nasal carriage rate can be reduced by segregating the pre and post-operative patients. They concluded that nasal colonisation of tetracycline-resistant strains was more than twice as common in the post-operative division of the ward compared with the pre-operative side. In making this conclusion they did not consider the effect of the length of stay on nasal carriage. It is more likely that the reduction in carriage rate resulted from the shorter length of stay of patients in the pre-operative section, and the fact that the post-operative wounds disperse more staphylococci.

2.4 Source of Infection (Ward Against Theatre)

In the practical handbook on the Control of Hospital Infection, LOWBURY et al.(74) defines the source of hospital infection as endogenous and exogenous (see Fig.I) The controversy is over whether ward cross-infection or operating theatre infection is predominant in post-operative wound infections. This may depend to some extent on the type of surgery, since infections acquired in the ward are usually in drained or leaking wounds. One would hope that with the advent of modern ventilation systems for operating theatres and the application of aseptic practices, the incidence of wound infections caused by airborne transfer in the operating theatre to be minimal. However, AYLIFFE and COLLINS (39) and WALTER et al.(40) have demonstrated post-operative

wound infection related to disseminating carriers in the vicinity of the operating table. McNEILL et al.(75) reported a correlation between the phage type of staphylococci found in the region of the operating field and post-operative infected wounds. Many others (35,41,42,49,76) failed to demonstrate a correlation between strains isolated from the air in the theatre and those isolated from post-operative infections.

A large number of studies have been carried out to investigate the significance of ward air on post-operative wound infection. GILLESPIE et al.(II), ROUNTREE et al (38) and SHOOTER et al.(37) reported in the late fifties and early sixties, that ward cross infection plays the predominant role in hospital infections. Recent studies by THOMSEN, LARSEN and JEPSEN (42,76) confirmed this concept by demonstrating significant correlations between phage types in the ward air and in the infected wounds. SELWYN et al. (77) experienced a similar correlation between environmental level of staphylococci and wound sepsis rate. An increase in ward settle-plate counts which preceded an outbreak of an epidemic in a burns unit, as reported by HAMBRAEUS (78, S=69), adds further weight to the concept of ward cross infection being the predominant cause. However, this study may not be fully representative due to the small sample size and the speciality of the patient category. Others(II,45) have been able to reduce the wound infection rate by introducing methods to reduce the level of ward contamination, such as, nasal prophylaxis and disinfection of blankets and pillows. Further, the association between the length of pre-operative stay in hospital and wound infection as discussed in Section 2.2, indirectly

emphasise the importance of ward contamination as a source of wound infection.

The ward or theatre controversy can be looked ^{at} in a different sense, using the actual time of clinical onset of infection as an index. WILLIAMS et al. (28, S=2555) observed sepsis within five days of operation only in 7 per cent of the cases, between the sixth and tenth day in 38 per cent of the cases and in the remaining 55 per cent sepsis was not observed until the eleventh day. Subsequent studies by BRUUN (45), COHEN et al. (8), McLEOD (5) and FARRER and McLEOD (79, S=319) confirm that the mean clinical onset of post-operative wound infection is usually between the sixth and the tenth post-operative day. In taking this interesting observation further, FARRER and McLEOD point out that staphylococci infections have a short incubation period of about one to two days, which is much less than the mean clinical onset experienced above. They describe an experiment in human volunteers, where the presence of a foreign body reaction in the form of sutures resulted in a dramatic reduction of the minimum inoculum required to produce pus, and that stitch abscesses occurred from 24 to 48 hours following the introduction into the skin of sutures injected with 3×10^4 cocci.

When these observations are interpreted literally, it suggests that if the wounds are infected in the operating theatre, the clinical onset of infection must occur within five days. Hence, since the mean (and the mode) onset was experienced between the sixth and the tenth day, the majority of infections must have been acquired post-operatively in the ward environment. However, there are some uncertainties involved in assessing the onset of infection. WILLIAMS

et al.(52) and RESNEKOV (80) have reported instances of very deep sepsis beneath perfectly healed parietal wounds but in which pyrexia and the other signs of sepsis have not appeared until the tenth or fourteenth day. It is likely that the appearance of infection after an operation may depend on the extent of the initial inoculum. Therefore the onset of infection is not a very accurate indicator of the source of infection. Also, the validity of the FARRER and McLEOD (79) experiment is somewhat doubtful because the cocci were applied rather artificially.

Further, if we consider that infections are acquired in the ward post-operatively, how can we explain the influence of factors such as type of operation, length of incision, length of operation, host factors, drainage and late positioning of operation, on wound infection, as discussed in Section 2.2. It may be that although the exposure of the patient is about 10 to 20 times greater in the ward compared with the theatre, the patient is more susceptible to infection during operation. This susceptibility is a function of the factors related to operations as discussed earlier. Finally, it must be stated here that hospitals vary in the importance of ward or theatre infection; hence both groups studying the source of hospital infection may be correct in assessing their own environment.

2.5 The Influence of Environmental Factors

Since WILLIAMS et al.(10) demonstrated the association between nasal carriage of resistant strains and subsequent wound infection, much effort has been directed towards reducing the nasal carriage rate. These efforts were expedited

since the emergence of the ward environment as the predominant source of post-operative staphylococci wound infection. The work was directed towards identifying sources of contamination in the ward, and devising methods to reduce both the level of environmental contamination and the nasal carriage rate (there is a relationship between the two, as discussed in Section 2.I).

The role of bed clothing as a source of ward contamination has been studied (14,81). Only a temporary reduction in daily settle-plate counts were noted after treating the bedding with detergent-antiseptics (14), and the practice of disinfecting blankets after use by each patient did not significantly reduce general bacterial or staphylococcal counts on exposed culture plates and also, the blankets were heavily re-contaminated after only a few days (81). The relative importance of various floor cleaning methods have been studied by many researchers (20,82,83,84). AYLIFFE et al.(83,85) in their studies on ward floors and surfaces as reservoirs of hospital infection, concluded that regular use of disinfectants in cleaning a ward floor does not reduce the equilibrium level of bacteria on the floor. The modern practice of carpeting ward floors have been compared with conventional floor covering and no difference in ward contamination was observed (86,87,88). Routine washing of isolation room wall does not reduce the level of contamination (16), and walls are the least contaminated surfaces in wards (15,83). Other common sources of bacterial contamination of wards, are the linen and laundry chutes (13), but the introduction of exhaust ventilation through proper design can reduce the risk of contamination (12). (It must be stated here that most of

the studies quoted in this paragraph have not considered the effect of these factors on actual wound infection or nasal carriage rates).

The potential of ultra violet (UV) irradiation in reducing bacterial counts in air, has been applied to the problem of infection control. AYLIFFE et al.(25, S=1674) were able to demonstrate a reduction in bacterial transfer from a cubicle to a corridor, by introducing ultra-violet barriers. The counts of total organisms and Staph.aureus on the floor of the airlock were significantly lower when irradiated with UV lights. However, it is not possible to derive the impact of UV irradiation on nasal carriage rate, from this study. The National Research Council (41,89) conducted a large controlled investigation to study the effect of UV irradiation in operating theatres. They concluded that although the introduction of a UV irradiation system reduced the number of bacteria in the operating theatre by more than half, the reduction in post-operative wound infection was only limited to refined-clean wounds. When this is viewed with the increase in infection in other categories of wounds such as clean-contaminated, contaminated and dirty wounds (in the UV treated group), the indications are that many other factors influence the incidence of wound infection to a greater degree than UV irradiation.

Outbreaks of infections in wards are normally arrested by vigorous application of aseptic principles and selective isolation techniques. In severe outbreaks, the practice of closing a ward and reopening after extensive cleaning, has reduced the rate of infections (90, S=2000). Although the infection rate can be reduced by this method of inducing

changes in the ward environment by closing and re-opening the ward, it may only be cost-effective in severe outbreaks of infection. On the other hand, there is some doubt on the effectiveness of changed environments in reducing infections. WORMALD (91, S=528) did not experience a reduction in staphylococcal contamination, when a pre-war burns unit was transferred to a purpose built building. However, the implication of this study cannot be generalised because, (a) the patients were all burn patients whose susceptibility was much higher than the normal patient and (b) the study in the old unit was carried out between 1963-64 and the study in the new unit between 1967-69, time periods too far apart to make effective comparisons between infection rates, particularly at a time when the role of staphylococcal infections was changing.

BOWIE et al. (92) in discussing the concept of controlling hospital infection by design, states that when isolation is effected by design, the environmental bacterial contamination rate is reduced by a factor of 35-75. There are many methods of introducing the practice of isolation, varying from single room isolation away from the main ward, to isolation by partial sub-division. The major considerations in selecting particular methods of isolation are, the cost involved in introducing the isolation method and the relative effectiveness of the isolation method in reducing hospital infection. As far as the cost is concerned, total isolation is the most expensive and partial sub-division, the least. WILLIAMS et al. (28,93) in comparing infection rates between patients in isolation wards and in non-isolation wards, found that isolation ward patients(2.7%) had a lower infection rate than other patients(6.1%). Further, they observed

that patients in the isolation wards became nasal carriers of tetracycline-resistant staphylococci more slowly than those in the non-isolation wards. JEPSEN et al. (76) found significantly fewer staphylococcal wound infections among patients placed in cubicles than among those in the open ward. In their investigation in a cubicle ward PARKER et al. (48, S=446) experienced a considerably lower nasal carriage rate of resistant strains, but no change in the nasal carriage of sensitive or penicillin-resistant strains. A 55 per cent reduction in post-operative wound infection following the transfer of a surgical unit from a "Nightingale" type multi-bed ward to a new "race-track" type ward with 40 per cent of its beds in single rooms and with controlled ventilation, was reported by SMYLIE et al. (94, S=3880) and DAVIDSON et al. (95). The significance of this environmental change was further confirmed from a subsequent multiple regression analysis (DAVIDSON et al. 96). LIDWELL et al. (24) in a study where patients were nursed in 4-bed rooms separated from a common corridor only by a low dividing wall, suggested that sub-division of this type does not hinder the spread of nasal colonisation compared with open "Nightingale" type wards.

Although the overall benefits derived from complete isolation have been accepted more or less universally, the relative effectiveness of different methods of isolation is full of controversy. This may be due mainly to the uncontrolled nature of most of the investigations. The majority of studies on particular isolation methods have been carried out without first establishing a relevant "control group". In making conclusions on the effectiveness of the isolation

method under study, comparisons were often made between infection rates in the current study and the rate of a different method reported by others. Such comparisons would induce an obvious bias into the conclusions, as the patient groups in the two studies may not be comparable in patient parameters and other multifarious ward parameters surrounding them. One of the major objectives of isolation is to reduce the degree of cross-transfer of air between patients. This can be achieved equally well by introducing proper ventilation systems. Early application of ventilation systems were mainly limited to operating theatres, where considerable reductions in post-operative wound infections have been obtained through proper selection of ventilation systems (97). Although there are cost constraints associated with the possible universal introduction of ventilation systems to hospital wards, certain experimental and special wards have been fitted with ventilation systems. Investigations in such wards can be used to measure the effectiveness of different ventilation systems. AYLIFFE et al. (25, S=1674) reported a significantly lower mean settle-plate counts in recirculator-ventilated cubicles than in the open ward and in a window-ventilated side room. They further reported that, in a plenum-ventilated cubicle, the mean settle-plate counts were significantly lower than in the other three areas. STEINGOLD et al. (98) were able to obtain a considerable reduction in bacterial air contamination and cross-infection, with the introduction of a new ventilation system in a ward. Contrary to these inferences, mechanical ventilation has not been effective in controlling the spread of an epidemic strain in a ward (LIDWELL et al. 64). A somewhat similar

observation has been made by WHYTE et al.(99) in their study comparing infection and nasal carriage rates between mechanically ventilated sub-divided wards and open wards with natural ventilation. They failed to obtain any evidence that the risk of post-operative wound sepsis or of acquired staphylococcal sepsis, was lower in the ventilated sub-divided wards. However, the nasal acquisition rate was lower in the ventilated wards among patients who stayed two weeks or less in the ward; but there was no difference in the acquisition rates of resistant strains.

A closer examination of bacterial transfer between patients in ventilated areas is made possible with the use of particle tracers. Using this method LIDWELL et al. (100), LIDWELL (101), HAMBRAEUS and SANDERSON (102) and FOORD and LIDWELL (26) were all able to demonstrate a reduction in particle transfer resulting from the introduction of ventilation systems. All these studies however, did not find a reduction in cross-infection which could be attributed to the benefits derived from the ventilation system. The failure of these studies together with the study by WHYTE et al.(99), (where the experimental ward had both the benefits of mechanical ventilation and sub-division) to reduce the infection rate, indicates that many other factors may override ventilation and isolation in determining the incidence of post-operative wound sepsis. Even if there were some benefits derived from the introduction of ventilation and isolation systems, it is difficult to know whether the original capital expenditure on the new system can be justified. From the varieties of aseptic practices experienced by AYLIFFE et al.(103), it is probable that cost benefit analyses

were often not carried out before introducing these changes.

2.6 Patient Parameters

Patients' age and sex are parameters unique to individual patients, independent from the patient's clinical condition or the type of operation to be performed. Two other parameters, length of stay in hospital which is a measure of the degree of exposure to the hospital environment, and antibiotic therapy (as prophylaxis) can also broadly be considered as independent patient parameters. The distribution of these patient parameters in a given patient community, may determine the nasal carriage rate and the wound infection rate, quite independently. In other words, these patient parameters can be incorporated into a measure of the susceptibility of the patients.

2.6.I Age of Patient

BRUUN (45) reported an increase in nasal carriage rate of all strains of staphylococci as well as multi-resistant strains, with increasing patient age in the three age groups, under 40, between 40 - 60 and over 60. However, studies by POLAKOFF et al (104, S=361) on surgical patients and NOBLE et al.(105, S=839) on a random sample selected from a normal population outside hospital, found that the nasal carriage rate decreased with advancing age. But these two studies concentrated only on the overall nasal carriage rate and not on the carriage rate of resistant strains. It is probable that with advancing age, hospitalised patients become carriers of resistant strains by losing sensitive or penicillin-resistant strains.

The influence of age on wound infection itself is much

more evident. CRUSE and FOORD (115, S=23649) in one of the largest prospective studies on wound infection, found age of patient to be one of the major determinants of the risk of post-operative infection. In BRUUN's study (45), wound infection rate also increased with age in the said age groups. COWLING (46, S=4898) reported a significantly higher wound infection rate among patients 40 years and over. The general significance of age on wound infection has been recognised by many others (41,67,106). A more specific relationship, where infection rate was lowest in the neonatal period fluctuating from 1 month through 19 years, and then increasing from 20 through 99 years has been reported by FARRER and McLEOD (79, S=319). Similar idiomatic relationships, where the sepsis rate increases progressively during the first 5 decades, then remaining steady and finally increasing in the ninth decade (8); and the lowest infection rate occurring in the 15 to 24 age group and increasing upto twice that rate in the 65 to 74 age group (107) have been reported.

ALTEMEIER (9) states that "two-thirds of the patients with hospital acquired septicamea, both gram-negative and gram-positive, fall within the two age groups, the new born and the elderly. Since the frontiers of surgery during the past 15 years have extended principally within the new born and elderly groups, the problem of post-operative hospital acquired infections has been accentuated". This statement may infer that the complexity of operations performed in the extreme age groups is responsible for the higher infection rate, and not the natural effect of age. COWLING (46) in fact attributes the difference in infection rates in his under 40 and over 40 groups to differences in the complexity

of operations in the two groups. However, in the more controlled N.R.C. (41) study, after correcting the wound infection rates for any bias that may arise from ^{wound} classification, duration of operation, pre-operative stay, urgency of operation, diabetes, steroid therapy, obesity and malnutrition, the infection rate still increased with age. There is only one large study (108, S=9447) that has failed to establish the significance of age on wound infection. The implication of this study cannot be considered seriously because it was carried out over a period of 21 years, in which time so many other relevant factors may have undergone changes.

Although the relationship between age and wound infection and nasal carriage has been established, the underlying reason for the relationship is not quite certain. ELMAN(47) states that the resistance of the older individual to various infections is in general much lower than it is in the younger individual. DU NOUY (109) observed that the efficacy of the repair process of wounds in the elderly deteriorates generally. On a different note, BAUMGARTNER (110) states that the antibody production is deficient among the elderly. These explanations together with the complexity of certain operations in the elderly may result in the higher infection rates that have been observed in the older patients.

2.6.2 Sex of Patient

A lower nasal carriage rate of all strains as well as resistant strains among female patients was reported by BRUUN (45). In carriers of tetracycline-resistant staphylococci strains, LIDWELL et al.(24) reported a lower carriage rate among female patients. A lower post-operative wound infection rate among female patients has been reported by

P.H.L.S.(3), N.R.C.(4I), FARRER and McLEOD (79, S=3I9), and LIDWELL et al.(63, S=7I4). Also when purulent wounds were studied by JEPSEN et al.(66, S=845), the female patients had a lower infection rate.

The rationale behind the lower nasal carriage and wound infection rates among female patients is difficult to explain. BETHUNE et al.(II7) reported that men disseminate more staphylococci than females, and AYLIFFE et al.(25) experienced a significantly lower mean settle-plate count when a ward was occupied by female patients. FEKETY et al. (II2) found that new born males are more susceptible to staphylococci skin infections than females. These three studies may give some indication as to why the females have a lower nasal carriage rate. They however do not give any explanation regarding the lower wound infection rate. The difference in wound infection rates may be due to differences in the types of operations performed on males and females. The N.R.C. study (4I) attributes the difference to the higher proportion of non-clean wounds among males, but even after the figures were corrected for this difference, males still manifested a slightly higher sepsis rate. This concept of the greater proportion of contaminated wounds among males resulting in higher infection rates, has also been supported by the study carried out by BRUUN (45).

2.6.3 Antibiotic prophylaxis

Normally antibiotics are administered to pre-operative patients as a prophylactic measure to reduce the risk of endogenous infections. These may be administered topically, orally or systemically. The effect of topical application is to destroy infecting organisms in the wound, oral application

reduces the bacterial flora in the colon and systemic application kills the bacteria during operation. Each method of application may induce many problems or side effects. The topical and oral applications may induce antibiotic-resistant strains of staphylococci and systemic application may induce certain drug problems.

The higher risk of nasal carriage and wound infection associated with the administration of antibiotics, is well documented. PARKER et al.(48, S=446) reported that patients who received antibiotics acquired multiple-resistant strains in the nose, two and a half times more rapidly than those who did not. LIDWELL et al.(24) made a similar observation, where patients who had received antibiotics had a high nasal carriage rate of tetracycline-resistant strains. When examined closer they found that patients receiving penicillin had a tetracycline-resistant carriage rate 2.6 times greater than those without antibiotics, and those receiving other antibiotics had a carrier rate 3.9 times greater than those who did not receive antibiotics. EDMUNDS (55, S=2863) noted a reduction in the acquisition of sensitive strains when antibiotics were given, and he has listed the association between different types of staphylococci strains and the different types of antibiotics administered.

The above studies specify the relationship between antibiotic use and nasal carriage rate. Prophylactic antibiotics are also known to cause a greater degree of post-operative wound infection. COWLING (46) reported a higher post-operative wound infection rate (7.1%) among patients who received antibiotic prophylactically, when compared with those who did not receive antibiotics (2%). COHEN et al.(8) noticed

the presence of more antibiotic-resistant strains of staphylococci in post-operative wounds when antibiotics were administered.

It is probable that antibiotics are administered mainly to patients who undergo complicated surgery, and hence the higher infection rate reported. Further it is also probable that antibiotics when administered, reduce only antibiotic sensitive strains, leaving behind all resistant strains. If we interpret the association between antibiotic prophylaxis and wound infection literally, then it is better to stop the practice of antibiotic prophylaxis completely. However, such a simplistic view ignores the proven benefits of chemotherapy. KEIGHLEY (7I) has reported that in certain types of surgery, short-term antibiotic prophylaxis is effective in reducing the incidence of post-operative wound infection. It may be that although a higher infection rate is observed in patients who received antibiotics (greater numbers of whom may be high operative risk patients), the majority of high-risk patients benefit from the prophylactic measures, by way of a reduction in expected (in the absence of prophylaxis) infection rates and the complexity of resulting infections. The explanation that antibiotics are administered to a greater number of high-risk patients, does not however, explain the higher nasal carriage of resistant strains observed among these patients. It is again probable that antibiotics produce a reduction in the carriage of sensitive strains, resulting in an increase in the remaining resistant strains.

2.6.4 Length of Stay in Hospital

Patients' exposure to micro-organisms in the ward environment is increased with increasing length of stay

in hospital. This phenomenon may be reflected in the nasal carriage rate, and if so, the nasal carriage can be used as a measure of exposure. Many studies (24,28,45,55,63,64,99,104,113) have reported an increase in the nasal carriage of tetracycline or multi-resistant strains of staphylococci, with increases in length of stay in hospital. The carriage of sensitive or all strains of staphylococci reduces with increasing length of stay (45,48,63,99,113), which implies that patients tend to lose sensitive strains and acquire more resistant strains with increasing length of stay in hospital. Instances where no overall increase in carriage rate with length of stay have been observed (WILLIAMS et al.93,S=606); these studies tended to quote carriage rates for all strains of staphylococci. In such studies it may be probable that the increase in the carriage rate of resistant strains is equal to the reduction in the carriage rate of sensitive strains, thus making the overall carriage rate to be constant over the period of time.

2.7 Application of Multiple Regression

When studies are carried out to investigate the significance of certain factors on wound infection (or nasal carriage), it is often difficult to attribute with confidence a change in the observed infection rate to any one of the related factors. It is generally through hind sight and not purely on scientific analysis that we make conclusions on the significance of certain parameters on wound infection and nasal carriage. Ideally, we must carry out studies on one variable at a time, keeping all other variables constant during the study. However, due to many practical difficulties

such controlled experiments cannot be conducted. Multiple regression analysis is a technique that can be used to overcome these practical difficulties. Once the independent variables (e.g. age, type of operation) in an experiment are identified, multiple regression technique would evaluate the relative importance of each variable on the dependent variable (e.g. infection rate or nasal carriage rate). The principle of multiple regression is described in most of the fundamental books of statistical theory.

LIDWELL (44) applied multiple regression analysis to the results of the P.H.L.S. survey (4) and established the significance of various operative procedures and patient factors on the risk of post-operative wound infection. He concluded that age over 60, male sex, long duration of operation, incision over 6 inches long, the insertion of a drain and certain types of operations, to be associated with a high risk of infection. Type of operation, wound contamination, insertion of a drain, nasal carrier state of resistant strains, duration of operation, and pre-operative hospitalisation resulted as significant factors on wound infection in a multiple regression analysis carried out by BRUUN (45). DAVIDSON et al. (96, S=1000) applied the multiple regression technique when a change in the ward environment was made, and found that the ward environment was a significant factor in wound infection, together with the type of wound (clean or dirty), the presence of bacteria in the wound at the end of the operation, age of patient, and the duration of operation. A subsequent study by LIDWELL et al. (24) used multiple regression analysis on factors that might effect the nasal acquisition rate, and found that age and antibiotic treatment to be the primary factors.

CHAPTER 3

IMPLICATIONS

3.I Critique of the Literature Survey

In the actual literature survey somewhere around 450 original articles were referenced, but only a selection are quoted in Chapter 2. Some of the reported investigations were based on extremely obscure experimental methodologies, which were responsible for much of the confusions surrounding this field of study. Experiments were often uncontrolled, based on small samples, and results reported even without the application of simple statistical tests to verify the validity of the observations. Some have even formed conclusions before carrying out a test, and for obvious reasons the tests confirmed their instinctive beliefs, quite contrary to the basics of scientific investigations. Nevertheless, non-controlled studies have provided useful evidence on the sources of infection and modes of spread. The majority did not take into account the fact that there may be other factors (apart from the one being tested) which may influence wound infection. A good example is the study quoted earlier (73), where it was demonstrated that nasal carriage in pre-operative patients can be reduced by segregating the pre and post-operative patients. On the surface, it appears to be a major genuine revelation; but when one considers the fact that post-operative patients stay longer in hospital than pre-operative patients, and that post-operative wounds disperse more staphylococci, their conclusions on the effectiveness of segregation seem to be somewhat dubious.

The interpretation of the literature is made more

difficult by the different terminologies that are used by different researchers. The term "nasal carriage rate" has been used by some to refer to the carriage of all strains of staphylococci, whereas others have used the term referring to the carriage of antibiotic resistant strains only. Further, nasal carriage rates reported in certain studies do not indicate whether they are carriage rates on admission or on a later day. Therefore, it appears that there is a great need to adhere to a standard terminology in this field of study. When reporting nasal carriage rates, the day (related to the day of admission) the carriage rate was studied, and the antibiotic sensitivity pattern of the strains must be mentioned. The practice of reporting wound infection and nasal carriage rates as a percentage, without any indication of the number of patients in the group must be prevented. The total number of patients in the study as well as in the groups in the analysis, together with the year and the period of study should be mentioned in future reports.

3.2 General Conclusions of the Literature Survey

The literature survey did not adequately resolve the many controversies surrounding this area of study. However, certain general conclusions can be derived from the literature discussed in Chapter 2. Hospitalised patients acquire antibiotic resistant strains of staphylococci in their noses. The reason why some patients become carriers and some do not, under similar environmental conditions is not too clear. It is probable that variations in individual resistant patterns are related to the nasal carriage of staphylococci. The relationship between the number of staphylococci in the ward air

and the risk of nasal carriage is a difficult one to quantify. The experience of LIDWELL et al. (25,63,64) that a reduction in aerial contamination results in a much less than proportionate reduction in nasal carriage, seems to be a likely explanation.

Whether there is a significant association between nasal carriage of resistant staphylococci and wound infection, is difficult to reject or accept in view of the literature cited. Most of the studies quoted were based on relatively small samples, and there was some confusion over the terminology used in different studies. None of the studies have made any attempt to rectify the observed carriage rates against any bias, that may have been induced from other factors such as age and length of stay. Also, in some of the studies it was not clear whether nasal carriage was observed before or after the onset of wound infection. If the carriage rates reported are those observed after the acquisition of wound infection, then the reported relationship would obviously be a spurious one. With so much uncertainty and variations in the experimental methodology, a true comparison cannot be made easily. However, nasal carriage in itself reflects two characteristics which are somewhat related to the risk of wound infection. Firstly, nasal carriage of resistant staphylococci is a measure of the patient's exposure to the ward environment as well as a measure of the level of ward contamination. Secondly, nasal carriage rate is an indication of the susceptibility of the patient. Therefore, when the implications of these two factors on wound infection are considered, nasal carriage of resistant staphylococci can be used as a measure of the risk of post-operative staphylococci

cross-infection (and to some extent on the risk of wound infection).

The factors associated with the risk of post-operative infection are more apparent. There is hardly any confusion over the significance of factors such as type of operation, contamination, drainage and other operative procedures on the incidence of wound infection. Certain patient parameters such as age, sex and antibiotic therapy, are also associated with the risk of infection. What is lacking is the emphasis on the relative importance of these operative and patient parameters, on the level of wound infection. The application of the multiple regression analysis has made some headway in this area.

The literature cited does not make it any easier to resolve the problem on the source of post-operative wound infection. Here too, doubtful experimental methodology and the use of confusing terminology have made the problem even more controversial. As the significance of both the ward environment as well as the theatre environment has been well documented, both these can be considered as sources of post-operative wound infection. If one accepts 6 - 10 days as the mean onset of post-operative infection (5,8,28,45,79), and the incubation period of staphylococci infection to be less than 48 hours, then it is highly probable that the majority of infections are ward infections. However, it must be recognised that the onset of infection is not a good indicator of the source of infection, particularly in instances of very deep sepsis. Therefore, both the ward and theatre environments are considered as sources of hospital infection; and recent experience (2,71) suggests that endogenous

infections are becoming much more frequent. If only staphylococcal wound infections are considered, BRUUN (45) in 1970 pointed out that about three-quarters of such infections are acquired in the ward. Since, multiple antibiotic-resistant staphylococci are acquired in wards, the use of the nasal carriage rate as an indicator of ward cross infection can be justified.

Nearly all the possible ward sites that may be contaminated have been studied. Many practices were introduced to reduce the level of aerial contamination in wards. Most notable ones are the introduction of UV barriers, isolation methods and mechanical ventilation. The impact of these practices on the reduction in aerial contamination has been demonstrated without any doubts. What is lacking however, are studies examining the effect of these on nasal carriage and wound infection. A mere relative reduction in aerial contamination is fruitless if it does not result in a reduction in nasal carriage and wound infection. It is probable that the airborne route is less significant as a route of cross infection. Also, the LIDWELL et al.(24,63,64) concept of the quantitative relationship between the level of aerial contamination and nasal carriage, may be appropriate in this area. This concept may also have implications on the cost-effectiveness of introducing these practices. Proper cost benefit studies must be carried out before implementing or introducing changed environmental factors into wards and theatres.

The significance of patient parameters on wound infection and nasal carriage has been well documented. The age of patient appears to be the most prominent parameter.

Although it has been argued that the elderly are more likely to acquire infections because they undergo complicated surgery, the type of surgery in itself can be considered as a function of patient's age. Further, the type of operation cannot influence the relationship between nasal carriage and age of patient. Therefore, the effect of age on wound infection and nasal carriage is independent of other factors. The relationship between length of stay in hospital and nasal carriage of resistant strains, is an absolute one; which can be used as a measure of the exposure to the ward environment, and also to some extent, as a measure of the patient's susceptibility to infection. There is some doubt over the significance of sex and antibiotic therapy on nasal carriage and wound infection. On antibiotic therapy it is difficult to distinguish the difference between cause and effect; whether the antibiotics were administered to patients with a higher risk of infection or whether the antibiotic treatment resulted in the higher rate of infection. There is no such bias in the relationship between antibiotic use and nasal carriage, and it is probable that sensitive strains are suppressed by the use of antibiotics resulting in a higher carriage rate of resistant strains. The lower wound infection rate among females may be a result of the less complicated surgery they undergo, and their lower nasal carriage rate. The reason for the lower nasal carriage rate among females is rather unknown.

Multiple regression analysis is useful in determining the relative significance of various factors on nasal carriage and wound infection. However, if this technique is applied indiscriminately to studies with small sample sizes to test

the significance of a large number of related factors, the emergence of spurious relative significances would be inevitable. Therefore it is better to limit this technique to large surveys.

3.3. Cross Sectional Surveys

The aetiology of staphylococci wound infections can be studied either using a continuous survey or a cross-sectional (or prevalence) survey. The more commonly used continuous surveillance method is useful in keeping track of fluctuations of endemic infections and demonstrating the occurrence of outbreaks of infection in individual hospitals. This method of surveillance however, has limited use in comparing infection rates of different hospitals. A meaningful comparison of infection rates between hospitals cannot be achieved due to the variations in definitions and methodologies in such studies. In cross-sectional (or prevalence) surveys a single team visits each hospital for a period of days or weeks, and since the same criteria is used by the team in judging infections, this is an appropriate method for inter-hospital comparisons. Further, when cross-sectional surveys are carried out, it is possible to obtain a large sample of patients in a short period of time, which would not be practical in continuous surveillances. Also, the sample obtained would be relatively free from any bias arising from the changing nature of staphylococci infections over the years.

Although EIKHOFF et al.(II4) have reported the appropriateness of using cross-sectional surveys for inter-hospital comparisons of infection rates, there are certain inconsistencies associated with such comparisons. Ideally, when

comparisons are made between hospitals, apart from factor(s) under study, the hospitals must be comparable in the susceptibility of the patient populations and in the overall ward practices and structures. For example, if comparisons are made between a general hospital and a specialist unit such as a skin hospital, there would be obvious differences in infection rates. Similarly, if a hospital which has a greater number of cubicled wards is compared with a hospital with a large number of open wards, there would again be a bias due to the differences in sub-division. However, if the comparisons are based on a very large survey, the differences in ward practices and structures may not be so important in comparing infection rates. In such cases, the differences in susceptibility of the two patient populations must be corrected, using some index defining the patient parameters.

3.3.1 The Birmingham Survey

With the intention of clarifying some of the uncertainties in this area, a large cross sectional survey was carried out between 1967 and 1973 by the Infection Research Laboratory, Dudley Road Hospital, Birmingham (4,51). The survey covered hospitals in the Birmingham region, where 38 hospitals were visited and repeat surveys made in 12 hospitals. Over 12000 patient records were collected from about 520 different wards. Most of those visited were general hospitals, both large and small, including hospitals in the teaching group; a number of small specialised units were also visited, including neurosurgical, thoracic, ophthalmic, orthopaedic, accident, skin and ear, nose and throat hospitals.

3.3.2 Technique of Survey

Before the first survey of a hospital, a preliminary

visit was made to discuss details of the study with senior members of the medical, nursing and administrative staff. Agreement for the survey was obtained from the Medical Staff Committee. In the survey, a team consisting of the Research Nurse and a Consultant Microbiologist or a Technician visited the wards, one ward per morning, and collected data which were entered on specially designed forms (Appendix A). Information about a patient's age, sex, date of admission, diagnosis, date of operation, wound sepsis or other infection and antibiotic treatment at time of visit, were recorded on one form, and details of ward structure and aseptic and domestic practices were recorded on other forms. The nurse or microbiologist attended the routine dressing of wounds and recorded the presence or absence of sepsis by criteria described below. Information on all acquired infections and on antibiotic treatment was obtained from case-notes, ward records and temperature charts and from discussion with the ward sisters. Criteria for infections other than those of wounds were similar to those used in a study by the Centre for Disease Control, Atlanta (GARNER et al. 1966). Nose swabs were taken from all patients and staff in the ward at the time of the visit and from all infected operation wounds or other open lesions. Many samples were taken from environmental sites, especially 'wet' areas or equipment.

The information on the forms was transferred initially to punched cards by the Regional Health Authority. After validation they were transferred to tape, and the analysis carried out using the University of Aston Computer ICL 1904S.

3.3.3 Bacteriological Methods

Wound and lesion swabs were cultured aerobically on

on blood agar and Mac-Conkey plates. Nose swabs were cultured on nutrient agar containing 1 per cent horse serum, diphenolphthalein diphosphate for recognition of presumptive Staph.aureus (BARBER & KUPER, 127) and tetracycline (10 μ g /ml). Tetracycline was not included in plates used for culturing nose swabs from maternity units, where cross-infection commonly occurs with antibiotic sensitive strains or strains resistant to penicillin only, probably because the adult patients were young females staying in hospital for a short time only. Swabs taken from a number of environmental sites were cultured on blood agar, MacConkey's medium, improved cetrimide agar (BROWN & LOWBURY, 128) and in nutrient broth. Some sterile fluids and disinfectants were also examined for possible contamination. Antibiotic sensitivity tests were made by a ditch-plate, or disk diffusion method, on strains of Staph.aureus isolated from noses and lesions, and on gram-negative bacilli isolated from lesions. Most strains of Staph.aureus isolated from wounds or lesions were phage typed (BLAIR & WILLIAMS, 129).

3.3.4 Definitions (Survey)

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, 41) 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. operations on the stomach, gall-bladder and bladder.

Contaminated:

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

The list of operations classified as clean, clean-contaminated and contaminated, are given in Appendix B.I.

3.4. The Present Work

The major implication of the literature survey was the need to establish some form of a susceptibility index, based on the significance of various patient parameters. Such an index can be used in future studies to adjust infection and nasal carriage rates for any bias derived from the incomparability of the patient populations under study. Hence, the primary objective of this study was to formulate such an index from the analysis of the survey data. Before the formulation of an index (a model) the significant patient parameters must first be isolated. The significance of age on wound infection and nasal carriage, and length of stay on nasal carriage, is evident from the literature survey. These two parameters can therefore be incorporated into an individual or a joint model without much doubt. The significance of sex and antibiotic usage is not so clearly visible in the literature survey. Their significance must be established before incorporating them to a model. On modelling itself, the most commonly used method of multiple regression analysis

will be employed in the first instance. Later, attempts are made to formulate a similar model using mathematical techniques.

The survey also had certain other objectives, when it was originally designed. In this area, primarily it was intended to offer indications of the changing nature of the problem of wound infection. In recent times such large cross-sectional surveys have not been reported by others, and hence, the results of this survey should indicate the current trend. Cross-sectional surveys are particularly useful and accurate in determining the current trend. Secondly, the survey was designed to investigate the significance of operative parameters such as type of operation, wound classification, wound drainage, pre-operative stay and associated factors. These two aspects of the objectives are considered in this study prior to the investigation of patient parameters. It must be recognised at this stage that it is not possible to test the association between nasal carriage and wound infection from this study, because cross-sectional studies do not indicate whether the nasal carriage was noticed before or after acquiring a wound infection.

A further objective of the survey was the examination of the significance of ward parameters on nasal carriage and wound infection. Over 200 ward parameters were recorded during the survey and from the design of the survey, it is possible to relate ward parameters to the rate of infection (or carriage) of the patient groups which were associated with those ward parameters. A crude comparison of infection or carriage rates would give a biased result, due to differences in patient parameters. This bias, however, can be avoided if a susceptibility index is used to correct the results.

The multiple regression model will be used to correct these results before investigating the significance of ward parameters. Even after correcting these results, much weight cannot be attached to these significances, because there are many interactions occurring when cross-sectional surveys are analysed. This correction is more than anything, used as an example of how the model describing patient parameters can be used in a practical sense. Ideally, the model should mainly be used in continuous surveys and other investigations in this area. Cross-sectional surveys are exceptions in this sense, because of the extremely large number of variables and interactions; even after correcting the results using the model, some bias would still persist.

PART - I

ANALYSIS

CHAPTER 4

PRIMARY ANALYSIS

4.I Definition of Wound Infections

In the survey, wounds were described as having (1) no infection (2) redness of edges and serious discharge (3) pus or (4) cellulitis. The presence of haematoma, sinuses or fistulae, wound breakdown, slough or deep abscess 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:

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

Moderate-Superficial inflammation of whole wound (or over onethird) with a serous 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 fistulae or widespread cellulitis or wound breakdown with an obvious inflammatory reaction and pus.

The grade of severity, although based on the above definitions, was a personal opinion of the observer. However, some consistency was ensured because all wounds were examined and assessed by one or the other of the two observers.

In the analysis, doubtful infections and certain

categories of operations, e.g. vaginal, rectal, traumatic and drainage of abscesses, have been excluded. The wound infection rate is the percentage of patients infected in a particular patient group under study and included mild, moderate and severe, but not doubtful infections.

4.2 Wound Infection Rate

Out of the 11716 patients in the survey 3354 had operations and the corresponding total wound infection rate was 15.4 per cent. When purulent wounds are used as a criteria of wound infection* the rate is only 6.9 per cent. Table I shows the classification of wound infections into types of wounds. As expected the infection rate was lowest in clean operations (8.6%) and highest in contaminated operations (41.3%) and in clean-contaminated wounds the infection rate was 21.1 per cent. The difference between these three categories is statistically significant ($\chi^2 = 286$, 2 D.F., $P < 0.001$).

Table I. Type of Wound and Infection Rate.

	Clean		Contam		Type of Wound Clean-contam		not known	Total
	ND	D	ND	D	ND	D		
No. in group	1553	560	134	232	393	476	6	3354
Percentage infected(all infections)	6.1	15.5	30.6	47.4	16.0	25.2	0	15.4
(Purulent wounds)	(3.4)	(6.3)	(18.7)	(31.9)	(9.2)	(10.3)	0	(6.9)

ND: not drained. D: drained.

* The purulent criteria is only used in Table I for the figures in parenthesis. Other infection rates relate to the definition given at the end of section 4.1, except for resistant staphylococci infection rates in section 4.2.1.

Drains were inserted in about a third of operated wounds and drained wounds had a significantly higher infection rate (25.0%) than undrained wounds (9.6%) ($\chi^2 = 145$, 1 D.F., $P < 0.001$). Table 2 shows infection rates in wounds with different types of drain. In 32 drained wounds the type of drain was not recorded at the time of the survey. Lower infection rates were found in wounds with smaller drains or closed drainage systems, e.g. 'Redivac', and the highest rate in wounds with more than one drain. The concept of lower infection rates in clean undrained wounds was also true when the purulent criteria was used (figures in parenthesis Table I).

Table 2. Type of drain and wound infection rate.

Type of Drain	Number of Patients	Percentage infected
Redivac ..	497	17.1
Corrugated ..	223	37.7
Large tube ..	273	28.9
Wick ..	19	26.3
Small tube ..	155	20.6
More than one drain ..	69	40.6
(not known) ..	32	12.5
Total ..	1268	25.0

4.2.I Bacteria of Infected Wounds

Swabs were taken from 906 wounds, including mild infections of drained sites and doubtful infections which were excluded from the wound infection rate analysis. The bacteria which were isolated are shown in Table 3. More than one organism was often isolated from a wound. Most of the swabs which did not yield one or more of these organisms showed no bacterial growth.

Table 3. Percentage of wounds which yielded bacteria.

	Percentage
Staph. albus ..	13
Staph. Aureus ..	24
E. Coli ..	17
Proteus sp. ..	15
Klebsiella-enterobacter sp. ..	11
Ps.aeruginosa ..	7

Table 5. Type of patient and wound infection rate.

		Number of Patients	Infection Rate(%)
General surgery	..	1647	19.2
Gynaecology	..	180	12.8
Obstetrics	..	87	4.6
Paediatrics	..	157	15.3
Orthopaedic	..	431	6.5
Geriatric surgery	..	36	25.0

The length of pre-operative stay in hospital is considered as a factor associated with the risk of infection. In this study 38 patients were operated on the day of admission (some of which were emergency operations), and about two-thirds of patients operated within the first three days after admission. Table 6 shows the relationship between pre-operative stay and wound infection. If the patients operated on the day of admission are disregarded as special cases (e.g. emergency), then there is a general increase in wound infection with increases in pre-operative hospital stay. The difference between these four latter groups was statistically significant ($\chi^2 = 35.3$, 3 D.F., $P < 0.005$).

Table 6. Pre-operative stay in hospital and infection rate

	Day of Admission	I - 3 days	4 - 6 days	7 - 9 days	over 9 days
No. in group	38	2189	384	211	532
Infection Rate(%)	21.0	13.0	17.4	15.2	23.1

There was not sufficient information recorded at the time of the survey to evaluate the significance of associated factors such as immuno-suppressive drugs, irradiation, malnutrition, obesity and diabetes. For similar reasons the source of infection (ward, theatre or self) could not be determined.

In wounds where swabs were taken, 14.1 per cent were colonised with antibiotic resistant Staphylococci aureus. When resistant Staphylococci is used as a criteria of wound colonisation in these 906 swabbed wounds, clean wounds (13.1%) and clean contaminated wounds (13.1%) had a lower colonisation rate than contaminated wounds (19.5%), but the difference was not statistically significant ($x^2 = 4.65$, 2 D.F., $P < 0.1$). In the swabbed wounds 526 contained drains and the remaining 285 wounds were not drained. When the same criteria of wound colonisation was applied, drained wounds (14.3%) showed a lower colonisation rate than undrained (15.1%) wounds, but the difference was not significant ($x^2 = 0.09$, 1 D.F., $P < 0.75$). The classification of the swabbed wounds into wound types, using resistant Staphylococci as a criteria, are shown in Table 4.

Table 4. Resistant Staphylococci Colonisation Rate in Swabbed Wounds

	Clean		Contaminated		Clean Con'td.		Excluded	Total
	ND	D	ND	D	ND	D		
No. in group	161	160	47	138	77	228	95	906
Percentage colonised (Resistant Staph. aureus)	13.0	13.1	25.5	17.4	13.0	13.2	10.5	14.1

ND- not drained D- drained

4.2.2 Other Factors Related to Infection

The classification of all patients into the types of patients is listed in Appendix B2. Over three quarters of operated patients fitted into seven major types and these are given in Table 5. The lowest infection rate was found among the obstetric, orthopaedic and gynaecology patients and the highest among geriatric patients.

Older age of patient and sex (male greater than female) were associated with a high incidence of wound infection, and these are discussed in detail in Chapter 5.

4.3 Nasal Carriage Rate

The total nasal carriage rate was 8.6 per cent. When the nasal carriage rate was broken down into operated and non-operated patient groups (Table 7), the operated group had a significantly higher nasal carriage rate than the non-operated group ($\chi^2 = 5.46$, I D.F., $P < 0.025$). This difference in carriage rates could not have been due to the possibility of a greater proportion of the operated patients being of a higher age group, because the age distribution in both the operated and non-operated groups was similar.

Table 7. Nasal carriage rates in operated and non-operated patients.

	Operated	Non-operated	Total
No. of patients	4159*	7557	11716
Nasal carriage rate(%)	9.5	8.2	8.62

* This figure includes 805 operated patients who were excluded from wound infection rate calculations in Tables I - 6

Like the operated patients, over three-quarters of all the patients in the survey, could be classified into seven major patient types. The nasal carriage rate for different types of patient, is shown in Table 8. The lowest carriage rate was observed among the gynaecology, obstetric, paediatric and orthopaedic patients and the highest carriage rate among geriatric patients. These categories of patients reflecting the highest and lowest carriage rates are somewhat similar to the categories of infection rates shown in Table 5.

Table 8. Type of patient and nasal carriage rate.

	Number of Patients	Carriage Rate
General surgery ..	2785	9.6
General Medicine ..	2172	10.5
Gynaecology ..	575	2.4
Obstetrics ..	1363	4.0
Paediatrics ..	659	4.0
Orthopaedic ..	835	8.5
Geriatric ..	494	23.5

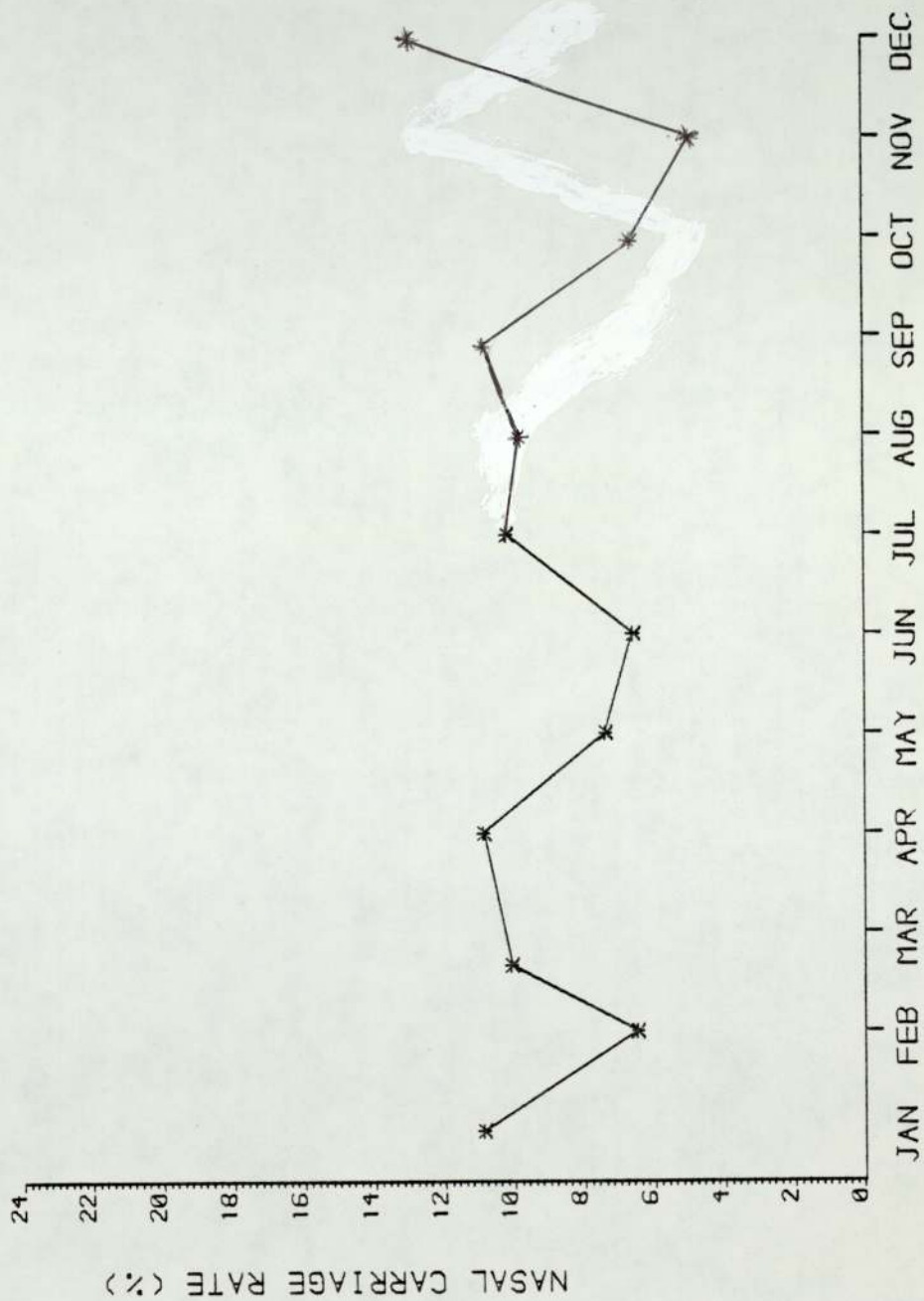
The possibility of seasonal changes in nasal carriage rates was studied and no correlation was found. The somewhat higher carriage rate in December (Figure 2) could be a result of the abnormally high proportion of highly susceptible patients that are left in hospital during the festive season (most of the not-so-severely-ill patients go home for Christmas^s).

Old age, sex (male more than female), length of stay in hospital and exposure to antibiotics were all associated with a higher incidence of nasal carriage. These patient parameters are discussed in detail in Chapter 6.

4.4 Consequence of Infection on Hospitalisation

The mean hospitalisation for patients with wound infections was 28 days and for non-infected operated patients 18 days. For patients with hospital acquired infections (excluding wounds), the mean length of stay was 33 days. For patients with wound infections or any acquired infections, the mean length of stay was 30 days, as opposed to the mean of 16 days for all other patients. The implications are, that infected patients stay twice as long in hospital compared with non-infected patients. (It must be stated here that the days in hospital refer to the time spent in hospital up till the day of survey, as opposed to a continuous survey

FIGURE 2



where actual length of stay can be evaluated. However, cross-sectional surveys also reflect the actual trends and these figures can be assumed to be representative of the true situation.)

CHAPTER 5

SIGNIFICANCE OF PATIENT PARAMETERS ON WOUND INFECTIONS

5.1 Introduction

The wound infection rate of 15.4 per cent reported in the previous chapter emphasised the problem of post-operative wound infection. The purulent wound infection rate reported therein is similar to the rates reported elsewhere (96, II6). The primary analysis confirmed the significance of parameters such as type of wound (clean Vs. contaminated), insertion of a drain, pre-operative length of hospitalisation and type of patient, on the risk of post-operative wound infection. It also indicated that old age and male sex are associated with a high incidence of wound infection. Age and sex are parameters unique to every individual patient, irrespective of his clinical or operative condition. Previous studies only viewed the age of patient as a qualitative concept, merely stating that high age is associated with a higher risk of acquiring a post-operative infection; and studies on the significance of the sex of patient have been somewhat inconclusive. Clearly there is a need to quantify the association between age and wound infection rate, and to establish the significance of sex of patient on wound infection. In this chapter, the significance of age is quantified using a curve fitting approach, and the significance of sex of patient is investigated by making allowances for any bias arising from associated factors such as type of wound, presence of drains and type of operation.

5.2 Age of Patient and Wound Infection Rate

In order to examine the association between post-operative wound infection and patients' age further, patient ages were classified into nine major groups both for convenience and to provide an adequate sample size for analysis. The wound infection rates for these age groups are shown in Table 9.

Table 9. Wound infection rate and age of patient.

<u>Age Group</u>	<u>No. in Group</u>	<u>Infection Rate</u>
Less than 1 ..	52	11.5
1 - 9 ..	177	13.6
10 - 19 ..	234	12.0
20 - 29 ..	310	11.3
30 - 39 ..	316	11.4
40 - 49 ..	458	13.1
50 - 59 ..	551	16.2
60 - 69 ..	614	21.2
70 & over ..	642	16.7
Total ..	3354	15.4

Most of the patients under one year old were neonates and most of the over 70 year old patients were classed as geriatrics. For most of the analytical studies these two extreme age groups were not included as their clinical conditions are not necessarily representative of the majority of patients. The differences in infection rates in the remaining seven age groups (1 to 69) were statistically significant ($\chi^2 = 31.0$, 6 D.F., $P < 0.005$).



The relationship between age and wound infection rate can best be represented by a quadratic equation of the form $Y = A - BX + CX^2$, where Y is the infection rate, X is the age and A, B and C are constants. For the data in Table 9 (age I - 69 only), the following quadratic equation gave the best fit, with a sum of squared deviation (SSD) of 0.5 which absorbs more than 99 per cent of the variance about the mean;

$$Y = 15.35 - 0.34X + 0.0065X^2$$

differentiating to obtain the minimum value for Y,

$$\frac{dy}{dx} = 0 \quad \text{at } X = 26$$

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

5.2.I Patient age, sex and wound infection rate

It is possible that the above trend of age is a function of the distribution of male and female patients in different age groups. In order to test this phenomenon, patient age groups were further classified according to sex (Table IO). Although female patients had a lower infection rate, the influence of age on both these groups was similar. The relationship between age and wound infection rate for both groups can be represented by quadratic equations. The equation for the male patient group is

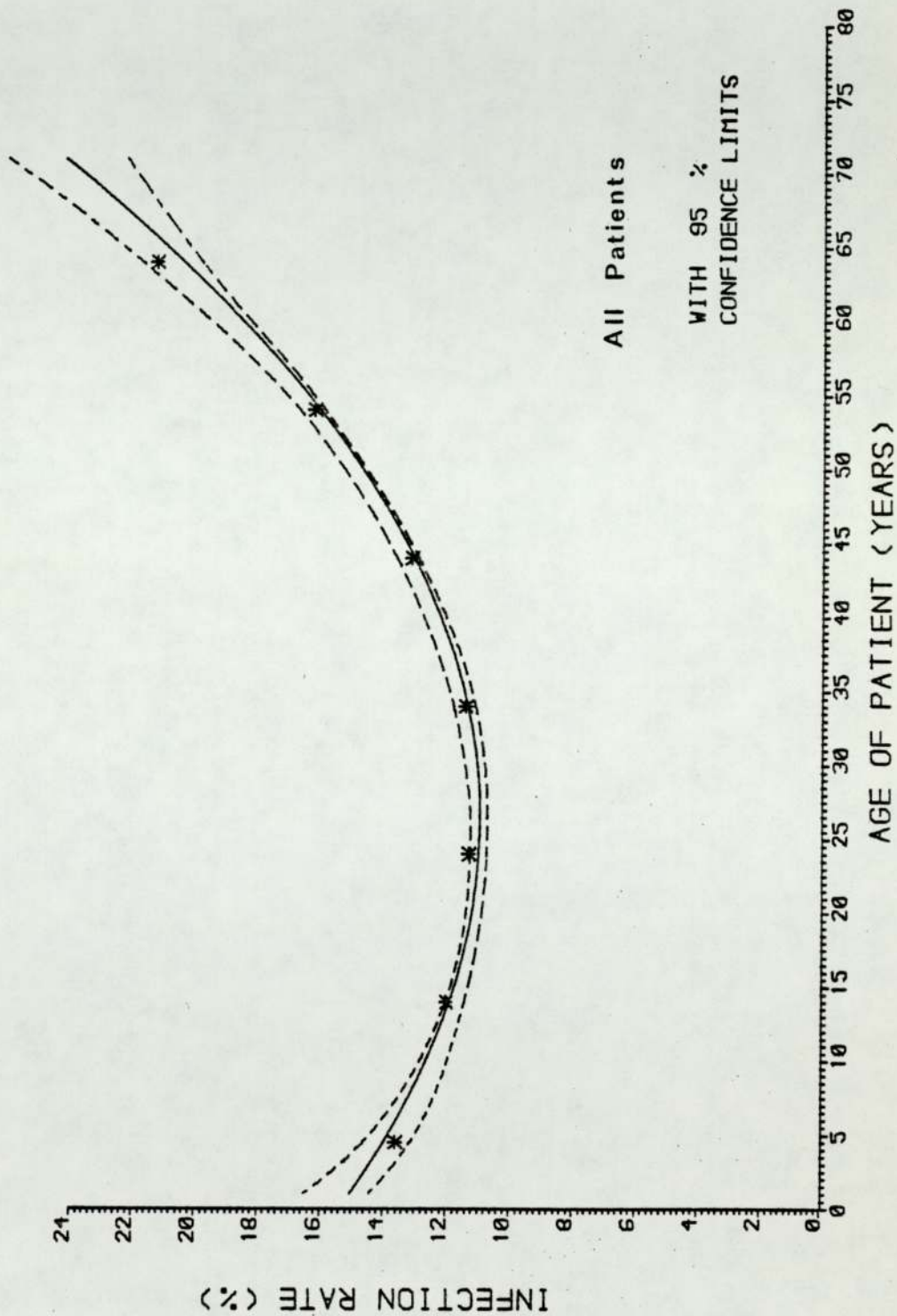
$$Y = 18.18 - 0.359X + 0.0067 X^2, \text{ SSD} = 5.4$$

which absorbs 93 per cent of the variance about the mean and has a minimum infection rate at 27 years. For female patients

$$Y = 9.49 - 0.118X + 0.0038X^2, \text{ SSD} = 6.5$$

which absorbs nearly 98 per cent of the variance about the mean and has a minimum infection rate at 15 years.

FIGURE 3



All Patients

WITH 95 %
CONFIDENCE LIMITS

AGE OF PATIENT (YEARS)

These two curves are shown in Fig. 4. The difference in infection rate due to the sexes was greater in the younger age groups.

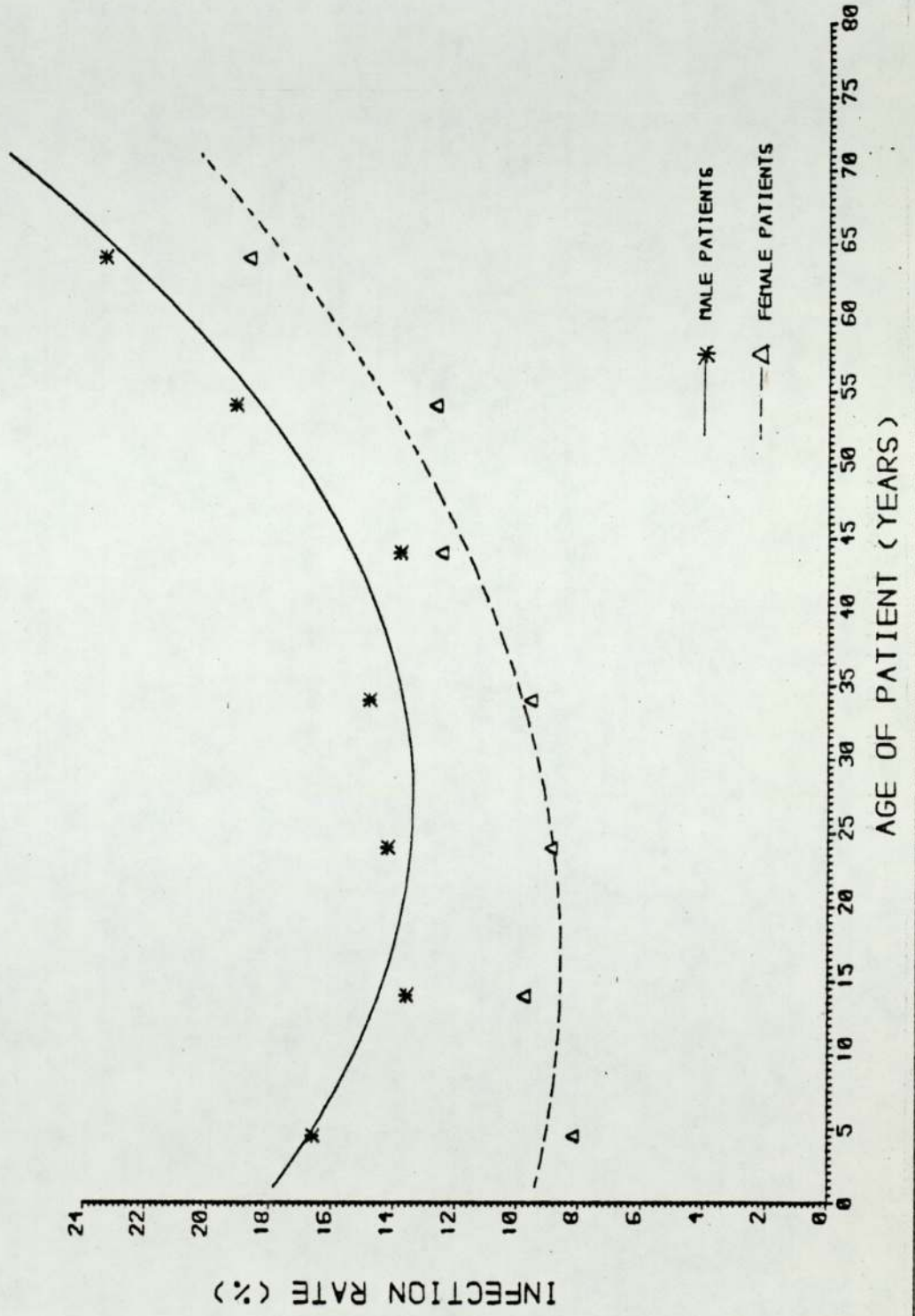
Table IO. Age, sex and wound infection rate.

Age Group	Males		Females	
	No. of Patients	Percentage infected	No. of Patients	Percentage infected
I - 9 ..	116	16.6	61	8.2
10 - 19 ..	132	13.6	102	9.8
20 - 29 ..	141	14.2	169	8.9
30 - 39 ..	108	14.8	208	9.6
40 - 49 ..	210	13.8	248	12.5
50 - 59 ..	299	19.1	252	12.7
60 - 69 ..	330	23.3	284	18.7
(70 & over)	(271)	(21.0)	(371)	(13.5)

5.2.2 Age, Type of Wound and Infection Rate

The relationship between age and wound infection rate could well be a result of the type of operations or wounds associated with particular patient ages. To examine this concept in detail, patients were divided into the three wound categories - clean, contaminated and clean-contaminated. The wound infection rates in these categories were then classified into the seven age groups as before (there were only 366 contaminated wounds, too small a sample to classify into age groups). The infection rate in different age groups for clean and clean-contaminated wounds are shown in Table II. Even after this classification the quadratic nature of the age curves was clearly evident.

FIGURE 4



The equation for clean wounds was

$$Y = 6.7 - 0.092X + 0.0024X^2, \text{ SSD} = 2.4$$

and for clean-contaminated wounds

$$Y = 19.5 - 0.335X + 0.0078X^2, \text{ SSD} = 15.9.$$

These two curves are shown in Fig. 5.

Table II. Age and wound infection rate for clean and clean-contaminated wounds

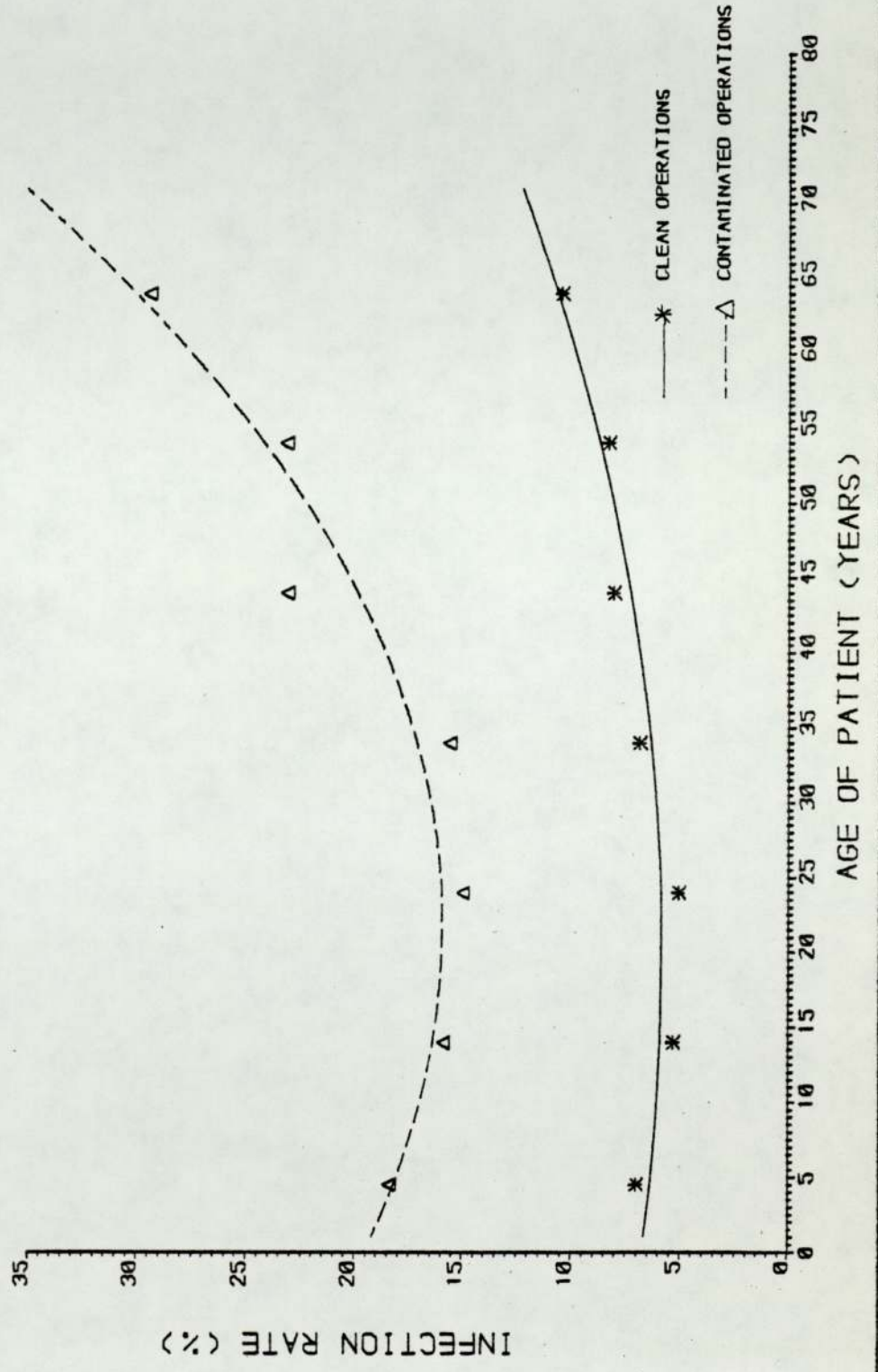
Age Group	Clean		Clean-contaminated	
	No. of Patients	Percentage infected	No. of Patients	Percentage infected
I - 9 ..	115	7.0	38	18.4
10 - 19 ..	133	5.26	82	15.85
20 - 29 ..	198	5.05	87	14.94
30 - 39 ..	219	6.85	77	15.58
40 - 49 ..	311	8.04	117	23.08
50 - 59 ..	351	8.26	134	23.13
60 - 69 ..	355	10.42	167	29.34
(70 & over)	(401)	(11.97)	(152)	(18.42)
Total*	2083	8.6	854	21.1

* excluding under 1 year olds.

5.3 Sex of Patient and Wound Infection Rate

As shown in Table I2, the male infection rate for all infections was significantly higher than the female infection rate ($x^2 = 18.8$, 1 D.F., $P < 0.005$). Also, when wound infection was defined using the purulent criteria, the significantly higher male infection rate still persisted ($x^2 = 12.1$, 1 D.F., $P < 0.005$). It is possible that the difference is due to the presence of a high proportion of older patients

FIGURE 5



among male patients, but as can be seen from Table I0, this is unlikely and further, male infection rate is higher in every age group. Evidence of higher male colonisation rates was obtained when the 906 wound swabs were analysed for resistant staphylococcal strains (Table I3). Here again the male patients (I6.9%) had a significantly higher staphylococcal wound colonisation rate than female patients (I0.7%) ($\chi^2 = 7.0$ I D.F., $P < 0.01$).

Table I2. Sex of patient and wound infection rate.

		Male	Female	Total
No. of Patients	..	I64I	I7I3	3354
Percentage Infected (All Infections)	..	I8.I	I2.7	I5.4
Percentage Infected (Purulent wounds)	..	9.8	6.5	8.I

Table I3. Sex of patient and resistant staphylococci
wound colonisation rate.

		Male	Female	Total
No. of Patients	..	504	402	906
Infection Rate	..	I6.9	I0.7	I4.I

5.3.I Sex of Patient, Type of Wound and Infection Rate

BRUNN (45) and the N.R.C. Study (4I) indicated that the higher male wound infection rate can be the result of a higher proportion of contaminated wounds among male patients. This is possibly true, because (as seen in Table I4) in clean wounds female patients (8.9%) had a slightly higher infection rate than male patients (8.2%); but the difference was not

statistically significant ($x^2 = 0.4$, I D.F., $P > 0.5$).

However, Table I4 also shows significantly higher male infection rates in contaminated wounds ($x^2 = 11.6$, I D.F., $P < 0.005$) and clean-contaminated wounds ($x^2 = 8.3$, I D.F., $P < 0.005$). This shows that male patients have a significantly higher infection rate following contaminated and clean-contaminated surgery.

Table I4. Sex of patient, type of wound and infection rate.

	Male	Female	Total
Clean ..	8.2 (932)	8.9 (1181)	8.6 (2113)
Contaminated ..	49.2 (195)	32.2 (171)	41.3 (366)
Clean-contaminated..	24.5 (511)	16.2 (358)	21.1 (869)

Number of patients given in brackets.

5.3.2 Sex of Patient, Wound Drainage and Infection Rate.

Another parameter of wound infection that may have introduced a bias into the observed higher male wound infection rate, is the presence of wound drains. In all drained wounds male patients (30,0%) had a significantly higher infection rate than female patients (19.7%) ($x^2 = 18.1$, I D.F., $P < 0.005$). In undrained wounds also the male infection rate (10.2%) was higher than the female infection rate (8.9%) but the difference was not statistically significant ($x^2 = 1.2$ I D.F., $P > 0.5$). This may imply that the male infection rate is higher only in drained wounds. However, further analysis showed that over 70 per cent of undrained wounds in both male and female groups were classified as clean wounds.

Since, in clean wounds there was no difference in male and female infection rates, the high proportion of clean wounds would have introduced a bias into the classification of undrained wounds. This was confirmed when undrained contaminated and undrained clean-contaminated wounds were analysed together, where male infection rate (23.9%) was significantly higher than the female infection rate (14.8%) ($\chi^2 = 6.9$, I D.F., $P < 0.01$). The infection rate following different types of operative wounds and type of drains for male and female patients, are given in Table I5. The possibility that the difference in infection rates is a result of the differences in the type of wound drains was also investigated, and as shown in Table I6, the male infection rate was significantly higher with all types of drains, except in the case of corrugated drains.

Table I5. Sex of patient, type of wound, drainage and infection rate.

	Type of Wound						Total
	Clean		Contaminated		Clean-contaminated		
	ND	D	ND	D	ND	D	
Male	4.7 (701)	18.6 (231)	40.0 (65)	53.8 (130)	19.2 (219)	28.4 (292)	18.1 (1641)
Female	7.2 (852)	13.4 (329)	21.7 (69)	39.2 (102)	12.1 (174)	20.1 (184)	12.7 (1713)

ND - Not drained. D- drained
Number of patients given in brackets.

5.3.3. Sex of Patient and Infection Rate Following Common Operations.

It was often said that the higher male infection rate is due to the more complex surgery male patients undergo (41, 45). In order to remove any such bias in the analysis,

infection rates in operations common to both male and female patients were analysed together. These operations were: Gastrectomy, Cholecystectomy, Appendicectomy, Pyloroplasty, Thoracotomy, Lobectomy, Cystotomy, Colectomy, Colectomy, Caecostomy, Hernia inguinal, Hernia repair, Varicose veins, Ligature veins, Laparotomy, Vagotomy and Nephrectomy.

About one-third of all the operations in the survey fell into this common operation category, and the corresponding male infection rate (21.3%) was significantly higher than the female infection rate (15.9%) ($\chi^2 = 4.72$, 1 D.F., $P < 0.05$). This observation confirmed that the significantly higher male infection rate is probably independent of any bias arising from the differences in types of operations.

Table I6. Sex of patient, type of drain and infection rate.

	Redivac	Corrugated	Large tube	Wick	Small tube	More than one drain
Male	23.2 (220)	36.4 (129)	31.4 (169)	44.4 (9)	25.0 (72)	57.1 (35)
Female	12.3 (277)	39.4 (94)	25.0 (104)	10.0 (10)	16.9 (83)	23.5 (34)

Number of patients given in brackets

CHAPTER 6.

SIGNIFICANCE OF PATIENT PARAMETERS ON NASAL CARRIAGE

6.1 Introduction

In Chapter 4 and 5, patient and operative parameters related to post-operative wound infection were examined. Staphylococcal cross-infection however, is largely dependent on the level of ward contamination. Nasal carriage of tetracycline-resistant Staph.aureus is a convenient method of measuring cross-infection transmitted on dry vehicles or in the air of the hospital. A nasal swab can easily be obtained from all patients, and tetracycline-resistance is a suitable measure of hospital acquisition except in neonatal wards. Therefore, the susceptibility to nasal carriage of resistant Staphylococci can be used as a measure of the risk of cross-infection. The analysis in 4.3, indicated that old age, male sex, length of stay in hospital and exposure to antibiotics to be associated with a higher incidence of nasal carriage. These four parameters can be classified as patient parameters because they are independent of the patients' clinical or operative conditions.

The significance of sex of patient and chemotherapy is investigated in this chapter, and the relationships between age and nasal carriage and length of stay and nasal carriage, are quantified using curve fitting techniques.

6.2 Age of Patient

The nasal carriage rate of tetracycline-resistant Staphylococci for different patient age groups are shown in the last column in Table I7. Since neonates rarely acquire

multiple-resistant strains, but many acquire strains which are antibiotic-sensitive or penicillin-resistant only, the under one year olds are excluded from further analysis. The majority of over 70 year old patients were long stay geriatric patients, and since they are not representative of the normal patients, they too are excluded from further analysis.

Table I7. Age of patient and nasal carriage rate

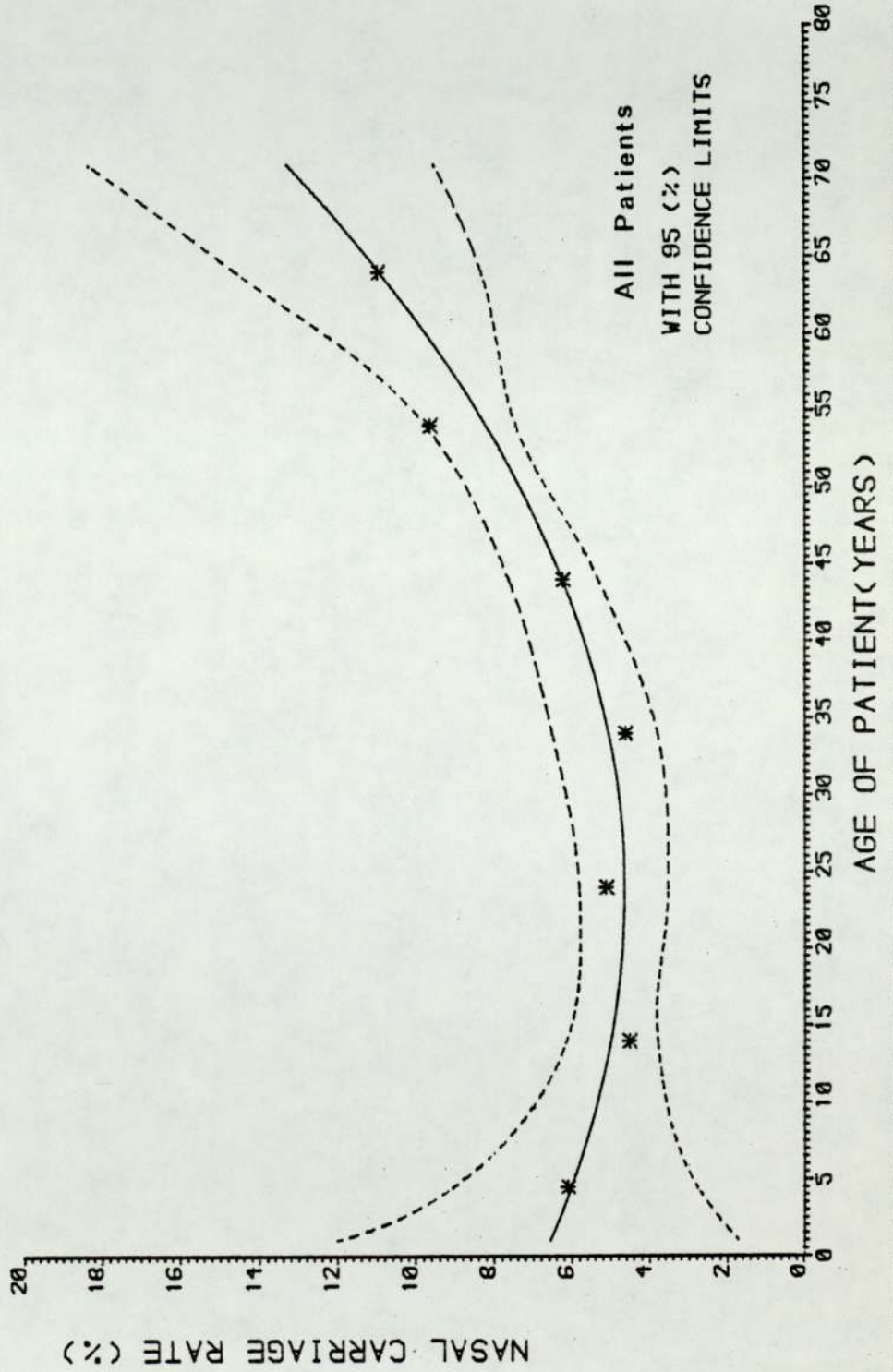
Age group	Males		Females		Total	
	%	Number	%	Number	%	Number
Under 1 Yr	3.2	506	4.4	453	3.7	959
I - 9	5.7	458	6.8	308	6.1	766
10-19	6.6	332	2.6	385	4.5	717
20-29	6.0	365	4.8	975	5.1	1340
30-39	5.2	367	4.3	624	4.6	991
40-49	6.4	594	6.1	606	6.2	1200
50-59	10.1	875	9.0	747	9.6	1622
60-69	12.1	1005	9.5	885	10.9	1890
70 & over	17.5	821	14.2	1410	15.4	2231
Total	9.3	5323	8.0	6393	8.6	11716

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

$$YN = 6.718 - 0.179X + 0.0038X^2, \text{ SSD} = 2.08$$

which absorbed about 95 per cent of the variance about the mean. This curve together with the 95 per cent confidence

FIGURE 6



limits are illustrated in Fig 6. The minimum carriage rate is at 23.5 years.

6.2.1 Age, Sex and Nasal Carriage

Examination of Table I7 shows that the quadratic relationship between nasal carriage and age of patient was quite independent of any bias arising from the sex distribution of the patient population under study. A similar age and nasal carriage function was observed in both the male and female patient groups (Fig.7). Quadratic equations were the best fit in both instances. For male patients the equation is:

$$YN = 7.17 - 0.164X + 0.0037X^2, \text{ SSD} = 4.06$$

with 90 per cent of the variance about the mean absorbed and a minimum carriage rate at 22 years. For female patients the equation is: $YN = 6.49 - 0.18X + 0.0037X^2$, SSD = 2.08 with 94 per cent of the variance about the mean absorbed and a minimum carriage rate at 24 years.

6.2.2 Age of Patient and Nasal Carriage for Operated and Non-operated Groups

It was reported in 4.3 that operated patients experienced a significantly higher nasal carriage rate than non-operated patients. The distribution of operated and non-operated patients in different age groups could have influenced the observed relationship between age and nasal carriage. However, further analysis (Table I8) confirmed this was not so. The quadratic nature of the relationship was clearly evident in both the operated and non-operated patient groups (Fig.8). For operated patients the equation is:

$$YN = 5.7 - 0.184X + 0.0045X^2, \text{ SSD} = 3.59$$

and for non-operated patients

$$YN = 9.49 - 0.286X + 0.0048X^2, \text{ SSD} = 7.14$$

FIGURE 7

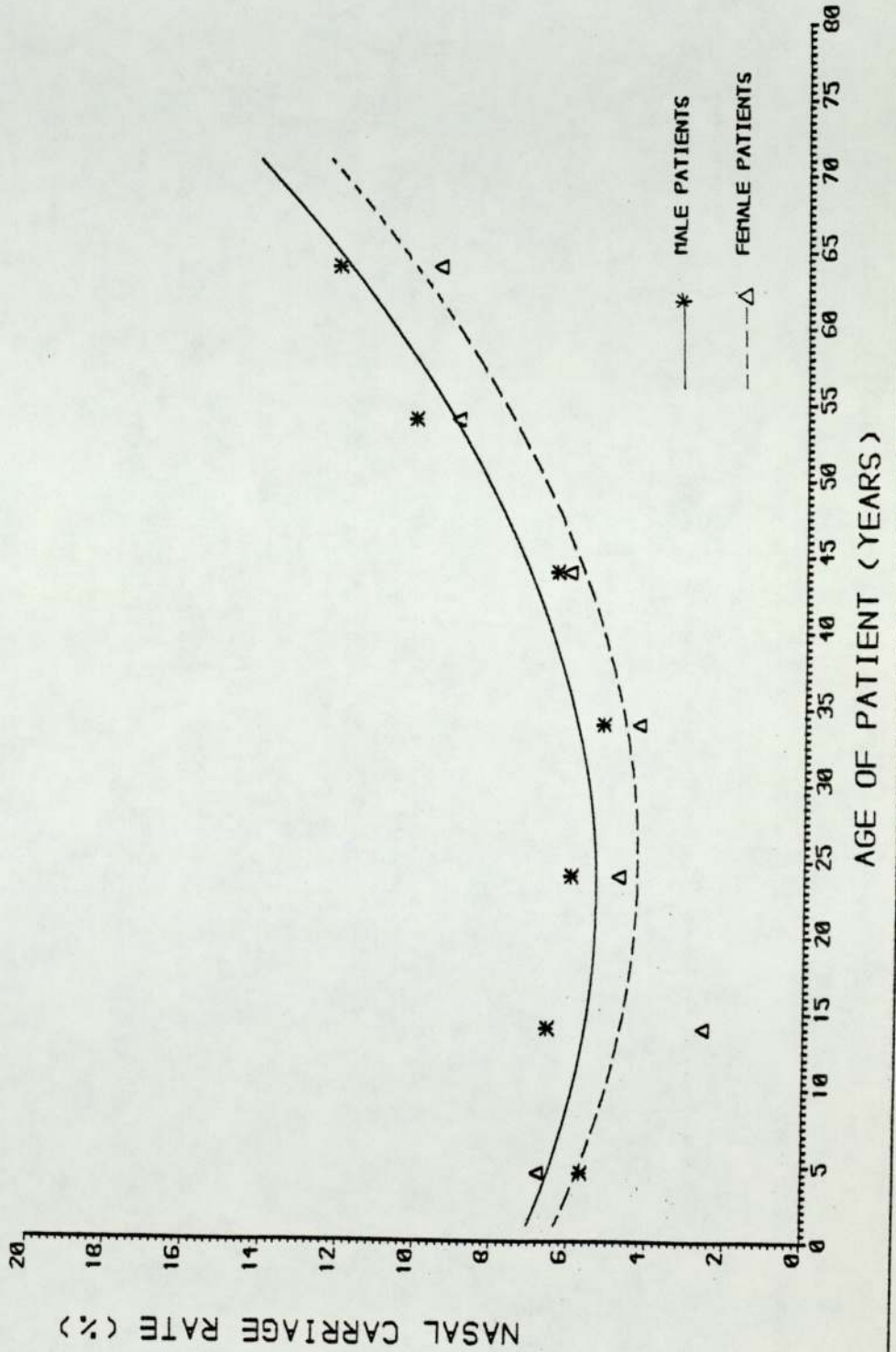


FIGURE 8

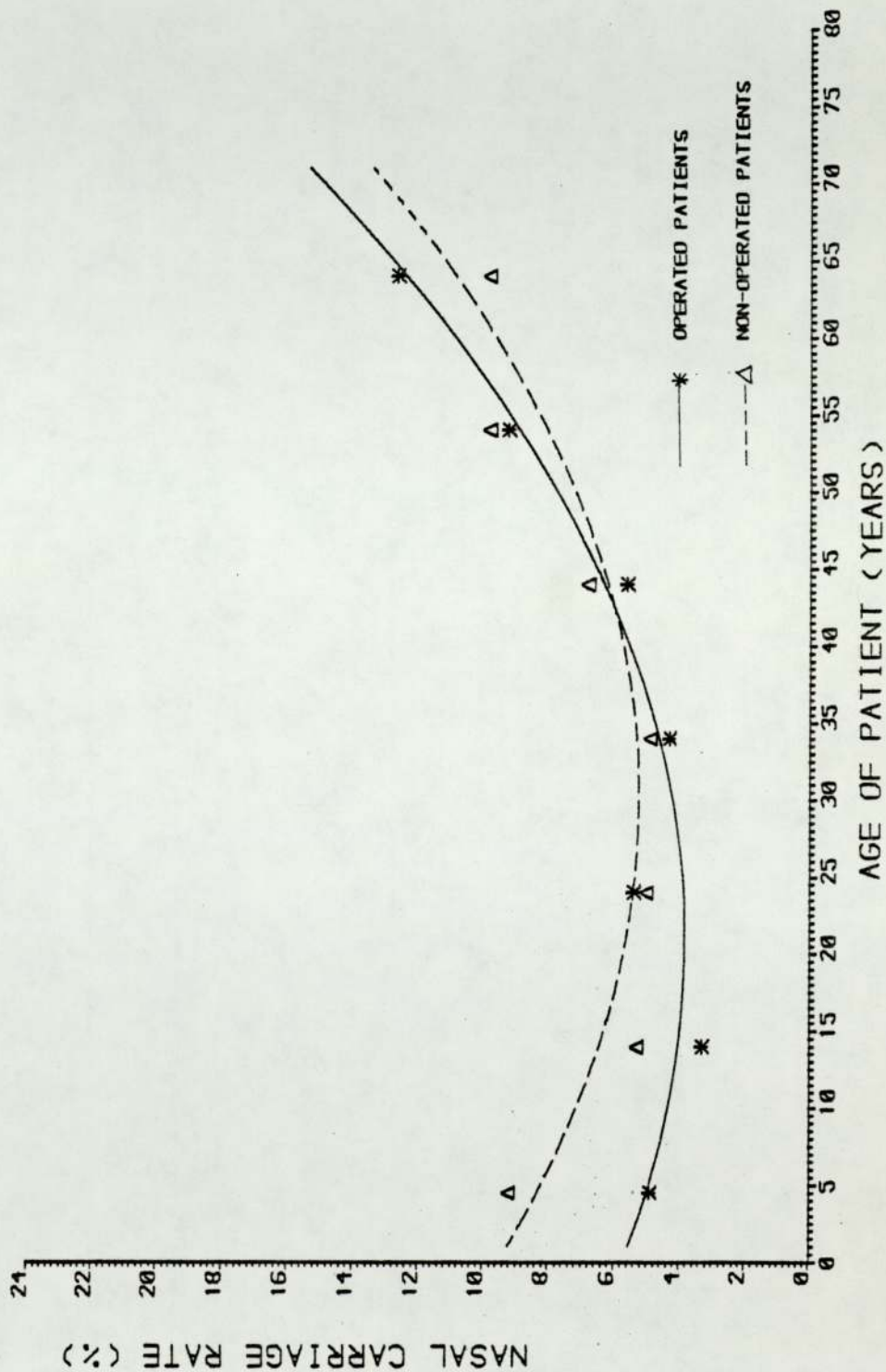


Table I8. Age, operation and nasal carriage rate.

Age group	Operated		Non-operated	
	%	Number	%	Number
I - 9 ..	4.9	224	9.2	347
10-19 ..	3.3	302	5.3	415
20-29 ..	5.4	427	5.0	913
30-39 ..	4.3	394	4.9	597
40-49 ..	5.6	549	6.8	651
50-59 ..	9.2	665	9.8	957
60-69 ..	12.6	730	9.8	1160

6.3 Chemotherapy

Patients receiving one or more antibiotics (or other chemotherapeutic agents) at the time of the survey, were included in the antibiotic group, and the nasal carriage rate of these patients (11.6%) was significantly higher than that of the patients who did not receive any antibiotics (7.5%) ($\chi^2 = 48.7$, 1 D.F., $P < 0.005$). Since antibiotics are in the majority administered to operated patients, the higher carriage rate may be a reflection of the lower resistance of these patients. Therefore, it was necessary to investigate the relationship between carriage rate and chemotherapy for operated patients and non-operated patients considered separately. In the operated group, patients receiving antibiotics had a significantly higher carriage rate than those who did not receive antibiotics ($\chi^2 = 11.9$, 1 D.F., $P < 0.005$). In the non-operated group also, patients receiving antibiotics had a significantly higher carriage rate ($\chi^2 = 35.2$, 1 D.F., $P < 0.005$). These observations are summarised in Table I9.

Table 19. Chemotherapy, operation and nasal carriage rate.

		Antibiotics	No antibiotics
Operated	..	11.6 (1451)	8.3 (2708)
Non-operated	..	11.7 (1671)	7.2 (5886)
Total	..	11.6 (3122)	7.5 (8594)

No. of patients in brackets

Before making any conclusions on the significance of chemotherapy on nasal carriage, the distribution of male and female patients in the antibiotic and no-antibiotic groups must first be considered (since male patients have higher carriage rates). When this analysis was carried out the antibiotic group had a significantly higher carriage rate in the male patient group as well as in the female patient group. Further, when these groups were broken down to operated and non-operated groups, the significance of the higher carriage rate in the antibiotic group was visible in all except the female operated group. Even in this group, the carriage rate of the patients receiving antibiotics was about 2 per cent higher. These observations are summarised in Table 20 and the details of the significance tests shown in Table 21.

About 27 per cent of the patients in the survey were treated with antibiotics. Ampicillin and tetracycline were the most commonly used antibiotics, which together accounted for more than half the total antibiotics being administered. The effect of the administration of individual chemotherapeutic agents is shown in Table 22. The statistical significance of each agent was tested against the no-antibiotic group for differences in carriage rate. A significantly

higher carriage rate is shown for patients treated with tetracycline, ampicillin and nitrofurantoin. Patients treated with benzyl penicillin or an oral penicillin showed a lower carriage rate than in the untreated group, but this was not significant. Other antibiotics such as fusidic acid or cephalosporins were not included, as their use was too infrequent.

Table 20. Chemotherapy, sex, operation and nasal carriage rate.

		Antibiotic		No Antibiotic	
		%	No	%	No
<u>Male</u>	Operated	13.4	764	8.9	1202
	Non-operated	12.4	856	7.3	2501
	Total	12.8	1620	7.8	3703
<u>Female</u>	Operated	9.6	687	7.8	1506
	Non-operated	10.9	815	7.1	3385
	Total	10.3	1502	7.3	4891

Table 21. Significance of chemotherapy.

Test group (Antibiotic Vs. No antibiotic)		χ^2 , I D.F	Status
Male operated	..	9.5	Significant (P< 0.005)
Male Non-operated	..	21.2	Significant (P< 0.005)
Female Operated	..	1.8	Not Significant (P>0.1)
Female Non-operated		13.3	Significant (P< 0.005)
All Male	..	33.7	Significant (P< 0.005)
All Female	..	14.0	Significant (P< 0.005)

Table 22. Nasal carriage in relation to type of antibiotic.

Antibiotic	No. in group	Carriage rate(%)	χ^2 I. D.F.	Significance
None	8594	7.5		
Streptomycin	267	9.4	1.31	NS (P > 0.5)
Erythromycin	43	11.6	1.02	NS (P > 0.5)
Nitrofurantoin	131	22.9	43.2	Sig(P < 0.005)
Sulphonamide	126	11.9	3.2	NS (P > 0.1)
Cloxacillin	281	10.0	2.6	NS (P > 0.75)
Penicillin	463	6.3	1.01	NS (P > 0.5)
Ampicillin	1058	10.4	10.7	Sig(P < 0.005)
Tetracycline	634	14.8	42.3	Sig(P < 0.005)
Neomycin	57	7.01	0.001	NS (P > 0.975)
Topical applications other than neomycin ..	221	8.1	0.07	NS (P > 0.9).

6.4 Length of Stay in Hospital

The length of stay in hospital of the patient was considered for this analysis to be the number of days spent in hospital upto the day the nose swab was taken. The length of stay was divided into 12 groups varying in size from 1 - 2 days to over 80 days. An interval of 2 days was taken for the first 10 days and then varying time intervals were taken to give reasonable group sizes for analysis. Table 23 gives the classification of nasal carriage rates of patients in the survey into categories depending on their length of stay in hospital.

From Table 23 it is evident that when all the patients are considered, the maximum rate of carriage was reached

by 31 - 40 days. The carriage rate, after a linear increase upto the 40 days in hospital, reached a plateau. Over the first 40 days a linear relation between carriage rate and length of stay fits the data very closely, with a correlation coefficient as high as 0.998. The best fit is given by the equation:

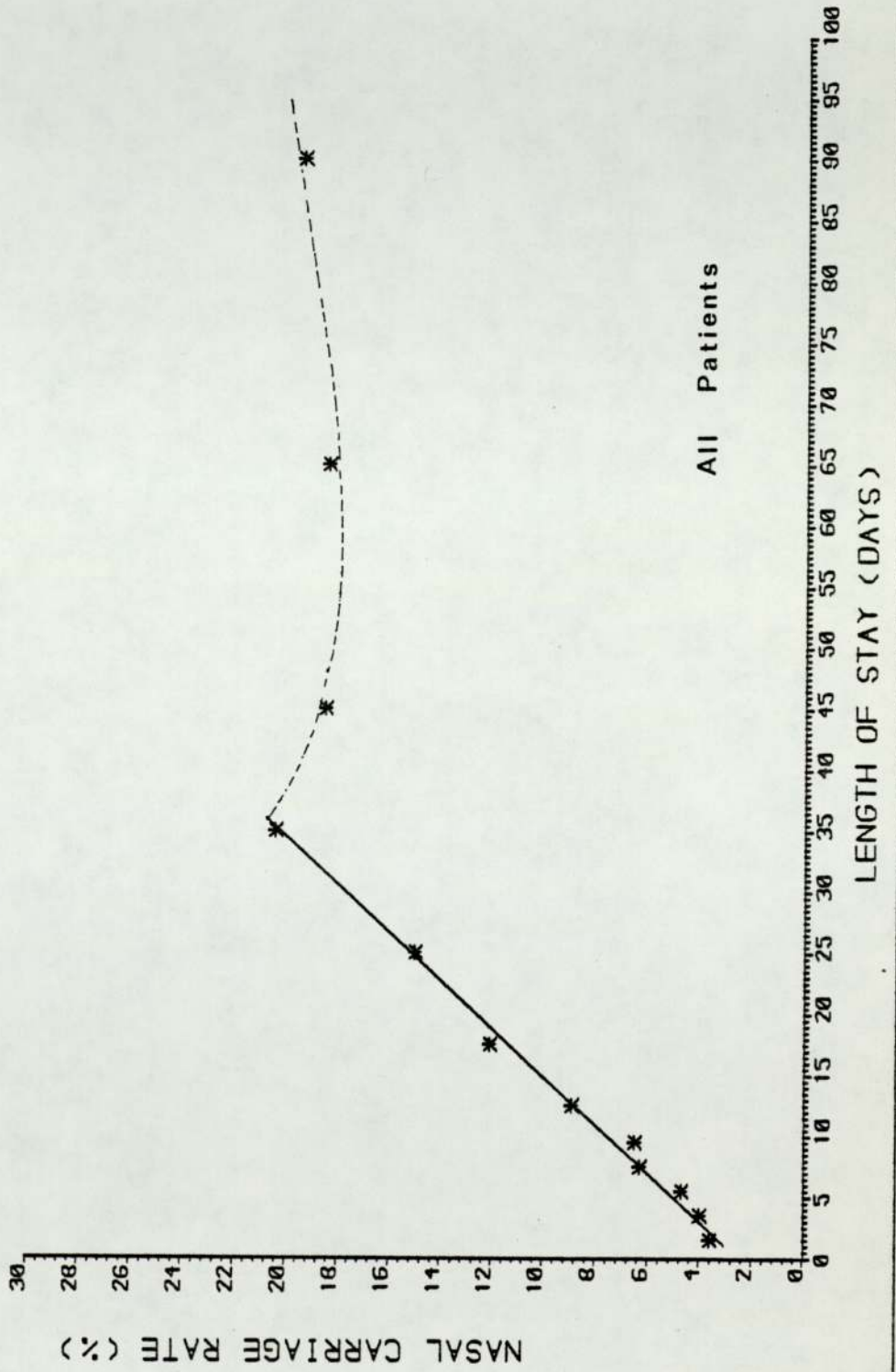
$$YN = 2.52 + 0.507T$$

where YN is the nasal carriage rate and T the length of stay. This relationship is shown graphically in Fig 9 where the linear regression is used upto the 40 day period and beyond the 40 day period, an emperical curve fitted to represent the observations.

Table 23. Nasal carriage rate and length of stay
in hospital

Days in hospital	All patients		Male		Female	
	%	No	%	No	%	No
I - 2	3.6	2362	4.0	1080	3.3	1282
3 - 4	4.0	1517	2.8	677	5.0	840
5 - 6	4.7	1206	5.7	543	3.9	663
7 - 8	6.3	1042	7.8	472	5.1	570
9 - 10	6.5	758	9.1	328	4.4	430
11 - 15	8.9	1388	10.1	655	7.9	733
16 - 20	12.1	792	12.7	401	11.3	391
21 - 30	15.0	916	16.6	458	13.3	458
31 - 40	20.4	446	21.1	218	19.3	228
41 - 50	18.5	275	24.8	133	12.7	142
51 - 80	18.4	396	15.5	174	20.7	222
Over 80	19.4	618	20.6	184	18.9	434
Total	8.6	11716	9.3	5323	8.0	6393

FIGURE 9



All Patients

6.4.1 Sex of Patient, Length of Stay and Nasal Carriage

Table 23 also shows the relationship between nasal carriage and length of stay for male and female patients. The male patients reached a maximum carriage rate at 41 - 50 days and the female group at 31 - 40 days. Like in the case for all patients, both the male and female carriage rates arrived at a plateau after a rapid linear increase. The carriage rate for both groups can again be represented by a linear function followed by an empirical curve. The regression equation for male patients upto the 41 - 50 day group was:

$$YN = 3.235 + 0.523T,$$

with a correlation coefficient of 0.988.

The regression equation for female patients upto the 31 - 40 day group was:

$$YN = 2.11 + 0.467T,$$

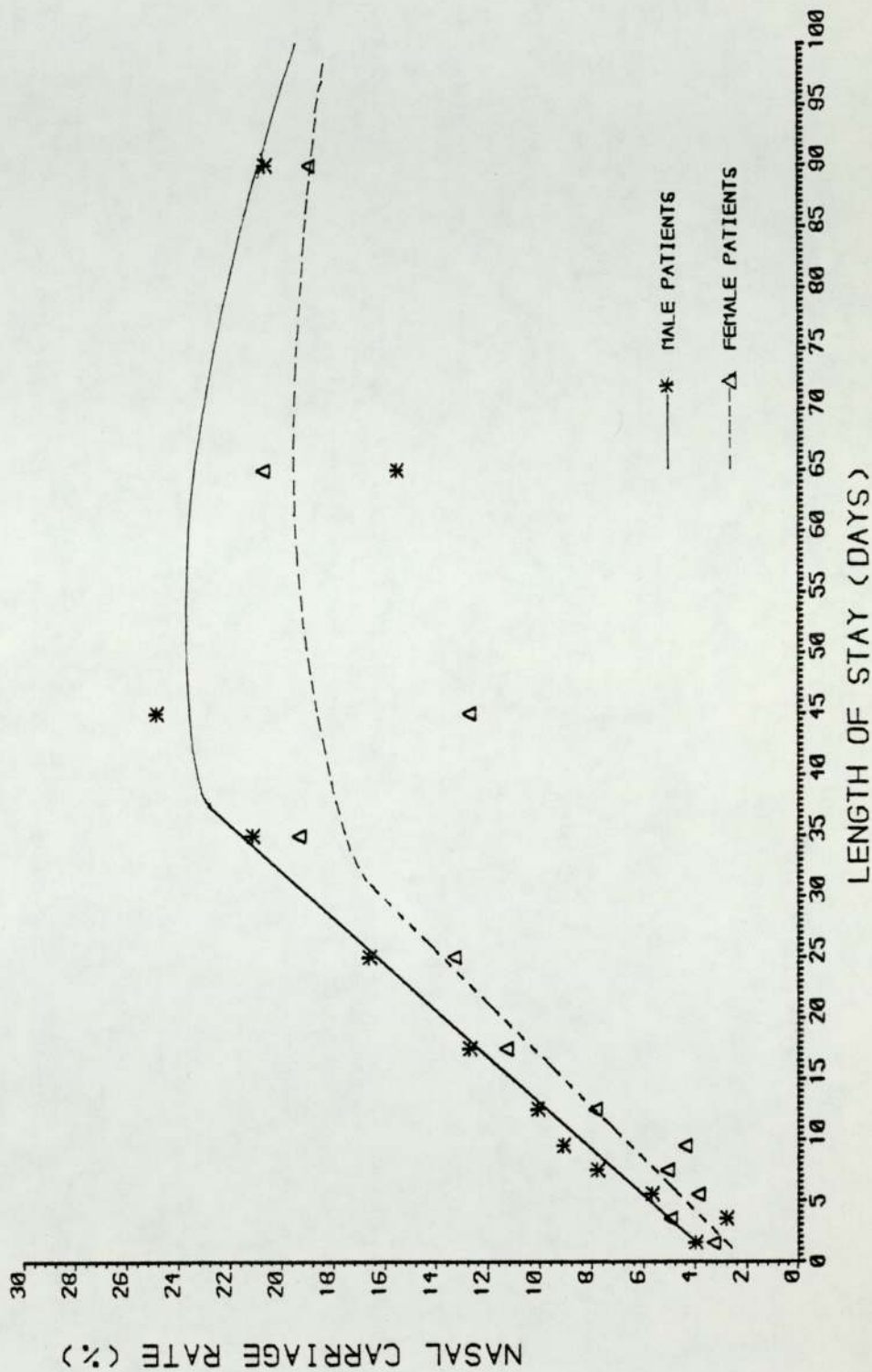
with a correlation coefficient of 0.982.

The male and female carriage rates are represented graphically in Fig. 10. This shows that the carriage rate for males was higher than that for females for all lengths of stay and that the male carriage rate reached a higher level, associated with the maximum carriage rate being attained somewhat later. The apparent fall in carriage rate after reaching a maximum is probably due to differences in sample sizes in the different age groups.

6.4.2 Age, Length of Stay and Nasal Carriage Rate

Since nasal carriage increases with age, the increase in carriage rate with length of stay might be due to the presence of a greater proportion of older patients (e.g. geriatric patients) who are often in hospital for long periods.

FIGURE 10



Patients were therefore classified into two major age groups, 0 - 59 years and 60 years and over and were further classified in terms of the length of stay categories previously described. The length of stay and carriage rate for these two age groups are shown in Table 24.

As expected, the patients in the over 60 year group have a significantly higher carriage rate than the 0 - 59 year old group ($\chi^2 = 180.0$, 1 D.F., $P < 0.005$). For patients staying upto 6 days in hospital, the difference between the two age groups was not significant ($\chi^2 = 2.33$, 1 D.F., $P < 0.1$), but the difference was significant in patients staying in hospital over 7 days.

Table 24. Age group, length of stay and nasal carriage rate.

Days in Hospital	Age group 0 - 59		Age group 60 & over	
	%	No	%	No
I - 2	3.5	1847	3.9	515
3 - 4	3.9	1161	4.5	356
5 - 6	4.1	896	6.5	310
7 - 8	5.9	709	7.2	333
9 -10	4.0	497	11.1	261
11-15	7.0	839	11.8	549
16-20	8.1	434	17.0	358
21-30	10.4	501	20.5	415
31-40	15.9	239	25.6	207
41-50	13.6	132	23.1	143
51-80	12.7	173	22.8	223
Over 80	16.1	167	20.6	451
Total	6.1	7595	13.3	4121

The relation between nasal carriage and length of stay for both age groups was similar to that previously described i.e. reached a stabilised state after a linear increase in carriage rate upto 30 - 40 days in hospital. This is shown in Fig. II. Both age groups reached the maximum carriage in 31 - 40 days, but the older patients showed a higher rate of increase. The linear regression equation for the 0 - 59 year group is :

$$YN = 2.44 + 0.352T,$$

with a correlation coefficient of 0.974.

For the over 60 year group the regression equation is:

$$YN = 3.42 + 0.666T,$$

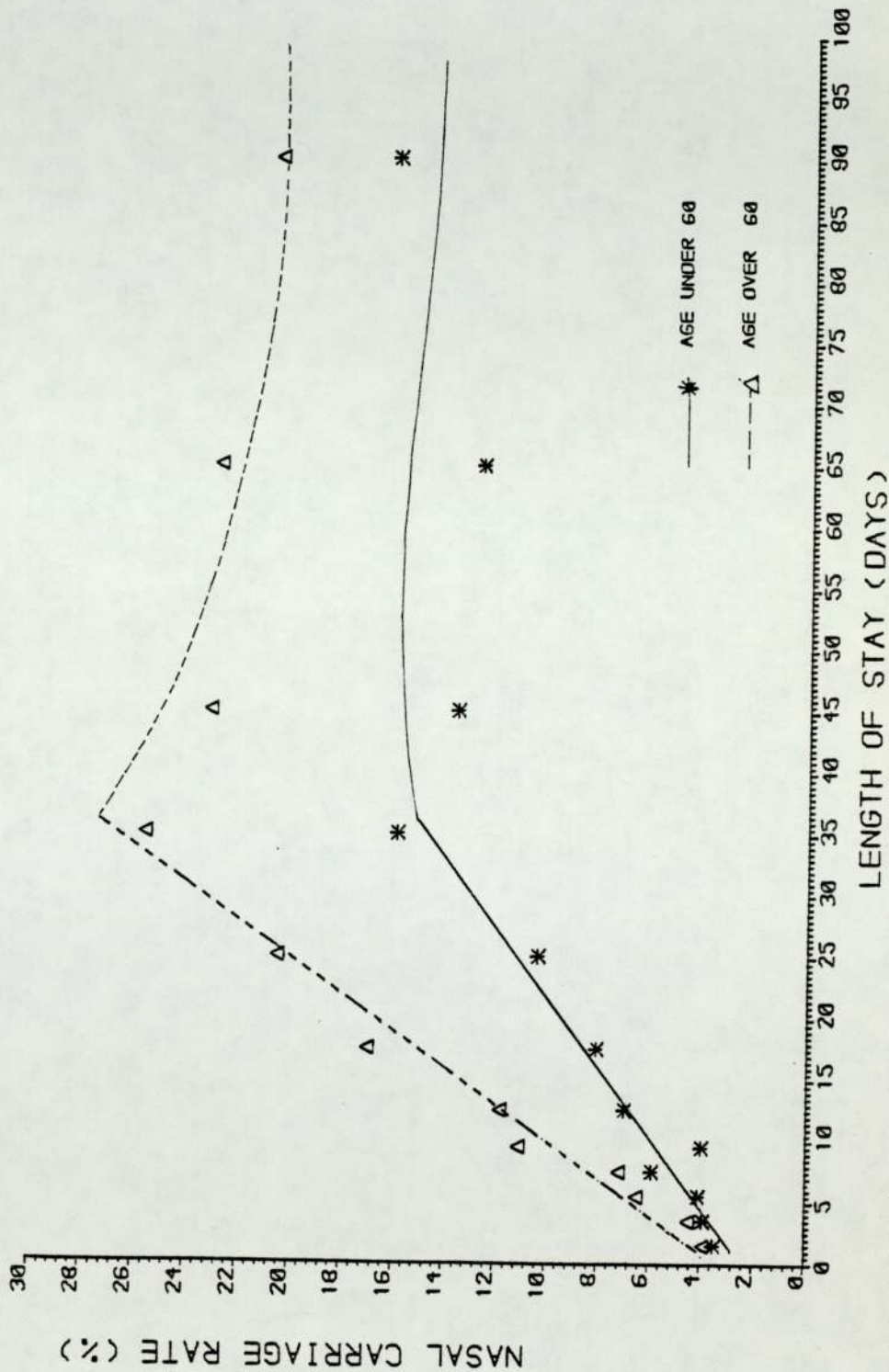
with a correlation coefficient of 0.991.

6.4.3 Operation, Length of Stay and Nasal Carriage Rate

In Chapter 4, a higher carriage rate was reported for operated patients than for non-operated patients. Since operated patients may stay longer in hospital, the distribution of operated patients in different length of stay groups may have influenced the observed relationship. To investigate this possibility, patients were classified into operated and non-operated groups and were further classified in terms of the length of stay categories previously described (Table 25).

Both the operated and non-operated groups reached a plateau around the 30 - 40 day group, after a linear increase in carriage rate, which confirms that the observed relationship between nasal carriage and length of stay is free from any bias arising from the distribution of operated and non-operated patients in different length of stay groups. The association between nasal carriage and length of stay for operated and non-operated groups is represented graphically

FIGURE 11



in Fig. I2. The regression equation for the operated patient group is:

$$YN = 1.29 + 0.575T,$$

with a correlation coefficient of 0.99

For the non-operated patient group the regression equation is:

$$YN = 2.3 + 0.504T,$$

with a correlation coefficient of 0.98.

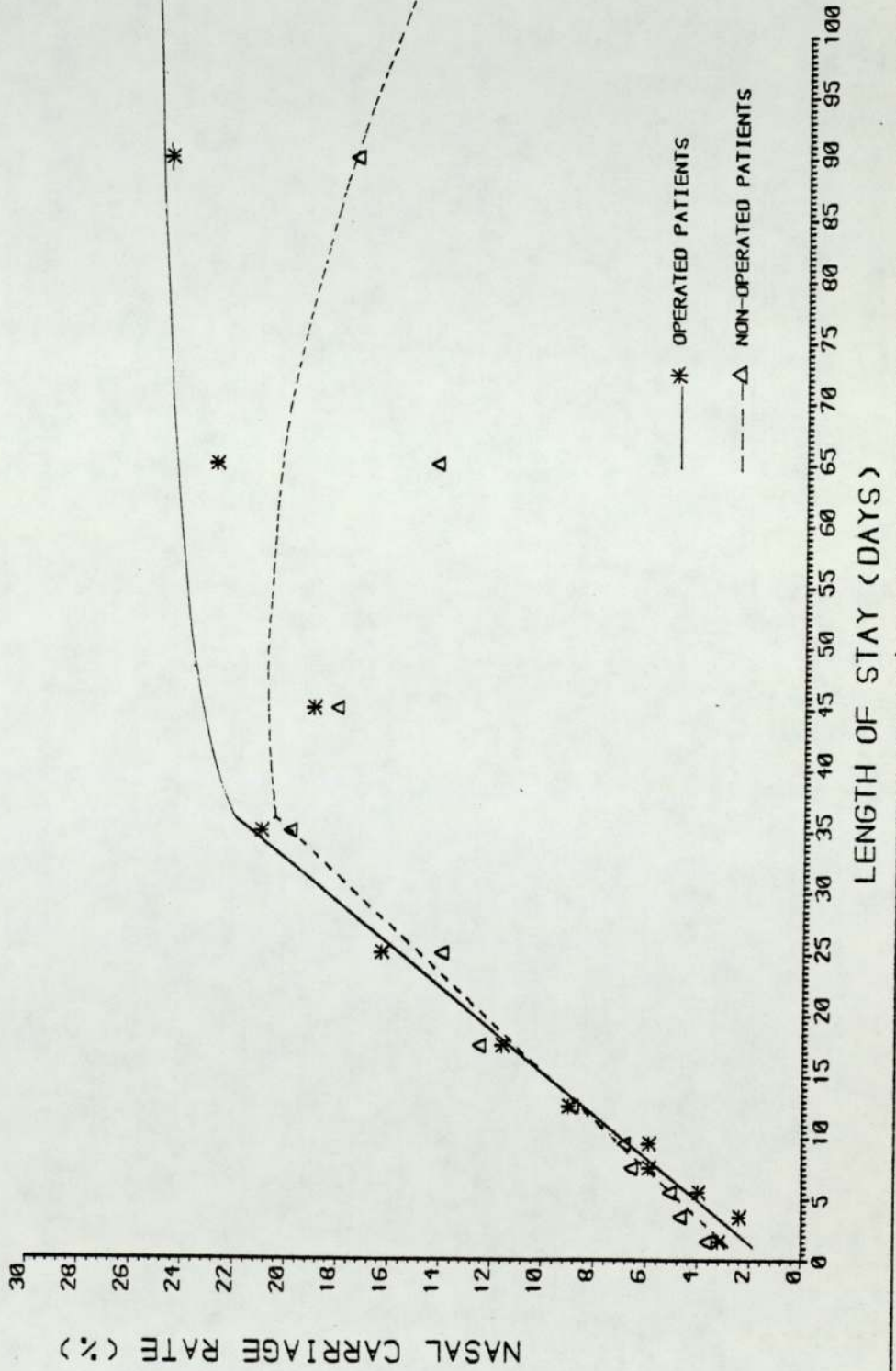
Table 25. Operation, Length of stay and nasal carriage rate.

Days in hospital	Operated		Non-operated	
	%	No	%	No
I - 2	3.2	532	3.7	1830
3 - 4	2.4	458	4.7	1059
5 - 6	4.0	423	5.1	783
7 - 8	5.9	440	6.6	602
9 -10	5.9	340	6.9	418
11-15	9.0	577	8.9	811
16-20	11.6	328	12.5	464
21-30	16.3	380	14.0	536
31-40	21.0	195	19.9	251
41-50	19.0	126	18.1	149
51-80	22.8	193	14.3	203
Over 80	24.6	167	17.5	451
Total	9.4	4159	8.2	7557

6.4.4 Age, Sex, Operation, Length of Stay and Nasal Carriage Rate.

Although the association between length of stay and nasal carriage has been established free from any bias

FIGURE 12



arising from age, sex or operation, it is possible that some interactions between these three factors could introduce some bias. To exclude this possibility the two major age groups under 60 and over 60 were classified into operated and non-operated age groups, and these categories were further classified into male and female groups. The nasal carriage rates for each length of stay group in all these categories were calculated. The relationship between nasal carriage and length of stay (i.e. reaching a stabilised state after a linear increase in carriage rate upto 30 - 40 day group) was strikingly similar in all these categories under study. The operated and non-operated division in the 0 - 59 age group is illustrated in Fig. I3, and in the 60 and over group illustrated in Fig. I4. The male and female carriage rates in these categories followed similar relationships. These observations confirm that the observed relationship between nasal carriage and length of stay is independent of factors such as age, sex, and operation or from any interaction of these factors.

6.5. Sex of Patient

The overall nasal carriage rate for male patients (9.3%) was significantly higher than the female (8.0%) carriage rate ($\chi^2 = 6.3$, 1 D.F., $P < 0.025$). As was seen in Table I7, the male carriage rate was higher in all age groups, except in the under 10 year old group. When the age under 60 and over 60 division was made, the difference between male and female carriage rates was significant in the over 60 group, but in the 0 - 59 group, although the male carriage rate was higher, the difference was not statistically significant. In both the operated and non-operated divisions

FIGURE 13

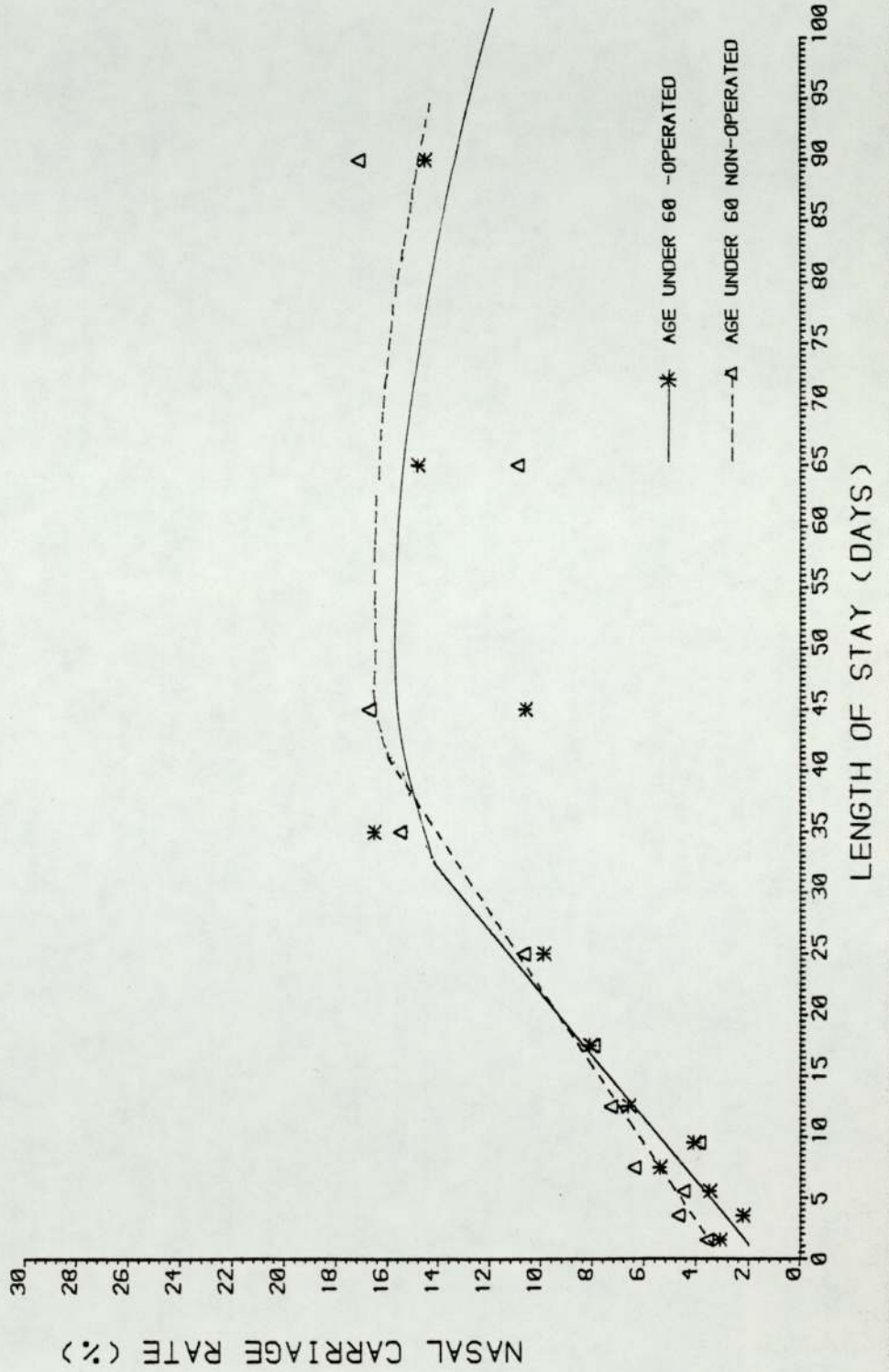
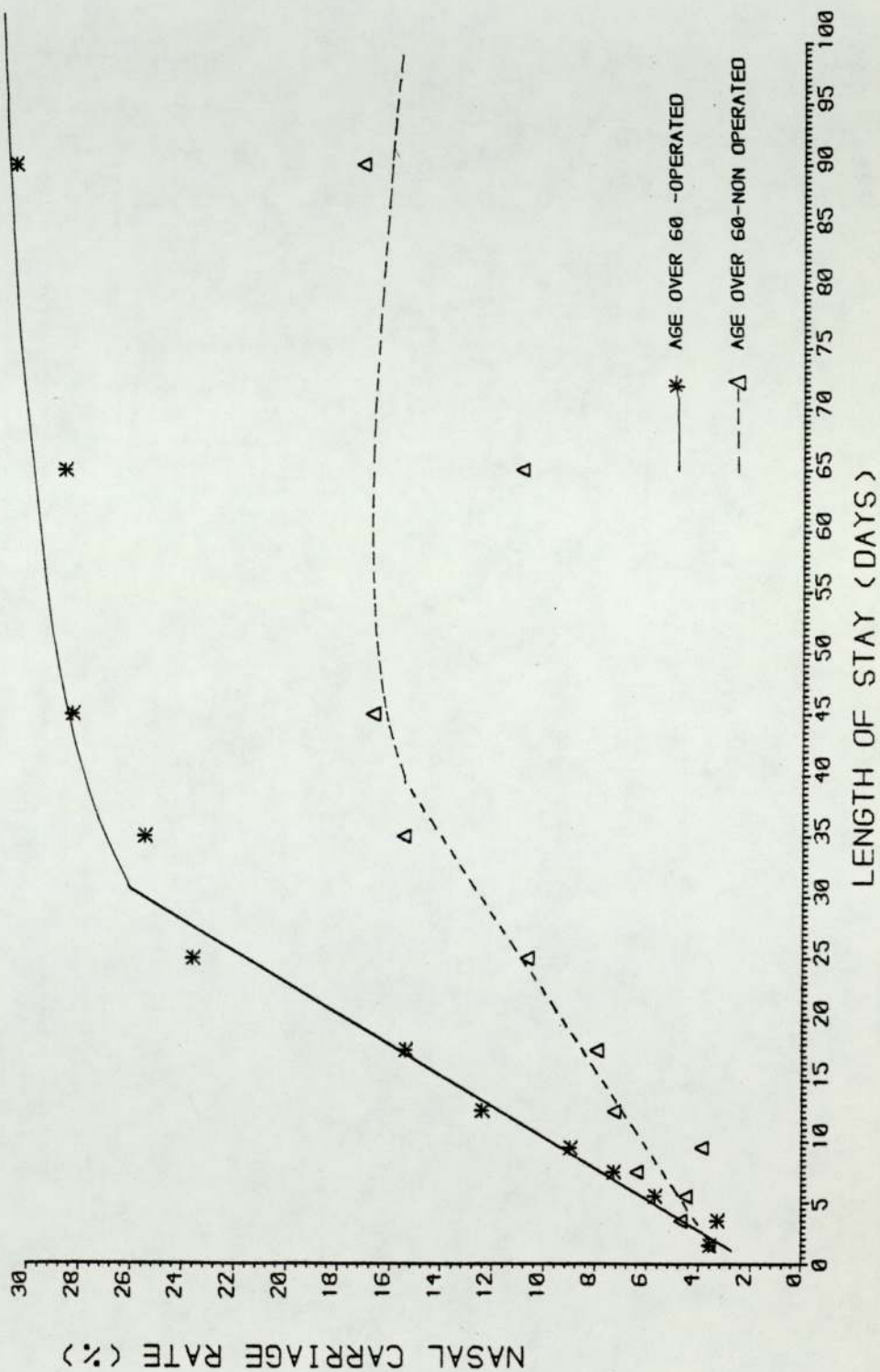


FIGURE 14



male patients had a higher carriage rate, but the difference was statistically significant only in the operated group. The higher male carriage rate could not have been an effect of any differences in length of stay, because the mean length of stay for male patients (15.5 days) was lower than the mean length of stay for female patients (18 days). Further, as was shown in Table 23, the male carriage rate was higher in almost all length of stay categories (except in the 3 - 4 day and 51 - 80 day categories). When the effect of antibiotics are considered, male patients receiving antibiotics had a significantly higher carriage rate. In the no-antibiotic group male patients had a higher carriage rate but the difference was not significant. The male and female carriage rates for different patient categories are given in Table 26.

Table 26. Sex of patient and nasal carriage rate.

	%	Male	Female	x ²	Significance
		No	%		
All patients	9.3	5323	8.0	6393	6.3 Sig(P < 0.025)
Age under 60	6.6	3497	5.6	4098	3.4 NS (P > 0.9)
Age over 60	14.6	1826	12.4	2295	4.1 Sig(P < 0.05)
Operated	10.6	1966	8.4	2193	6.0 Sig(P < 0.025)
Non-operated	8.6	3357	7.8	4200	1.4 NS (P > 0.75)
Antibiotics	12.8	1620	7.8	1502	5.0 Sig(P < 0.025)
No antibiotics	7.8	3703	7.3	4891	0.7 NS (P > 0.5)

Sig - Significant

NS - Not significant

CHAPTER 7

DISCUSSION ON THE IMPLICATIONS OF THE SURVEY ANALYSIS

7.1 Primary Analysis

The primary analysis confirmed the significance of operative parameters such as type of wound (clean Vs. contaminated), insertion of a drain, pre-operative length of hospitalisation and type of patient as significant determinants of the incidence of wound infection. Similar observations were made in the N.R.C. (41) study. The wound infection rates for different types of drains reported here further emphasise the relationship between certain aspects of operative techniques and wound infection. Out of the 906 wound swabs taken 24 per cent showed signs of Staphylococcal wound colonisation, and over half of these staphylococci were resistant to antibiotics (other than penicillin). The study confirmed that the incidence of staphylococci wound infections was now reduced when compared with earlier studies (P.H.L.S, 3) and these are replaced by gram-negative bacilli.

The nasal carriage rate of 8.6 per cent in this study confirmed the presence of antibiotic resistant strains of Staph.aureus in hospital environments at the time of the survey. The higher carriage rate reported in operated patients may be due to their lowered resistance. The relative nasal carriage and wound infection rate showed a striking similarity when the patients were classified into types of patient (Table 5 and 8). In both these tables low nasal carriage and wound infection rates were observed among obstetrics and high rates among geriatrics. This similarity adds further confirmation to the usefulness of using nasal carriage rate as a possible measure of hospital infection.

7.2 Patient Parameters and Wound Infection

7.2.I Age and Wound Infection

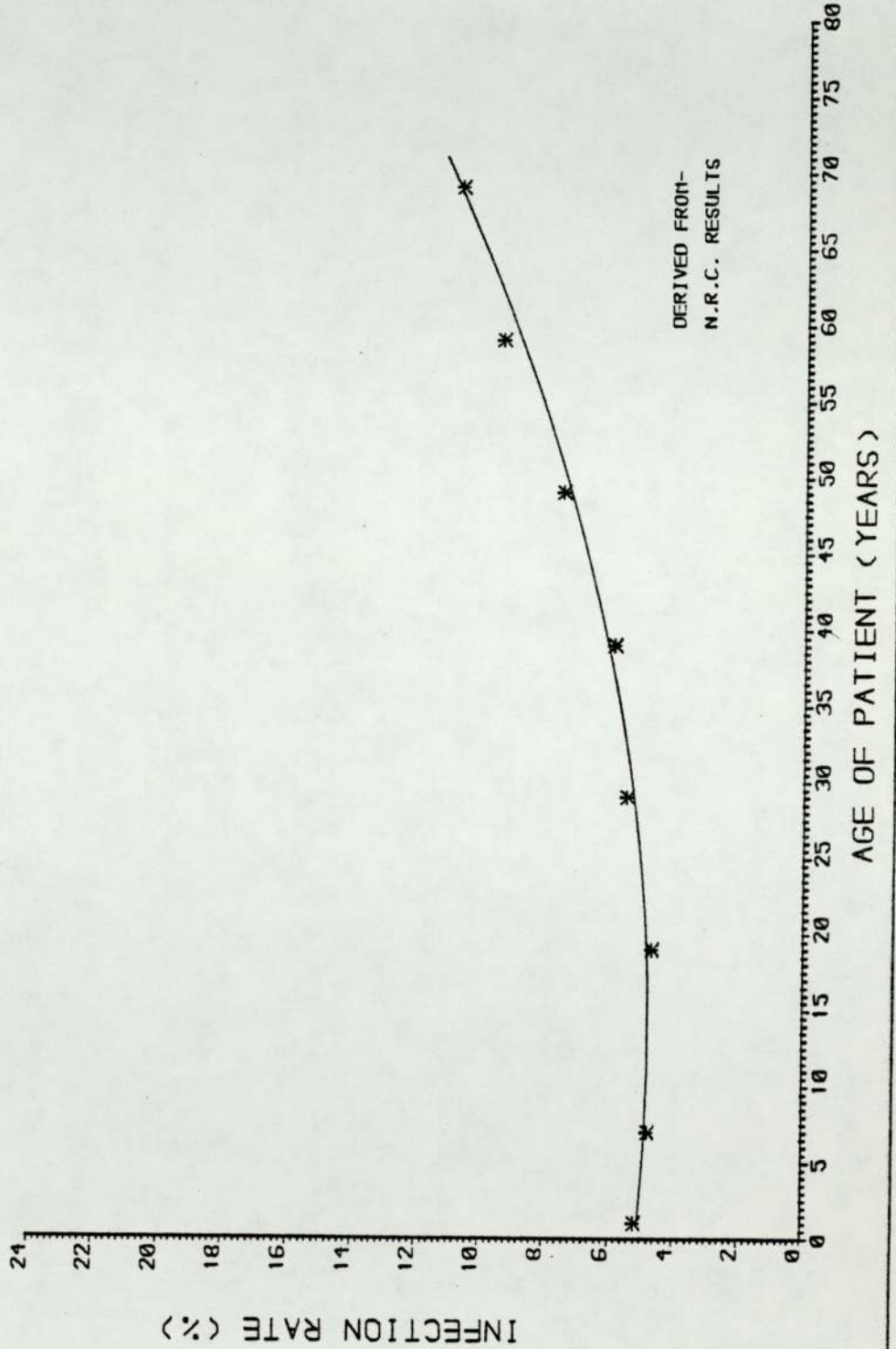
The significance of patient age on wound infection as reported by others (41,45,67,106) was confirmed in this study. This study differs greatly from those previous studies in that attempts were made to quantify the significance of age. The quadratic curves were very good fits to the observed results. Using the quadratic equations derived, it is possible to evaluate the probability of acquiring an infection at any given age. The constant 'A' in the quadratic equation of the form $Y = A - BX + CX^2$ can be considered as a measure of the ward or theatre contamination factor, which is quite independent of any age effects. The other constants B and C are related to the age. If this concept is generally true, then the constant A would vary to a certain extent from hospital to hospital, and the constants B and C to a lesser extent when population characteristics (National, Regional or Racial) are changed. However, in a given period of time these constants can be assumed to be constant in a particular hospital.

Confirmation on the concept of quadratic age curves can be obtained from the N.R.C. (41) survey, which is one of the largest control surveys carried out on post-operative wound infection. When the N.R.C. results were subjected to similar curve fitting techniques by the author, a quadratic appeared to be the best fit for the data. The equation was:

$$Y = 5.1 - 0.05X + 0.0019X^2 \quad (\text{SSD} = 0.41)$$

The N.R.C. results and the fitted curve are illustrated in Fig I5. This confirms the quadratic nature of the age curve developed here. The constants in the N.R.C. curve are

FIGURE 15



lower than the constants in this study, indicating a much lower overall infection rate for all ages. However, this could also be due to differences in the definitions of wound infections.

7.2.2 Sex of Patient

An in-depth investigation on the significance of the sex of patient on wound infection rate was carried out, mainly because this is one of the problems that was not adequately resolved in the literature survey. Male patients had a significantly higher infection rate in contaminated and clean-contaminated wounds, and although females had a higher infection rate in clean wounds the difference was not significant. Similar observations were made by the N.R.C. (41) study, which attributed the difference between male and female infection rates to the greater proportion of contaminated wounds among males. The significantly higher male infection rate was independent of the presence of wound drains or type of drain. As a further criterion, the pre-operative stay in hospital was compared for the two groups, and the distribution of patients according to pre-operative stay was similar in both groups, which excluded the possibility of a bias arising from differences in pre-operative stay in hospital. The comparison of infection rates in operations common to both males and females also confirmed that males have a higher rate of infection.

7.3 Patient Parameters and Nasal Carriage

The quadratic nature of the relationship between age and nasal carriage rate was clearly evident, and this curve was similar to the quadratic relationship between age and wound infection rate described in Chapter 5. Further, the point of minimum carriage rate (23.5 years) was similar

to the point of minimum wound infection rate (26 years), which reflects the closeness of the two relationships. The relationship between age and nasal carriage was independent of the sex of patient, but as was expected, the quadratic curve for male patients is at a higher level than the female curve. When the operated and non-operated division was made, the quadratic nature of the age function was prominent in both categories, emphasising the unbiased accuracy of the relationship between age and nasal carriage rate. Unlike the wound infection rate, there was no previous large survey such as the N.R.C. study to compare the observed relationship between age and nasal carriage, in order to ascertain further confirmative evidence. However, since it has been demonstrated that the relationship is independent of sex of patient and operation, the relationship must represent a real effect. This reflects the fact that the elderly and the very young are more susceptible to nasal colonisation with antibiotic resistant Staph. aureus.

A significant increase in nasal carriage rate was observed in the group of patients who received one or more antibiotics. This was equally true when the patients receiving antibiotics were further classified into operated and non-operated groups, which excludes the possible bias arising from the fact that antibiotics in the majority are administered to operated patients who are more susceptible. When the patients were divided into male and female groups, the significantly higher carriage rate in the antibiotic treated group still persisted. Even when interactions between operation and sex were considered, the antibiotic treated group had a significantly higher carriage rate in all groups, except in the female operated group (here too the antibiotic

treated group had a carriage rate about 2 per cent higher than the no-antibiotic group). These observations confirmed that patients treated with antibiotics have a significantly higher nasal carriage rate. When antibiotics are used sensitive strains are often removed and hence, resistant strains are selected. High carriage rates were observed in ampicillin and tetracycline treated patients, and these two antibiotics were the most commonly used. However, the increased carriage rate in the nitrofurantoin treated group was somewhat unexpected. This relationship may be due to the fact that the patients treated with nitrofurantoin and also carrying resistant staphylococci were often elderly patients who had been in hospital for longer than the average period. They also often had fractures or bed-sores, and were likely to have a urinary tract infection caused by ampicillin or sulphonamide-resistant organisms. The association between antibiotic therapy and nasal carriage has been demonstrated by many others(8,24,48,55).

The nasal carriage rate increases with length of stay in hospital linearly upto about the 30 - 40 days in hospital, and then reaches a stabilised state. This relationship prevailed when the analysis was extended to the following groups: male or female , age under 60 or over 60 and operated or non-operated. Each group reflected the significance of its own parameter (e.g. in the case of age group, under 60 group showed a lower carriage rate in every length of stay category), as well as demonstrating the significance of the carriage rate reaching a stabilised state after a linear increase upto the 30 - 40 days stay in hospital. The possibility that some interaction between these groups being responsible for the

observed relationship was excluded after further analysis. The linear increase in carriage rate with length of stay is somewhat easy to explain because the exposure to the microorganisms increases with increasing length of stay in hospital, but the stabilised state after the linear increase is somewhat puzzling. One explanation is that an exposure of 30 - 40 days is more than sufficient to induce an acquisition to a possible susceptible patient, which in other words mean that all the susceptible patients would acquire a strain within the first 40 days in hospital. Another explanation is that the true situation is overshadowed by the bias arising from relatively small sample sizes present in the length of stay groups over 40 days. The first explanation is more likely, because although the sample sizes are relatively (related to sample sizes in the survey) small, they are large enough compared with the sample sizes in many other studies. A third possible bias may arise from the very nature of the survey methodology (i.e. cross-sectional as opposed to continuous). It is assumed that the cross-sectional survey reflects the association between nasal carriage and length of stay in a closed patient environment. Although this assumption can be true in the early length of stay groups, some inaccuracy may be built into latter length of stay groups due to the fact the patients in a group are made up of patients from many different wards.

In the past, others have reported nasal carriage rates in different length of stay groups, but most of them were limited to 5 - 9 weeks stay in hospital, probably due to the problem of securing a large enough sample beyond this period. The linear increase in carriage rate was clearly evident

in all of the studies reporting the association between carriage of resistant strains and length of stay in hospital (24,28,45,48,55,63,64,99). In the majority of these studies the maximum carriage rate was observed around the fifth or sixth week in hospital. Linear regression equations can be fitted with great accuracy to most of these observed carriage rates. These reports based on continuous studies confirmed the observation made from this cross-sectional survey, i.e. a linear increase in carriage rate upto the 30 - 40 days in hospital. The concept of reaching a stabilised state after this period cannot be confirmed from other sources, because the reported carriage rates were often limited to the sixth week in hospital. However it can be concluded from a continuous study by LIDWELL et al. (100, S=4300) extending over 19 weeks that the carriage rate reaches a plateau after a linear increase upto the 45 days in hospital (as was experienced in this study), which was followed by a further rise in the rate of nasal carriage upto as high as 40 per cent when the duration of stay in hospital exceeded 130 days. But in this study, a great majority (over 78%) of patients staying over 6 weeks in hospital were over 60 years old, hence the implication of the reported further rise in carriage rate after the 85 days stay may be overshadowed by the age effect.

Male patients demonstrated a higher carriage rate in all categories under study, although the difference between the male and female carriage rates were not significant in the age under 60, non-operated and no-antibiotic groups. This may infer that the higher male carriage rate becomes more profound in the presence of other adverse factors such as age over 60, operation and antibiotic therapy.

The mean length of stay in hospital for female patients was about 20 per cent higher than the male mean length of stay. Due to this excess exposure to the ward environment, female patients should have reflected a higher nasal carriage rate, but the opposite was true. These observations may indicate that, since the observations are free from any bias arising from combinations of other associated factors, the difference between male and female carriage rate is a real effect. The reason for this lower carriage rate in females is uncertain. Lower carriage rate for female patients has been reported before (24). Other reports such as men disseminating more staphylococci than women(III), lower settle plate counts when a ward was occupied by female patients (25) and new-born males being more susceptible to staphylococci skin infections (II2), may offer some explanation. It may also be likely that the different texture of the skin in males and females has a bearing on the differences in carriage and dispersal.

7.4 Implications

From this analysis, age , sex, length of stay in hospital and exposure to antibiotics appeared as significant parameters related to the risk of nasal colonisation of resistant staphylococci. The significance of these four parameters in this analysis was derived in isolation, without accounting for the relative significance of each parameter. A multiple regression analysis would be useful in determining the relative significance of these parameters. If these parameters could contribute to a higher multiple correlation coefficient in the regression analysis, it would be possible to formulate a regression model based on these four parameters, which

can be used as a measure of the susceptibility to nasal colonisation of a patient or a patient population. Since nasal colonisation can be used as a measure of ward cross-infection and the fact that in Chapter 5, age and sex were associated with the risk of wound infection, such a model can also be used as a measure of the risk of wound infection.

Important conclusions can be derived from this analysis on the effectiveness of cross-sectional surveys as an aid in epidemiological studies. Although the cross-sectional surveys are based on random samples, the comparability of the results in this study with other reports based on continuous studies, shows the ability of cross-sectional studies to depict reality. The age and wound infection curve was similar to the one derived from a continuous study, and the length of stay curves were similar to curves reported in many continuous studies. Now, since it has been established that cross-sectional surveys are capable of mimicking reality, such surveys should be extensively used in epidemiological studies, particularly due to the speed at which large samples can be collected from cross-sectional surveys.

PART - II

MODELS

CHAPTER 8

MULTIPLE REGRESSION ANALYSIS

8.I Introduction

The analysis carried out in Part I, established the significance of certain patient parameters on wound infection and nasal carriage. This analysis however, does not give an indication of the relative significance of individual parameters on infection and carriage. Further, the results may be biased if there are correlations between certain parameters. For example, if the majority of male patients have undergone contaminated operations, since wound contamination is a significant parameter associated with wound infection, male sex would also result as a significant parameter. These shortcomings in the analysis carried out in Part I can be rectified with the aid of statistical techniques.

Multiple regression analysis is the most commonly used technique in determining the relative significance of a number of independent variables. A correlation matrix can be used to examine the possibility of high correlations between variables which may introduce a bias into the analysis. In the data the infection and carriage rates are defined as categorical (non-metric) variables, having one of two values, infected (carrier) or not infected (non-carrier), corresponding to the value of 1 or 0. Multiple regression is not ideally suited for this kind of data, because at best the multiple regression coefficient would be 0.5. However, this categorical dependent variable can be transformed into a canonical (metric) variable by grouping the data, which would

then be suitable for multiple regression analysis. To perform this transformation, patients were categorised into groups containing combinations of patient parameters, and infection and carriage rates were calculated for individual groups. These transformed data were then used in the regression.

8.2 Multiple Regression Applied to Wound Infection

To carry out the regression, four independent parameters were chosen. These are patient's age, sex, wound drainage and type of wound (classified as clean, contaminated or clean-contaminated). Age was classified into 7 groups varying from I - 70 years with a class interval of 10 years and the mid-points of the class taken as the age. 96 groups were formed from the 12 combinations of the variables sex, wound drainage and three wound classifications; and the classification of these groups into age combinations. Infection rate for each group was calculated. The number of patients in each group was used as a weighting factor in the regression analysis, which would counteract any bias arising from unrepresentative infection rates derived from small sample sizes.

$$Y = a + b_1X_1 + b_2 X_2 + b_3X_3 + b_4X_4 + b_5 X_5$$

Before carrying out the regression, a mutually exclusive set of variables must be established to represent the patient parameters. Since age is a canonical variable it can be represented as the linear variable X_1 , but the categorical variables sex, wound drain and wound classification cannot be represented in a similar manner. In representing these parameters, a variable can be given the value 1 when the variable is in one state, and the value 0 when the variable is

in the other state. For male sex the variable X_2 can be given the value 1, and for female sex the value 0. Similarly, the variable X_3 can be assigned the value 1 for drained wounds and the value 0 for undrained wounds. Since the wounds are classified as clean or contaminated or clean-contaminated, at least two variable are needed to represent these three types of wound descriptions. The variable X_4 can be assigned the value 1 for contaminated wounds and the value 0 for any other state, and the variable X_5 the value 1 for clean-contaminated wounds and the value 0 for any other state. Then, where X_4 and X_5 both take the value 0, it would represent a clean wound.

Table 27. Correlation Matrix - Wound Infection

	Age	Sex(M)	Drains	Contam	Clean- Contam	Clean
Age	1.0	-0.05	0.19	-0.06	-0.04	-0.01
Sex (M)	-0.05	1.0	-0.05	-0.03	0.27	-0.13
Drains	0.19	-0.05	1.0	0.18	0.05	-0.30
Contam.	0.06	-0.03	0.18	1.0	-0.18	-0.46
Clean-Contam.	-0.04	0.27	0.05	-0.18	1.0	-0.66
Clean	-0.01	-0.13	-0.30	-0.45	-0.66	1.0
Infection rate	0.17	0.20	0.53	0.63	0.21	-0.63

The correlation matrix in Table 27 shows that there is not a high correlation between the variables age, sex wound drainage and wound description. This observation confirms that the significant parameters on wound infection isolated in the analysis in Part I, is free from any bias arising from interactions (correlations) between the variables. Since, there are no high correlations between the variables, the results of the regression analysis would not have any inbuilt bias.

Table 28. Multiple Regression Analysis on Wound Infection I

Variable Name	Regression Coefficient	t Statistic	Part Correlation
Age	0.079	3.5	0.34
Sex(M)	3.302	2.0	0.21
Drains	11.529	6.4	0.56
Contam.	27.707	9.89	0.72
Clean-contam.	10.193	4.63	0.44

Multiple correlation = 0.923.

Model:

$$Y = 0.079 \times \text{Age} + 3.302 \times \text{Sex} + 11.529 \times \text{Drains} + 27.707 \times \text{Contam} + 10.193 \times \text{Clean-contam}.$$

The result of the regression analysis using the variables age, sex, wound drainage and wound description, is shown in Table 28. The 't' statistic is the ratio between the regression coefficient and its standard error, and this can be used to test the regression. A variable with a 't' statistic greater than 1.96 is statistically accepted to be significant. When this criterion is applied, all the variables in the regression are significant. Further, the multiple correlation of 0.923 in the regression is extremely high, which further confirms that these four variables largely determine the risk of post-operative wound infection.

The analysis in Table 28 however, does not include a separate coefficient for clean wounds. The regression coefficient for clean wounds is included as a function of the coefficients for age and sex. A separate regression coefficient can be attributed to the variable clean wounds by introducing a constant to the regression equation. When the variables

X₄ and X₅ are both zero (i.e. clean wounds), the constant in the regression equation would represent the regression coefficient for clean wounds. Table 29 shows the result of the regression analysis when the constant is used. Although this modification has improved the multiple correlation slightly (from 0.923 to 0.924), the regression coefficients for the constant, age and sex are not significant now, since the 't' statistics for these variables are less than 1.96.

Table 29. Multiple Regression Analysis on Wound Infection 2.

Variable Name	Regression Coefficient	t Statistic	Partial Correlation
Constant	2.749	1.27	0.13
Age	0.043	1.22	0.13
Sex	2.499	1.42	0.15
Drains	11.275	6.25	0.55
Contam.	27.428	9.79	0.72
Clean-contam.	9.824	4.44	0.42

Multiple correlation = 0.924

Model:

$$Y = 2.749 + 0.043 \times \text{Age} + 2.499 \times \text{Sex} + 11.275 \times \text{Drains} + 27.428 \times \text{Contam.} + 9.824 \times \text{Clean-contam.}$$

These regression models can be used to determine the probability of acquiring an infection in hospital. When the parameter values are fed into the model, it calculates the probability of acquiring an infection. The model is also a measure of the relative significance of individual patient parameters. The most significant parameter is wound contamination, followed by drainage and clean-contamination.

The significance of age even at 70 years is much less than the significance of these parameters, and for certain age groups the effect can even be smaller than the effect of male sex.

8.3 Multiple Regression Applied to Nasal Carriage

The initial analysis indicated that age, sex, length of stay in hospital and exposure to antibiotics, are associated with the nasal carriage of Staph.aureus. These four parameters are now used in the multiple regression analysis. Since age and length of stay are linear variables, age was classified into 8 groups and each of these groups was classified into 12 length of stay groups, making a total of 96 groups. These groups were further classified into sex and antibiotic groups, making a final total of 384 groups for analysis. 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 generated from small group sample sizes.

$$Y = b_1X_1 + b_2X_2 + b_3X_3 + b_4X_4$$

In performing the analysis the variables X_1 and X_2 were assigned to age and length of stay. 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 correlation matrix is shown in Table 30. None of the correlation coefficients between the four patient parameters is large enough to introduce any bias into the relationship between the carriage rates and the parameters.

Table 30. Correlation Matrix - Nasal Carriage.

	Age	Days	Sex	Antibiotics
Age	1.0	0.26	-0.01	0.04
Days	0.26	1.0	-0.05	-0.03
Sex	-0.01	-0.05	1.0	0.00
Antibiotic	0.04	-0.03	0.00	1.0
Carriage rate	0.42	0.56	0.1	0.16

Table 31. Multiple Regression Analysis on Nasal Carriage-I

Variable Name	Regression Coefficient	t Statistic	Partial Correlation
Age	0.087	9.06	0.42
Days	0.187	12.22	0.53
Sex	1.816	2.88	0.15
Antibiotics	2.826	4.01	0.20

Multiple correlation = 0.852

Model:

$$YN = 0.087 \times \text{Age} + 0.187 \times \text{Days} + 1.816 \times \text{Sex} + 2.826 \times \text{Antibiotics.}$$

The result of the multiple regression analysis is shown in Table 31. All the regression coefficients are statistically significant as the 't' statistics are considerably greater than 1.96 and the multiple correlation of 0.852 is high, which confirms the goodness of the fit. From the regression model it is evident that exposure to antibiotics and male sex contribute more to the risk of nasal carriage than age and length of stay in hospital. But for age over 30 years and length of stay over 15 days, the contribution

of exposure to antibiotics and male sex towards the risk of becoming a nasal carrier becomes less important when compared with age and length of stay.

Table 32. Multiple Regression Analysis on Nasal Carriage -2

Variable Name	Regression Coefficient	t Statistic	Partial Correlation
Age	0.022	0.75	0.04
Age ²	0.0009	2.33	0.12
Days	0.187	12.26	0.53
Sex	2.295	3.48	0.18
Antibiotics	3.177	4.43	0.22

Multiple correlation = 0.854

Model:

$$YN = 0.022 \times \text{Age} + 0.0009 \times \text{Age}^2 + 0.187 \times \text{Days} + 2.295 \times \text{Sex} + 3.177 \times \text{Antibiotics}.$$

The regression model developed in Table 31 only considers age as a linear variable. The analysis in Part I indicated that the age curves are quadratic, which implies that an age term as well as an age-square term jointly determines the observed relationship. Hence an age-square term was introduced to the regression model, and the resulting regression is shown in Table 32. The addition of the age-square term slightly increased the multiple correlation from 0.852 to 0.854. All the regression coefficients except the coefficient for age, are statistically significant.

The two regression models so far discussed were deliberately forced through the origin in order to determine the significance of the major parameters. This is somewhat

artificial because both the models intersect the carriage rate axis at the origin. It is more likely that the intersect is at a constant distance away from the origin. The constant may also account for the significance of other parameters on nasal carriage quite unrelated to the patient parameters. Therefore, a constant term was introduced to the regression as shown in Table 33. The addition of the constant again slightly increased the multiple correlation. The regression coefficients for the constant, age and age-square is non-significant. The introduction of the constant term has also made the age coefficient negative. When the constant, age and age-square terms are taken together, they represent a quadratic function, quite similar to the quadratic age curves experienced in Chapter 6. Therefore, although the coefficients of these three parameters are not significant when taken separately, they represent the quadratic curve when taken together, and hence, the coefficients may well be significant when considered as a joint single function.

Table 33. Multiple Regression Analysis on Nasal Carriage -3

Variable Name	Regression Coefficient	t Statistic	Partial Correlation
Constant	0.642	0.51	0.03
Age	-0.0015	0.03	-0.00
Age Square	0.0011	1.93	0.10
Days	0.185	11.87	0.52
Sex	2.217	3.27	0.17
Antibiotics	3.127	4.32	0.22
Multiple correlation = 0.855			
Model: $YN = 0.642 - 0.0015 \times \text{Age} + 0.0011 \times \text{Age}^2 + 0.185 \times \text{Days} + 2.217 \times \text{Sex} + 3.127 \times \text{Antibiotics}$.			

8.4 Graphical Representation of the Regression Model

The regression model derived from Table 33 can be represented graphically in a three dimensional axis system. The axis are the age, length of stay and the carriage rate (Fig. I6). A three dimensional surface can be generated from the age and length of stay components of the regression on nasal carriage rate. On the age plane a quadratic curve represents the age effect, and on the length of stay plane a linear function represents the length of stay effect. The intercept of this surface on the carriage rate axis represents the constant in the regression. This surface is based on the assumption that the other two categorical variables, sex and antibiotics, have taken the value 0. The graphical model can now be modified to account for the other states of the variables, sex and antibiotics. When these parameters are present, the surface would be shifted upwards, which in effect increases the value of the constant by the coefficient of the variable. Therefore, for the four combinations of sex and antibiotics (male antibiotic, male no-antibiotic, female antibiotic and female no-antibiotic), four surfaces similar in nature but shifted by a constant from each other, would result. This is shown in Fig. I6A.

8.5 Application of the Regression Model

A major objective of this study was to determine methods of correcting results of experimental studies carried out on ward and theatre parameters, for any bias arising from differences in the distribution of patient parameters. The major patient parameters related to nasal carriage and wound infection were described in Part I, and these parameters have

FIGURE 16

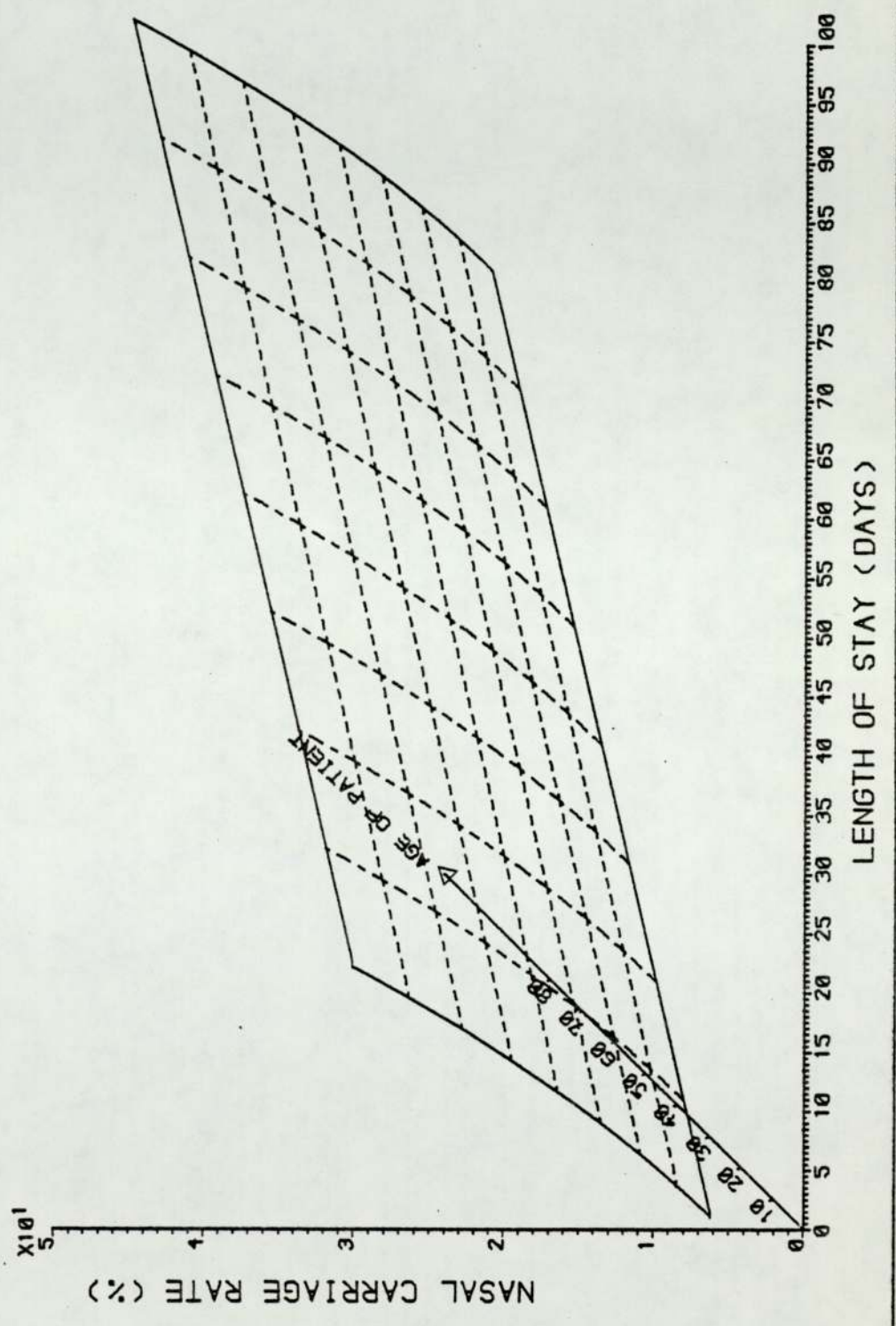
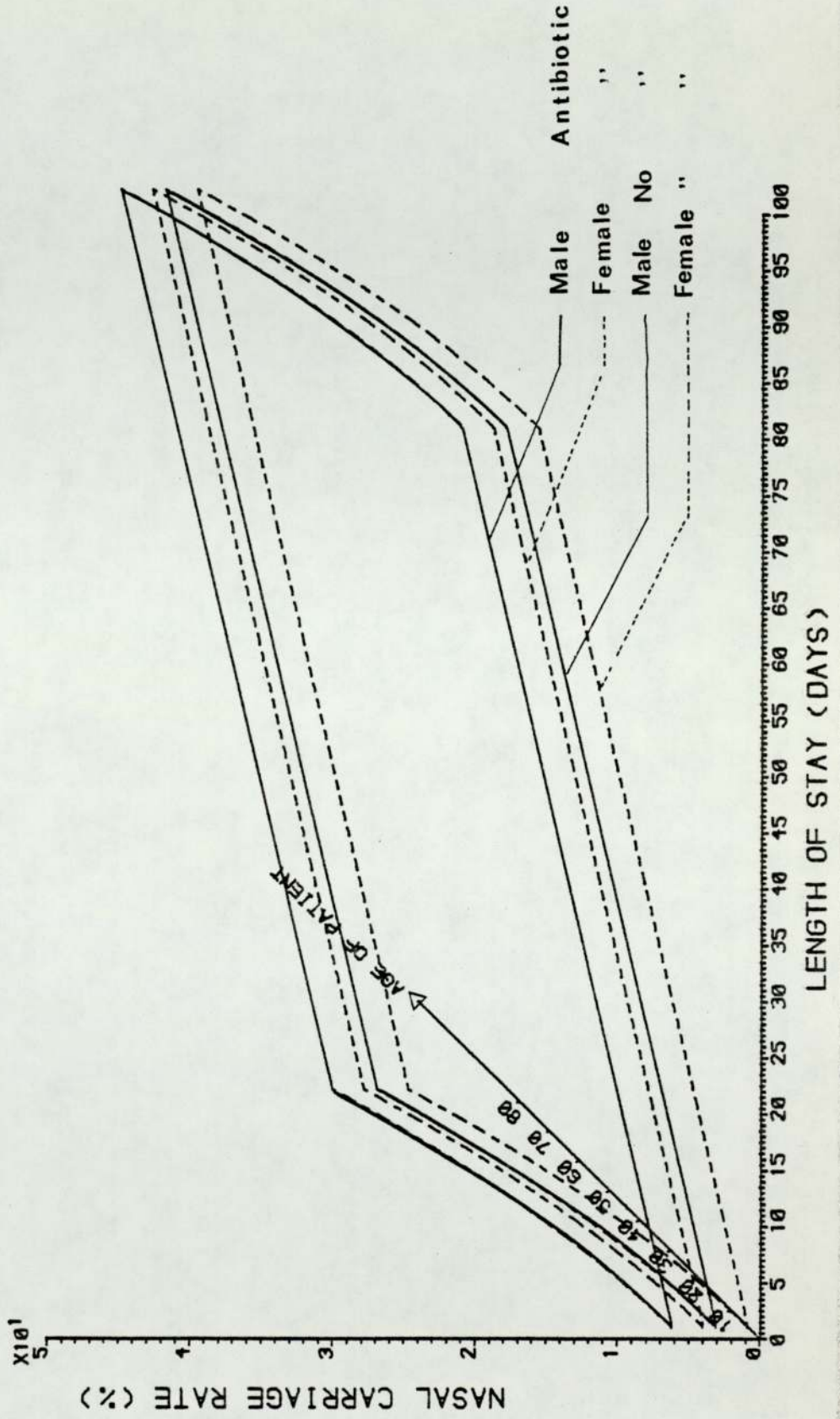


FIGURE 16 A



been incorporated into regression models in this chapter. These models can now be used to correct any experimental result for bias arising from patient parameters. For example, if a study was carried out to determine the significance of ward parameters on nasal carriage, by comparing carriage rates in two wards with differences in ward practices, the model must first be used to determine the expected carriage rates in the two wards derived purely from patient parameters. The expected carriage rate is calculated by summing up the probabilities of nasal carriage for individual patients derived from the model using each patient's characteristics such as age, sex, length of stay and antibiotic therapy and then dividing this total probability by the number of patients. The observed and expected (based on the regression model) carriage rates in the two wards can now be used to determine statistically, whether the ward parameters are significant or not.

Information regarding ward facilities, structures and practices were collected when the survey was carried out. Infection rates and carriage rates for individual wards were calculated based on the patients in each ward. Further, patients in different wards, but exposed to similar ward parameters (e.g. similar distance between beds, similar ward floors, etc) were grouped together and infection and carriage rates for these ward parameters were calculated. Although there were many differences in infection and carriage rates among different ward parameters, any straightforward conclusions derived from these figures would be invalid for the following two reasons. Firstly, the patient parameters within these groups may be different and if not corrected,

would result in biased conclusions on the significance of certain ward parameters. So, for obvious reasons, the infection and carriage rates must first be corrected for differences in patient parameters. The second reason is derived from an inherent weakness in cross-sectional surveys in determining the significance of the many ward parameters (assimilated from a large number of wards with diverse ward parameters). For example, the analysis may show that clean kitchens are associated with lower carriage rates, but it is possible that the majority of patients who were classed as being in wards with clean kitchens were also in cubicled wards. If cubicalisation is associated with low carriage rates, clean kitchens would also result as being associated with low carriage rates.

The first difficulty, the significance of patient parameters can be overcome using the regression models and calculating the expected carriage rates. However, the second difficulty cannot be overcome easily. The only possible solution is to carry out a correlation analysis between all the ward parameters in the study. The correlation analysis will indicate the similar ward parameters associated with a given group of patients. Then the corrected carriage rates (using the regression) can be interpreted empirically bearing in mind the correlations that exist between ward parameters. Such an analysis, although not very accurate, would indicate the significance of ward parameters. However, due to time constraints this further analysis could not be included in this study, and this approach is mentioned in the suggestions for further work in Chapter 13.

CHAPTER 9

PRELIMINARY MODELLING APPROACH

9.I Introduction

The patient parameters described in Part I indicated the significance of individual parameters on wound infection and nasal carriage. The information obtained from this primary analysis was subjected to a series of multiple regression analyses in Chapter 8. The resulting multiple regression equations were useful in indicating the relative significance of the patient parameters on wound infection and nasal carriage. Multiple regression is mainly a means of fitting curves through a series of observed relationships, allowing relative weighting factors to be given to each individual variable in the regression. Such analyses, however do not give any explanation of the underlying reasons for the observed relationships, i.e. the increase or decrease in carriage and infection rates in the presence of certain patient related parameters.

Parameters such as sex, chemotherapy, wound drainage and type of wound can only be one of two states corresponding to zero or unity. These parameters can be defined as step functions which would introduce a step wise increase in infection or nasal carriage rate in the presence of one or more of these parameters. The graphical representation of this concept was discussed in the regression models in Chapter 8. The reason for the increase in infection or carriage rate in the presence of these factors is somewhat self-explanatory. The presence of drains, wounds described as contaminated or clean-contaminated are all indications of different surgical procedures, which would for obvious reasons increase the

probability of infection. Antibiotics induce a step wise increase in nasal carriage rate for reasons described in previous chapters. What is unknown is the reason for the step wise increase in infection and carriage rate among male patients. This may be a result of a genetic difference between the sexes. Once the step wise functions are dealt with, we are left with two continuous functions, age and length of stay in hospital. The remainder of this chapter is devoted to devising graphical and mathematical concepts which could explain the quadratic nature of the age curves and the curvilinear nature of the length of stay curves.

9.2 Age of Patient

The relationship between age and wound infection rate may be overshadowed by many other parameters such as, type of operation and type of wound. However, the relationship between age and nasal carriage rate is unlikely to be complicated by other such parameters. Therefore, ignoring the effect of sex and antibiotics, it is fair to assume that the relationship between age and nasal carriage is the product of the relationship between age and susceptibility of the total patient population. Further, the susceptibility of the total patient population can be assumed to be the product of two age related factors. These are (a) the increase in the proportion of patients with acquired resistance to infections (due to previous exposure to the micro-organisms), with advancing age and (b) the deterioration of existing resistance mechanisms due to ageing in the total patient population.

It is likely that the majority of patients would have been exposed to most of the micro-organisms within the first few decades of life, and consequently, acquiring resistance due to the exposure. Hence the proportion of patients who have acquired resistance would increase with age, and the rate of change (i.e. slope of the curve) of acquiring resistance in the total population would decrease with advancing age. On the other hand, the deterioration of existing resistance mechanisms due to ageing is insignificant in the first few decades of life. But, the rate of change (i.e. slope of the curve) of deterioration for the total population would increase from the middle ages and would greatly increase in the old ages.

These two concepts of acquired resistance and the deterioration of resistance mechanisms can be incorporated into a graphical model to explain the observed relationship between nasal carriage rates and age. First of all it must be made clear that the relationship between age and nasal carriage rates derived in Chapter 6 is based on the characteristics of the total patient population under study. The quadratic curves derived in Chapter 6 do not depict for an individual patient the probability of becoming a nasal carrier as age increases from 1 to 80 years. The curve only predicts the probability of becoming a carrier for the majority of patients in an age group. With this concept in mind, the graphical model can now be developed.

As explained earlier, the rate of acquiring resistance to infection decreases with age for the total population. The relationship between the proportion (or percentage) of patients who have acquired resistance and age can be assumed

to be an exponential. Since susceptibility (defined as lack of resistance) is the inverse of acquired resistance, the susceptibility and age function reduces exponentially. On the other hand, susceptibility related to ageing (defined as the deterioration of existing resistance mechanisms) can be assumed to be exponential. These two curves are shown in Fig. I7. It must be emphasised again that these curves are for the total patient population as opposed to referring to individual patients. The total susceptibility curve can now be developed by adding the two susceptibility functions. As can be seen in Fig. I7, the resulting total susceptibility curve is very similar in nature to the quadratic curve shown in Chapter 6. So the assumption of two age related susceptibility functions working together in determining the possibility of nasal carriage for the total patient population is probably valid.

Further evidence on the ageing phenomenon can be derived from research on cancer. Certain incidences of cancer are age specific, where the incidence of cancer increases progressively with age. COOK et al. (II7) applied the age specific incidence rates of cancer collected by the International Union against Cancer for many cancer sites in eleven countries to the following model:

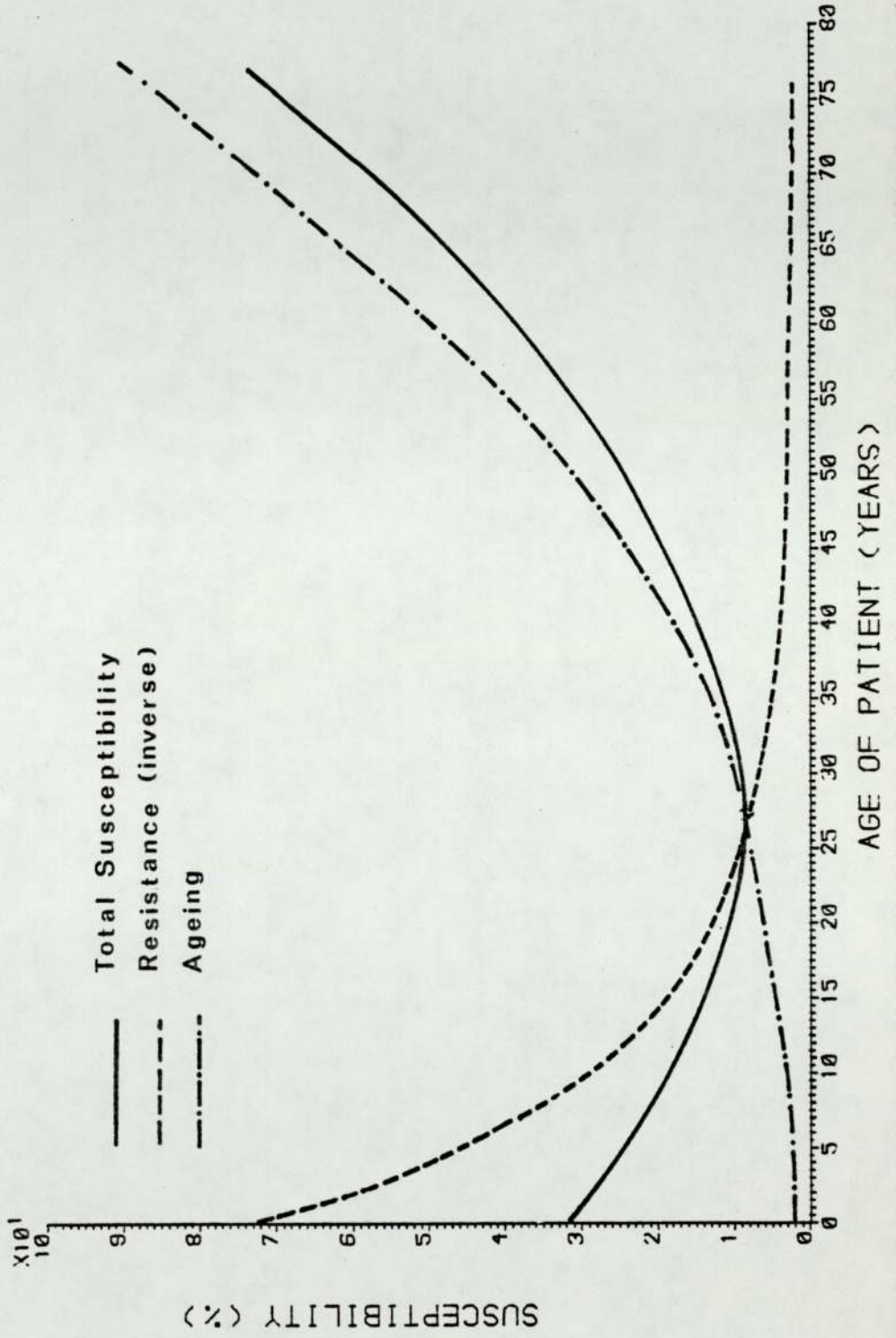
$$YX = cX^q$$

where YX is the incidence rate at age X and c and q are constants, which can be transformed to

$$\log (YX) = \log .c + q \log (X).$$

The data related to the incidence of cancer is somewhat unreliable outside the age group 30 - 80 years, because of the problem of insufficient sample sizes and the specialist

FIGURE 17



nature of cancers involved at the extremes of life. COOK et al. (117) using the log equation plotted the data between the said age group on a double logarithmic scale and as shown in Fig. 18, the age specific incidence rate in many cancer sites followed the model.

When the age related nasal carriage rates and wound infection rates experienced in this study (between the ages 30 - 70) were plotted on double logarithmic scales, both were straight lines, which confirmed the appropriateness of the above mathematical model in the area of hospital infection. The results obtained from the N.R.C. (41) study were also plotted on the same scales and this too was a straight line. These graphs are shown in Fig. 19.

9.3 Length of Stay in Hospital

There has been a number of theoretical models formulated on the epidemiology of many diseases (118,119,120,121, 122,123,124). These models are capable of estimating the expected infection rate with variation in time. The majority of these models fall into the 'deterministic' model category, which means that the future state of an epidemic is determined when the initial set of conditions is established. Since the association between length of stay in hospital and nasal carriage rate may behave similar to the epidemiology of diseases which are time dependent, these modelling concepts can be applied to the epidemiology of staphylococcal nasal carriage.

The basic deterministic models are based on the following concept. If an infected individual is introduced into a patient community of N susceptibles, since each

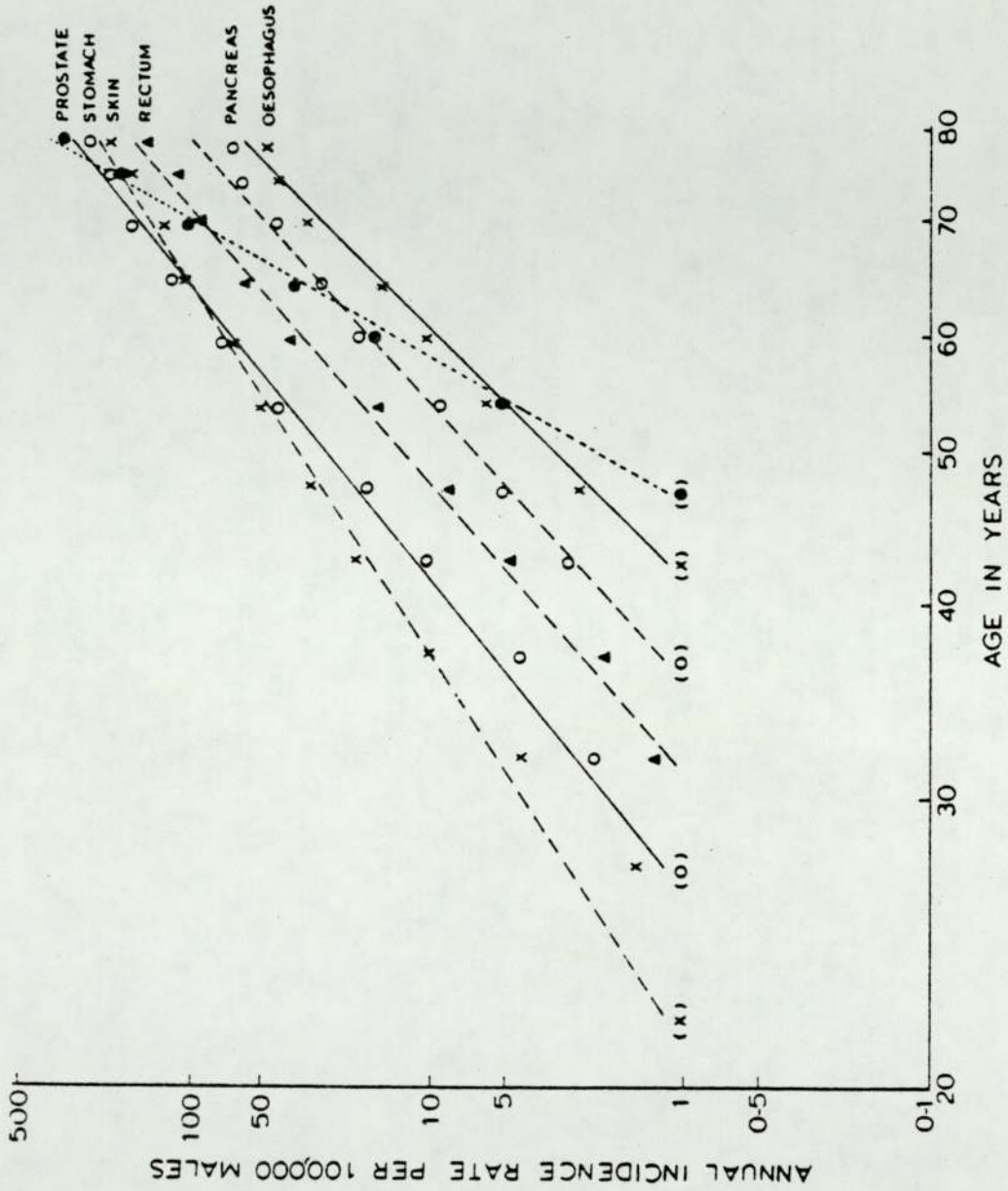
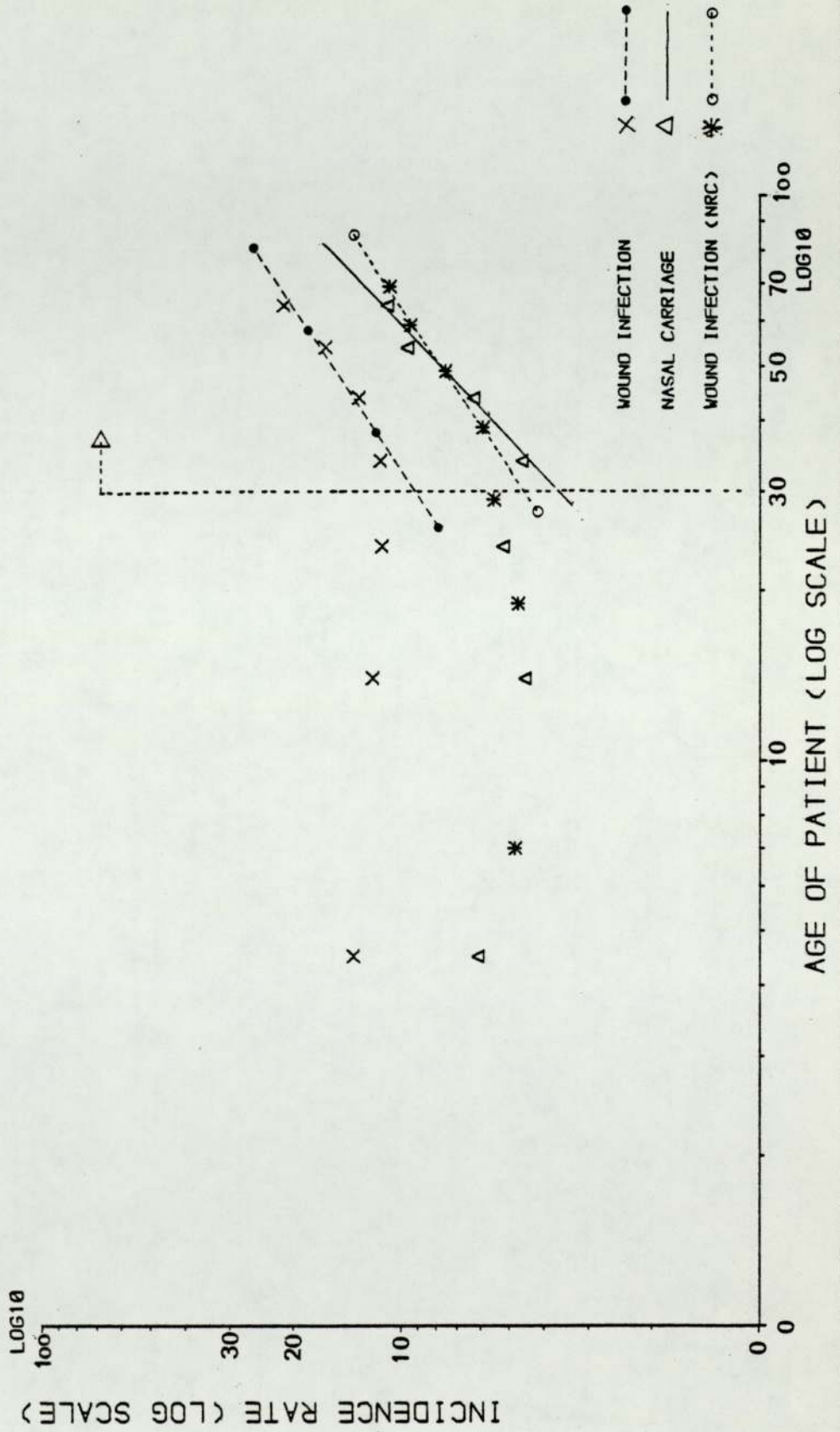


Figure 18 Annual age-specific incidence rates for cancer of selected sites among men, on logarithmic scale, England and Wales
Source: Cook, Doll, and Fellingham

FIGURE 19



patient in the community can be assumed to have a constant probability of infecting any susceptible member of the community, the number of new infections is proportional to the product of the number of infected cases and the number of susceptibles. Further, if N is large, the number of new cases per unit time can be considered to be equal to the expected proportion. Now if Z is the number of infected persons at time T and r the rate at which the interaction between one infective and one susceptible individual leads to the susceptible becoming infected, then the solution of the equation

$$\frac{dz}{dT} = rz (N - z) \dots\dots\dots (I)$$

will enable the determination of the number of infections at each variation in time. This model however, assumes that every member of the population will become infected ($z = N$ when $t \rightarrow \infty$). But the relationship between nasal carriage and length of stay in hospital that has been experienced in this study and previous studies suggests that the maximum carriage rate of resistant staphylococci rarely exceeds 30 per cent. This indicates that the proportion of patients susceptible to nasal carriage is about 0.3. The model assumes the proportion to be 1.0 or in other words that every one is susceptible. This assumption can now be changed to suit the relationship between nasal carriage and length of stay. If the proportion of susceptibles are a constant 'c' for a given population of N individuals, the number of susceptibles will be Nc. Then equation (I) becomes

$$\frac{dz}{dT} = rz (Nc - z) \dots\dots\dots(2)$$

$$\frac{dz}{z(Nc-z)} = rdT \dots\dots\dots(3)$$

multiplying both sides by Nc

$$\frac{Nc dz}{z(Nc - z)} = Nc r dT \dots\dots\dots(4)$$

or $\int \frac{dz}{z} + \frac{dz}{(Nc-z)} = \int Nc r dT \dots\dots\dots(5)$

solution to this differential equation yields

$$\log z - \log(Nc-z) = rNcT + K \dots\dots\dots(6)$$

The constant K will be determined by the initial condition.

As an initial condition we can take I to be the number of carriers at time T = 0.

Substituting this initial condition in (6)

$$\log I - \log (Nc-I) = K \dots\dots\dots (7)$$

substituting the value for K in (6)

$$\log z - \log(Nc-z) = rNcT + \log I - \log(Nc-I)$$

$$\text{or } \frac{z (Nc-I)}{(Nc-z)I} = \exp (rNcT)$$

which reduces to

$$z = \frac{NcI}{(Nc - I)\exp(-rNcT)+I} \dots\dots\dots(8)$$

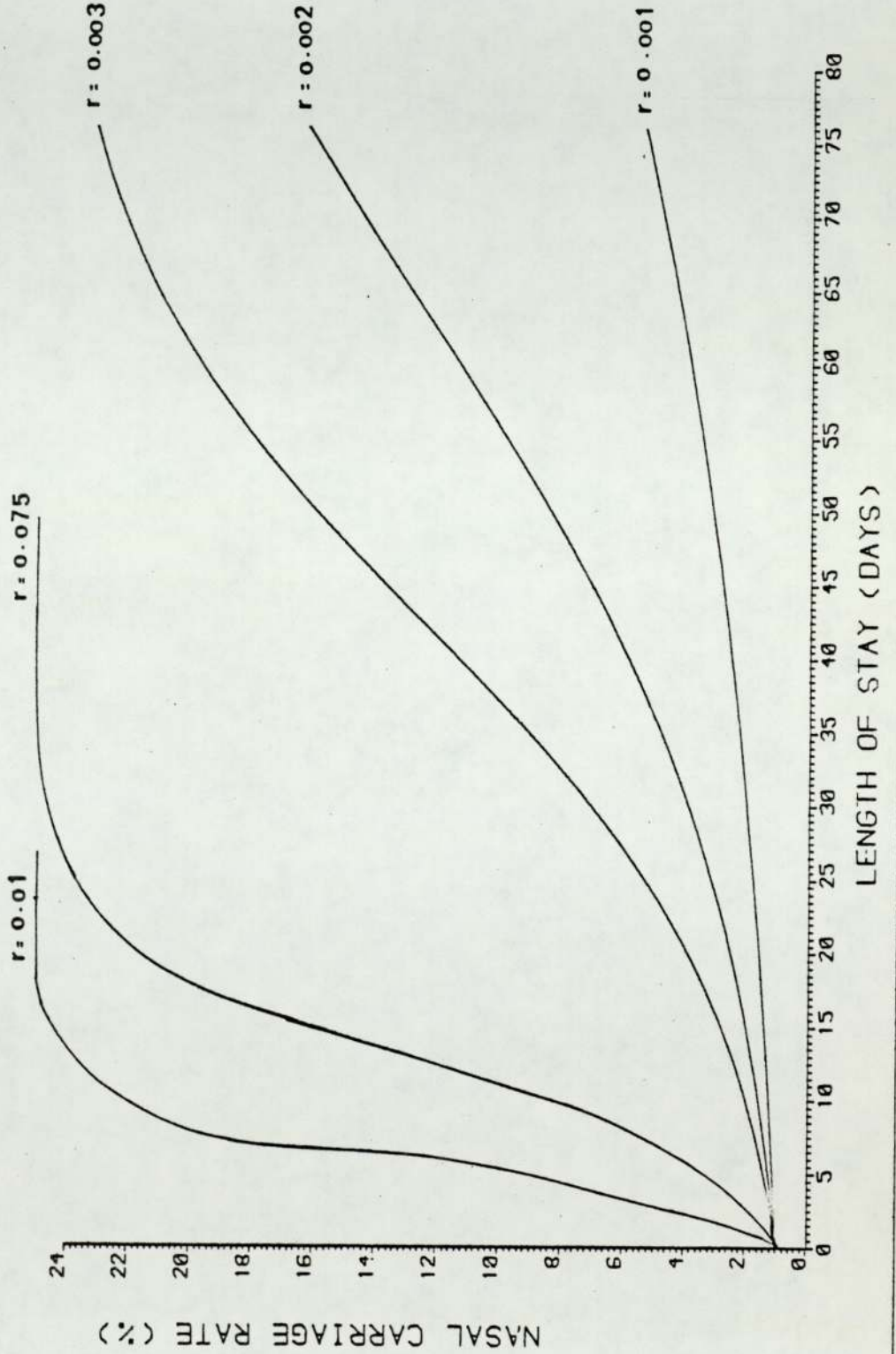
when $T \rightarrow \infty$ $z \rightarrow Nc$ and when $T = 0$ $z = I$

z is the number of carriers at time T, which can be transformed into a carriage rate by dividing equation (8) by N and multiplying by 100. Then $\frac{z}{N} \times 100$ will be equal to the nasal carriage rate YN

$$\therefore YN = \left[\frac{NcI}{(Nc-I) \exp (-rNcT) + I} \right]^x \frac{100}{N}$$

Fig. 20 shows the relationship between nasal carriage rate and length of stay derived from the model using a population of 100 individuals with one carrier at a time T = 0, and 0.25 of the patients being susceptible. Five different values for the rates of interaction r is considered to show the significance of this parameter.

FIGURE 20



CHAPTER 10

DEVELOPMENT OF A COMPREHENSIVE MATHEMATICAL MODEL

10.1 Introduction

The modelling approaches so far considered, the multiple regression and the mathematical model on age and length of stay, both have certain advantages and disadvantages. The multiple regression models incorporate all the variables into the models, but do not have any explanation as to the behaviour of the model. On the other hand, the mathematical models developed in Chapter 9 give sufficient theoretical explanation on the behaviour of the singular variables, age and length of stay, but these are treated in isolation and cannot be applied without first establishing a relative comprehensive relationship between these variables. Clearly, the objective of this study is to postulate a comprehensive model incorporating all the relevant variables. In this chapter such a model is developed incorporating the established variables, age and length of stay and adding a further variable, the number of patients in hospital. The significance of this further variable (number of patients), on infection and nasal carriage rates is discussed in 10.2.

10.2 Significance of the Distribution of Number of Patients

In previous studies, when nasal carriage rates were compared between different wards or hospitals, it was always inherently assumed that the distribution of number of patients in different age, sex or length of stay groups was similar in both patient populations under study. The majority of them making such comparisons were even unaware that they were

making this assumption, because they disregarded the significance of patient parameters. Obviously, if one is comparing the usefulness of a new aseptic practice by carrying out a controlled study in two selected wards, the results may be biased if the distribution of patient parameters is different in the two wards. Even if the wards were selected carefully to reflect similar age and length of stay distributions, there may still be a bias present if the distribution of the interaction between these two parameters are different.

The multiple regression model on nasal carriage developed in 8.3 can be used to overcome this problem. The carriage rates are corrected for variations in patient parameters or their interactions. Before the application of the model, details of patient parameters on every patient must be collected. This may be easy in comparing patient populations in a few wards, but if the comparisons are extended to inter-hospital or international level, many practical difficulties must first be encountered. For instance, if we are monitoring the changing nature of staphylococcal nasal carriage in the U.S.A. and the U.K. using a regression model, information regarding all the individual patient parameters must first be collected. This problem can be overcome if the distribution of the number of patients in different age and length of stay groups can be incorporated to a model as a separate variable. Although the number of patients in a group was used as a weighting factor in the regression model, the distribution of number of patients in different age and length of stay groups cannot be incorporated into the regression model as a variable. Because, in defining infection rate (as the percentage infected in a group) for the regression analysis, the number of patients

in a group was assumed constant. In developing a new theoretical model, this assumption of the number of patients being constant can be modified. Even when defining the infection rate, the assumption of a constant number can be modified. But first the distribution of the number of patients with regard to age and length of stay must be established.

10.2.I Defining the Numbers Distribution Using the Survey Data

When the number of patients in individual age and length of stay groups were classified, it was apparent that the number of patients increased with age and decreased with length of stay. This general trend was true for almost all of the age and time groups, and before carrying out the curve fitting, it was necessary to fit a series of geometric progressions to the observed data, in order to smooth out the few observations which were unrepresentative of the general trend. Table 34 shows the relationship between number of patients, age and length of stay for the original data and also for the modified data using the geometric progression.

This modified numbers distribution can now be used to find the relationship between age and number of patients using curve fitting techniques. For the age and number distribution in the length of stay 5 day group, a quadratic of the type $N = lx^2 + mx + n$ fits the data.

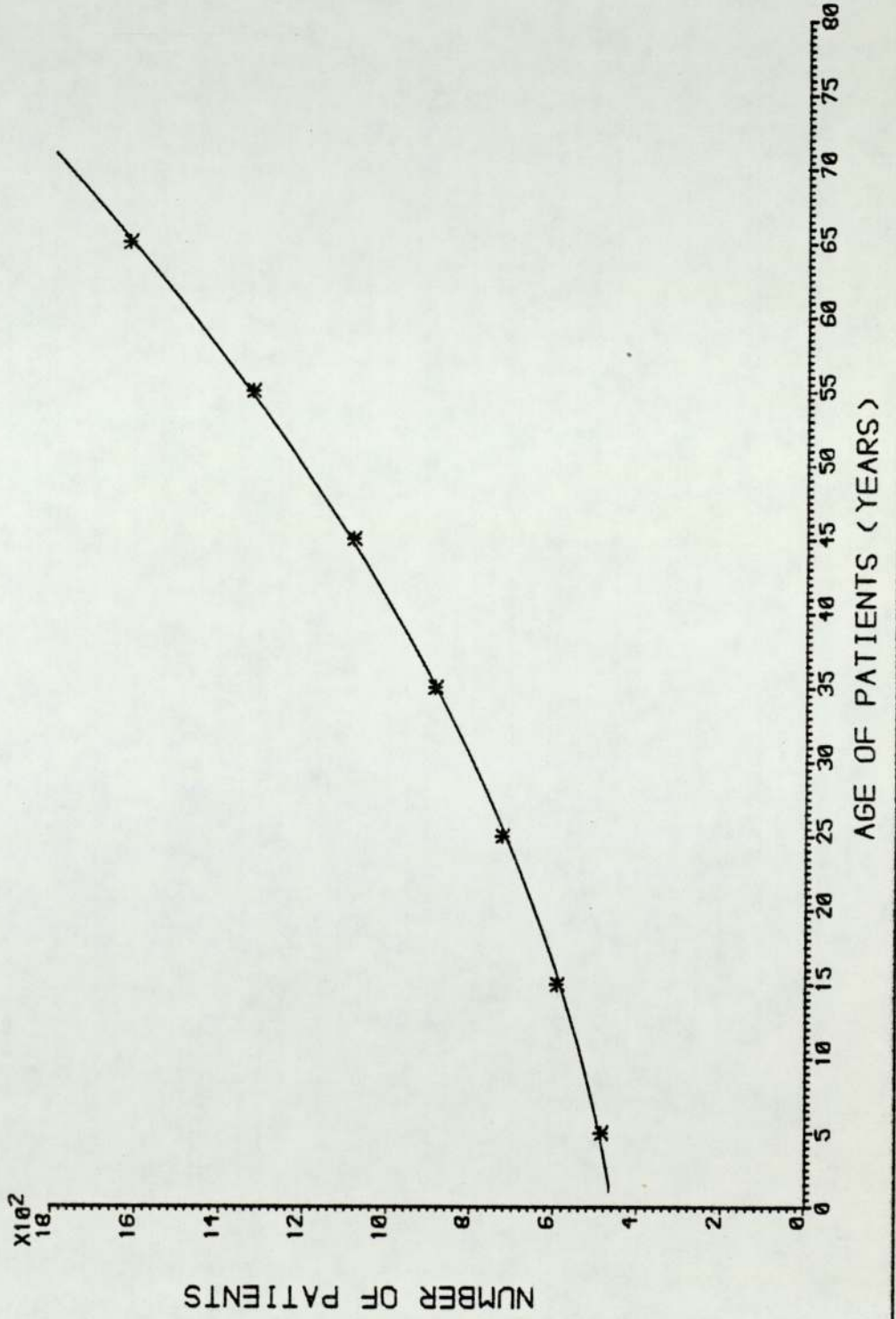
The equation is:

$$N = 0.184X^2 + 5.77X + 460 \quad \text{SSD}=324.8$$

This relationship between the number of patients and age is represented in Fig. 2I.

The distribution of number of patients and length of stay in the age 5 group, can be represented by a curve of

FIGURE 21



the type $N = N_0 T^{-u}$ where N_0 is the intercept on the N axis and u a constant.

The equation is:

$$N = 6776.5 T^{-1.54} \quad R = 0.994$$

which can be approximated to

$$N = 6776.5 T^{-3/2}$$

The relationship between the number of patients and length of stay is shown in Fig.22.

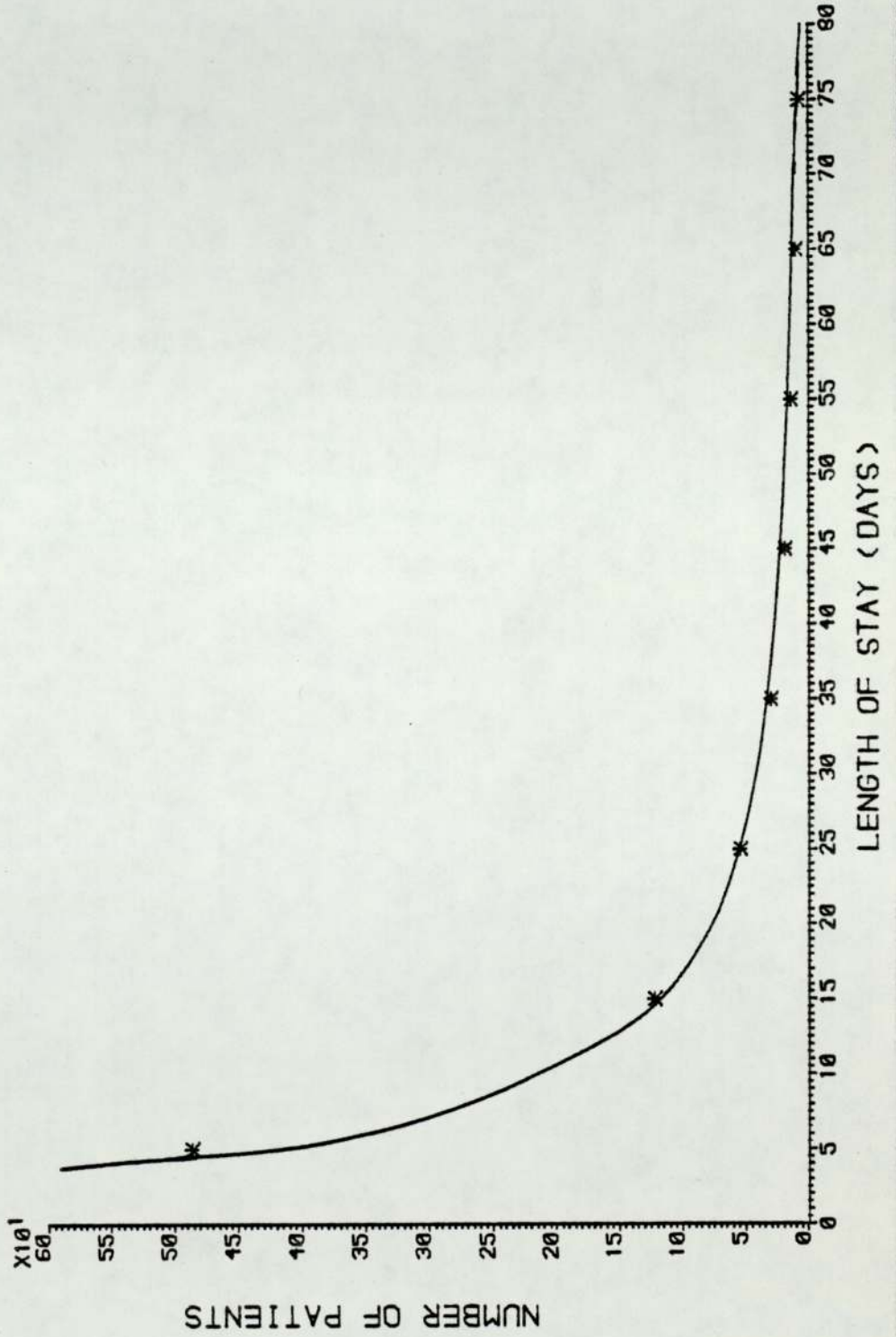
Table 34. Number of patients in age and length of stay groups

Days	Age:- 5	15	25	35	45	55	65
5	486 (486)	594 (487)	726 (1014)	887 (689)	1084 (753)	1324 (903)	1618 (963)
15	122 (117)	149 (112)	182 (155)	223 (165)	272 (236)	332 (383)	406 (421)
25	54 (45)	66 (38)	81 (78)	99 (64)	120 (102)	147 (140)	180 (185)
35	30 (26)	37 (25)	45 (29)	55 (32)	67 (27)	82 (79)	100 (89)
45	19 (14)	23 (14)	28 (16)	35 (12)	42 (27)	52 (37)	63 (53)
55	14 (12)	17 (11)	21 (13)	26 (6)	31 (14)	38 (21)	47 (42)
65	10 (8)	12 (9)	15 (10)	18 (5)	22 (9)	27 (14)	33 (28)
75	8 (5)	10 (4)	12 (2)	15 (3)	18 (4)	22 (6)	27 (16)

Original data in brackets

Now the relationship between age and numbers in the length of stay 5 day group and between length of stay and numbers in the age 5 year group had been established. These two base curves can be extended to produce the surface equation for the distribution of numbers. Since age below 1 year and length of stay less than one day are not representative

FIGURE 22



of the majority of patients, the surface equation should only be generated for values of X and T greater than or equal to one. Therefore as shown in Fig. 23, the surface will be generated from the new axis system N' T' X with the origin at X = I and T = I. In Fig. 23 the age curve is drawn in the T = 5 plane and the length of stay curve in the X = 5 plane, the intercept of the age curve in the T = 5 plane can be taken as a point in a T curve at X = 0 and T = 5, and by extrapolation the intersect of the age curve (T = 5) on the T' plane for X = I will be:

$$N_2 = 0.184 + 5.77 + 460$$

or equally,

$$N_2 = 466$$

This is a point on the T curve (X = I plane) at T = 5. Therefore the value at T = I or the intersect of the N' T' plane :

$$N_0 = \frac{466}{5^{3/2}} = 5210$$

Using $N_0 = 5210$ an age curve in the T = 0 plane can be found parallel to the T = 5 plane curve. The equation of this curve is also of the type :

$$N = 1.X^2 + m.X + N_0$$

with the coefficients:

$$N = 0.184 X^2 + 5.77 X + 5143 .$$

Now an age curve in the $N' X$, $T = I$ plane and a length of stay curve in the $N' T'$, $X = I$ plane have been established. Both curves originate at the point N_0 in the N axis where $N_0 = 52I_0$. The axis system can now be brought back to the $N X T$ system, and values of X and T would determine values for N based on the equations:

$$N = N_0 T^{-3/2}$$

and

$$N = l.X^2 + m.X + N_0$$

A surface equation can now be generated using these two base curves. Since the age curve is the predominant one in determining the number distribution, the base age curve can be used to generate length of stay curves for the surface. In other words the origin for the length of stay curve at different age groups will be defined by the base age curve. Hence the surface equation is :

$$N = \frac{l.X^2 + m.X + N_0}{T^{3/2}}$$

The origin of the surface is at $T = I$ and $X = I$ and the surface equation is only valid for values of $X > I$ and $T > I$. The numbers distribution generated from this equation is shown in Fig. 24 .

10.3 Formulation of the Basic Model

P the probability of becoming a nasal carrier is a function of age, length of stay and the distribution of number

of patients (ignoring sex and antibiotic therapy at this stage, because they are step functions which can be incorporated to the model at a later stage). The distribution of number of patients is a function of age and length of stay. This can be represented mathematically as :

$$P = f (X,T,N) \dots\dots\dots (1)$$

and $N = f (X,T) \dots\dots\dots (2)$

By total differentiation :

$$\Delta P = \frac{\partial P}{\partial X} \cdot \Delta X + \frac{\partial P}{\partial T} \cdot \Delta T \dots\dots\dots (3)$$

or equally, dividing through by ΔN :

$$\frac{\Delta P}{\Delta N} = \frac{\partial P}{\partial X} \cdot \frac{\Delta X}{\Delta N} + \frac{\partial P}{\partial T} \cdot \frac{\Delta T}{\Delta N} \dots\dots\dots (4)$$

in the limit :

$$\frac{dP}{dN} = \frac{\partial P}{\partial X} \cdot \frac{dX}{dN} + \frac{\partial P}{\partial T} \cdot \frac{dT}{dN} \dots\dots\dots (5)$$

10.3.I Relationship Between Number of Carriers and Total Number of Patients.

As explained in 9.3 in developing the model for length of stay and nasal carriage rate, the probability of nasal carriage depends on the interaction between the number of carriers and susceptibles. This implies that the number of

carriers varies as a function of the total number of patients. This leads to the assumption that the rate of change of number of carriers with respect to the total numbers present is a function of the number of carriers. This function can be further assumed to be the product of a constant 'V' and the number of carriers 'ni', which can be written mathematically as:

$$\frac{dni}{dN} = V \cdot ni \quad \dots\dots (6)$$

Solution to this simple differential equation yields:

$$\text{Log}(ni) = V \cdot N + B_1 \quad \dots\dots (7)$$

or
$$ni = B_2 \cdot e^{VN} \quad \dots\dots (8)$$

where
$$B_2 = e^{B_1}$$

Now the probability of nasal carriage is defined as :

$$P = \frac{ni}{N} \quad \dots\dots (9)$$

Substituting for ni

$$P = \frac{B_2 \cdot e^{VN}}{N} \quad \dots\dots (10)$$

Therefore

$$\frac{dP}{dN} = \frac{VN \cdot B_2 \cdot e^{VN} - B_2 \cdot e^{VN}}{N^2} \quad \dots (11)$$

$$\frac{dP}{dN} = \frac{B_2 \cdot e^{VN}}{N} \cdot \frac{[VN - 1]}{N} \quad \dots (12)$$

From I0 and I2

$$\frac{dP}{dN} = \frac{P.[VN - I]}{N} \dots\dots (I3)$$

Equation I3 can now be substituted into the differential equation 5 :

$$P.\frac{[VN - I]}{N} = \frac{\partial P}{\partial X} \cdot \frac{dX}{dN} + \frac{\partial P}{\partial T} \cdot \frac{dT}{dN} \dots\dots (I4)$$

10.3.2 Defining a Relationship Between Age and Length of Stay

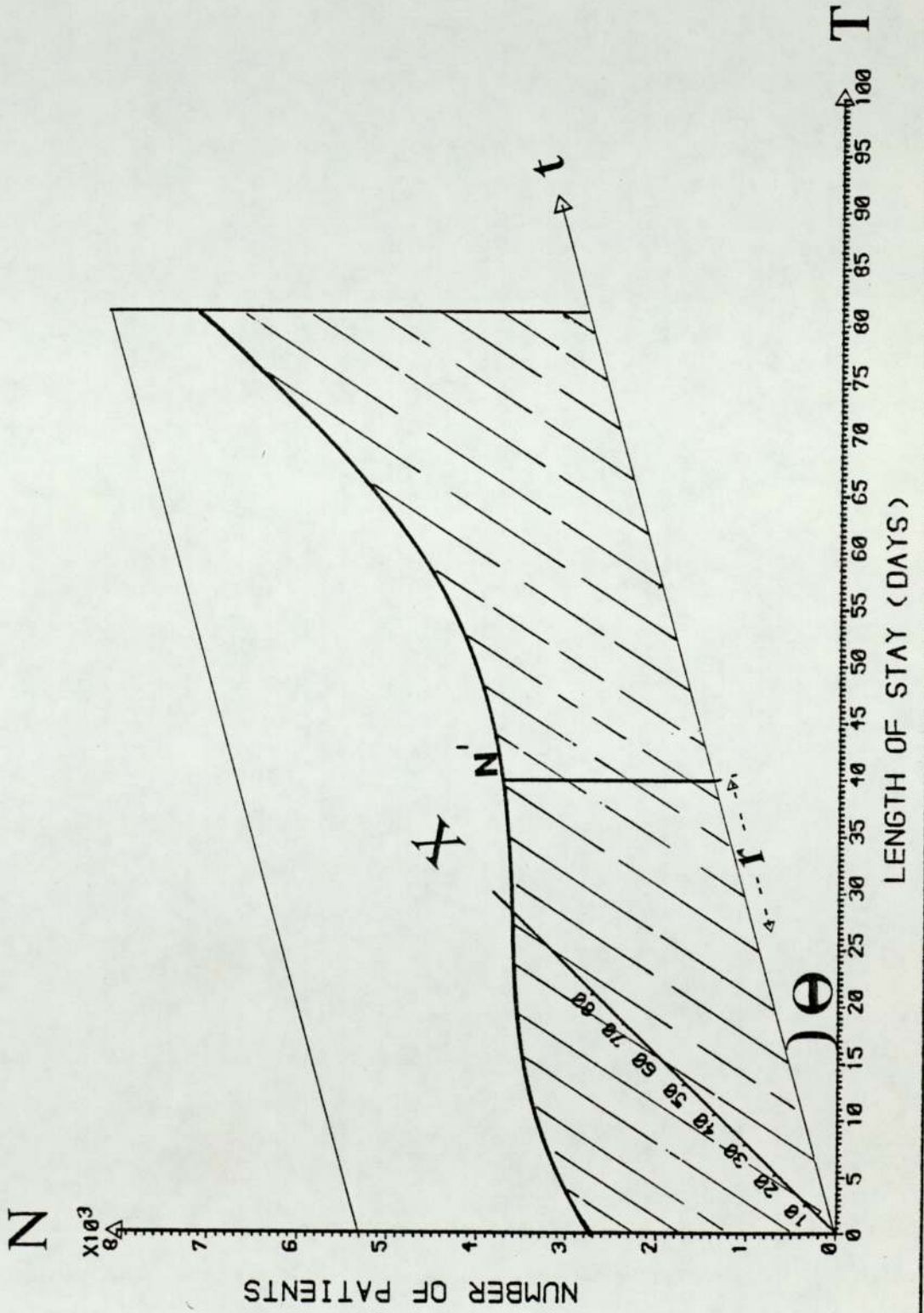
The differential equation in (I4) can be solved if $\frac{dX}{dN}$ or $\frac{dT}{dN}$ can be established. Neither can be found using

the surface equation $N = f(X,T) = \frac{1.X^2 + m.X + No}{T^{3/2}}$

because no direct relationship between X and T exists. Therefore in order to differentiate this equation, a relationship between X and T must first be assumed.

A relationship can be established by assuming X and T are linearly related. As shown in Fig. 25, an axis t can be drawn at an angle 'θ' to the T axis in the X T plane. If a plane is now drawn perpendicular to the Ot axis this will intersect the numbers surface, and the surface would represent as a single curve on the plane. Any point on this curve can be represented by t, and if a relationship between X and t and, T and t can be found, then t would be a unique parameter representing the relationship between X and T in the Ot plane. An infinite number of t axes can be drawn by varying θ, to cover the whole range of values

FIGURE 25



in T and X . Similar relationships between X , T , and t would hold at any angle θ .

The relationships can be established from simple geometry:

$$T = t. \text{Cos } \theta \quad \dots\dots (I5)$$

$$X = t. \text{Sin } \theta \quad \dots\dots (I6)$$

and $\text{Tan } \theta = \frac{X}{T}$, which will be a constant along t .

Also,

$$\frac{dX}{dN} = \frac{dt}{dN} \cdot \frac{dX}{dt}$$

but $X = t. \text{Sin } \theta$

$$\therefore \frac{dX}{dt} = \text{Sin } \theta$$

hence, $\frac{dX}{dN} = \frac{dt}{dN} \cdot \text{Sin } \theta \quad \dots\dots (I7)$

Similarly,

$$\frac{dT}{dN} = \frac{dt}{dN} \cdot \frac{dT}{dt}$$

but $T = t. \text{Cos } \theta$

$$\therefore \frac{dT}{dt} = \text{Cos } \theta$$

hence, $\frac{dT}{dN} = \frac{dt}{dN} \cdot \text{Cos } \theta \quad \dots\dots (I8)$

Now I7 and I8 can be substituted for $\frac{dX}{dN}$ and $\frac{dT}{dN}$ in I4

$$P \cdot \frac{[VN-I]}{N} = \frac{\partial P}{\partial X} \cdot \left[\frac{dt}{dN} \cdot \sin \theta \right] + \frac{\partial P}{\partial T} \cdot \left[\frac{dt}{dN} \cdot \cos \theta \right] \quad \dots (19)$$

But the partial differentials $\frac{\partial P}{\partial X}$ and $\frac{\partial P}{\partial T}$ must also be changed to account for the new parameter t .

$$\frac{\partial P}{\partial X} = \frac{\partial P}{\partial t} \cdot \frac{\partial t}{\partial X}$$

but $\frac{\partial t}{\partial X} = \operatorname{Cosec} \theta$

hence $\frac{\partial P}{\partial X} = \frac{\partial P}{\partial t} \cdot \operatorname{Cosec} \theta \quad \dots \dots \dots (20)$

and $\frac{\partial P}{\partial T} = \frac{\partial P}{\partial t} \cdot \frac{\partial t}{\partial T}$

but $\frac{\partial t}{\partial T} = \operatorname{Sec} \theta$

hence $\frac{\partial P}{\partial T} = \frac{\partial P}{\partial t} \cdot \operatorname{Sec} \theta \quad \dots \dots \dots (21)$

Substituting for $\frac{\partial P}{\partial X}$ and $\frac{\partial P}{\partial T}$ from 20 and 21, in 19

$$P \cdot \frac{[VN-I]}{N} = \frac{\partial P}{\partial t} \cdot \left[\frac{dt}{dN} \right] + \frac{\partial P}{\partial t} \cdot \left[\frac{dt}{dN} \right] \quad \dots \dots \dots (22)$$

To find $\frac{dt}{dN}$ the new variable t can be substituted for X and T in the surface equation using 15 and 16.

$$N = \frac{1 \cdot X^2}{T^{3/2}} + \frac{m \cdot X}{T} + N_0$$

after substitution :

$$N = \frac{1. (t^2 \cdot \sin^2 \theta) + m. t \cdot \sin \theta + N_0}{(t \cdot \cos \theta)^{3/2}} \quad \dots (23)$$

or
$$N = \frac{M_1 \cdot t^2 + M_2 \cdot t + N_0}{M_3 \cdot t^{3/2}} \quad \dots \dots \dots (24)$$

Where; $M_1 = 1 \cdot \sin^2 \theta$, $M_2 = m \cdot \sin \theta$, and $M_3 = \cos^{3/2} \theta$

Hence:

$$\frac{dN}{dt} = \frac{t^{3/2} \cdot [2M_1 + M_2] - (3/2) \cdot t^{1/2} [M_1 t^2 + M_2 t + N_0]}{M_3 \cdot t^3}$$

$$\frac{dN}{dt} = \frac{[4M_1 \cdot t^2 + 2M_2 \cdot t - 3M_1 \cdot t^2 - 3M_2 \cdot t - 3N_0]}{2M_3 \cdot t^{5/2}}$$

$$\frac{dN}{dt} = \frac{[M_1 \cdot t^2 - M_2 \cdot t - 3N_0]}{2M_3 \cdot t^{5/2}}$$

Taking the inverse to find $\frac{dt}{dN}$:

$$\frac{dt}{dN} = \frac{2M_3 \cdot t^{5/2}}{[M_1 \cdot t^2 - M_2 \cdot t - 3N_0]} \quad \dots \dots \dots (25)$$

This equation can now be substituted in 22 in order to solve the differential equation .

10.4 The Solution of the Differential Equation

Substituting for $\frac{dt}{dN}$ in I9 from 22:

$$P \left[\frac{VN-I}{N} \right] = \frac{\partial P}{\partial t} \left[\frac{2M_3 \cdot t^{5/2}}{M_1 t^2 - M_2 t - 3No} \right] + \frac{\partial P}{\partial t} \left[\frac{2M_3 \cdot t^{5/2}}{M_1 t^2 - M_2 t - 3No} \right] \dots \dots (26)$$

which leads to the 'auxillary equation' :

$$\int \frac{N}{P[VN-I]} \cdot dP = \int \frac{[M_1 t^2 - M_2 t - 3No]}{[2M_3 \cdot t^{5/2}]} \cdot dt$$

or ,
$$\int \frac{dP}{P} = \int \left[\frac{VN-I}{N} \right] \cdot \frac{[M_1 t^2 - M_2 t - 3No]}{[2M_3 \cdot t^{5/2}]} \cdot dt$$

$$\int \frac{dP}{P} = \int \left[\frac{V(M_1 t^2 - M_2 t - 3No)}{2M_3 \cdot t^{5/2}} - \frac{I}{N} \cdot \frac{(M_1 t^2 - M_2 t - 3No)}{2M_3 \cdot t^{5/2}} \right] \cdot dt$$

Substituting for N, and simplifying:

$$\int \frac{dP}{P} = \int \left[\frac{V(M_1 t^2 - M_2 t - 3No)}{(2M_3 \cdot t^{5/2})} - \frac{(M_1 t^2 - M_2 t - 3No)}{2t(M_1 t^2 + M_2 t + No)} \right] \cdot dt$$

$$\int \frac{dP}{P} = \int \left[\frac{V}{2M_3} (M_1 t^{-1/2} - M_2 t^{-3/2} - 3No t^{-5/2}) - \frac{M_1 t}{2F_1} + \frac{M_2}{2F_1} + \frac{3No}{2tF_1} \right] \cdot dt$$

where $F_1 = M_1 t^2 + M_2 t + No$

The integration yields:

$$\begin{aligned} \text{Log (P)} &= \frac{V}{2M_3} (2M_1 t^{1/2} + 2M_2 t^{-1/2} + 2N_0 t^{-3/2}) \\ &\quad - \frac{M_1}{2} \left[\frac{1}{2M_1} \text{Log}(F_1) - \frac{M_2}{2M_1} \cdot F_2 \cdot \text{Tan}^{-1} (F_3) \right] \\ &\quad + \frac{3N_0}{2} \left[\frac{1}{2N_0} \text{Log} \left(\frac{t^2}{F_1} \right) - \frac{M_2}{2N_0} \cdot F_2 \cdot \text{Tan}^{-1} (F_3) \right] \\ &\quad + \frac{M_2}{2} \cdot F_2 \cdot \text{Tan}^{-1} (F_3) + M_4 \end{aligned}$$

$$\text{where } F_2 = \frac{2}{(4M_1 N_0 - M_2^2)^{1/2}} ; \quad F_3 = \frac{2M_1 t + M_2}{(4M_1 N_0 - M_2^2)^{1/2}}$$

and M_4 is the constant of intergration.

Re-arranging:

$$\begin{aligned} \text{Log(P)} &= \frac{V}{M_3} (M_1 t^{1/2} + M_2 t^{-1/2} + 2N_0 t^{-3/2}) - \frac{1}{4} \text{Log}(F_1) \\ &\quad + \frac{3}{4} \text{Log} \left(\frac{t^2}{F_1} \right) + M_4 \end{aligned}$$

or,

$$\begin{aligned} \text{Log(P)} + \frac{1}{4} \text{Log} (F_1) - \frac{3}{4} \text{Log} \left(\frac{t^2}{F_1} \right) \\ = \frac{V}{M_3} (M_1 t^{1/2} + M_2 t^{-1/2} + 2N_0 t^{-3/2}) + M_4 \end{aligned}$$

$$P \cdot F_1^{1/4} \left[\frac{F_1}{t^2} \right]^{3/4} = e^{M_4} \cdot e^{\frac{V}{M_3} (M_1 t^{1/2} + M_2 t^{-1/2} + 2N_0 t^{-3/2})}$$

Re-arranging:

$$\frac{P F_1}{t^{3/2}} = W t^{3/2} \cdot e^{\frac{V}{M_3} (M_1 t^{1/2} + M_2 t^{-1/2} + 2N_0 t^{-3/2})}$$

where $W = e^{M_4}$

Re-substituting values for F_1

$$P(M_1 t^2 + M_2 t + N_0) = W \cdot t^{3/2} \cdot e^{\frac{V}{M_3} (M_1 t^{1/2} + M_2 t^{-1/2} + 2N_0 t^{-3/2})}$$

Re-substituting M_1 , M_2 , and M_3

$$P (1. \sin^2 \theta \cdot t^2 + m \cdot \sin \theta \cdot t + N_0) = W t^{3/2} \cdot e^{\frac{V}{\cos^3 \theta} (1. \sin^2 \theta t^{1/2} + m \sin \theta t^{-1/2} + 2N_0 t^{-3/2})}$$

Re-substituting values for X and T in the t plane:

$$t = \frac{T}{\cos \theta} \quad \text{and} \quad t = \frac{X}{\sin \theta}$$

$$P (1.X^2 + m.X + N_0) = \frac{WT^{3/2}}{\cos^{3/2} \theta} \cdot e^{\frac{V}{\cos^3 \theta} (1 \sin^{3/2} \theta X^{1/2} + m \sin^{3/2} \theta X^{-1/2} + 2N_0 \sin^{3/2} \theta X^{-3/2})}$$

which reduces to:

$$P = \frac{WT^{3/2} \cdot e^{V \cdot \tan^{3/2} \theta \cdot (1.X^{1/2} + m.X^{-1/2} + 2N_0.X^{-3/2})}}{\cos^{3/2} \theta \cdot (1.X^2 + m.X + N_0)}$$

W is the constant of integration which can be evaluated using the boundary conditions.

10.5 Graphical Representation of the Model

Before finding out the constant of integration using the boundary conditions, a value must be assigned to the constant V which defines the association between the number of carriers and the total number of patients. If the value of V is too large the exponential will go out of the range. For the boundary conditions, nasal carriage rate was considered to be 25 per cent at age 70 years and length of stay at 70 days. This figure was chosen because the maximum carriage rate normally experienced is about 25 per cent, and the maximum is experienced in extreme age and length of stay groups. Further if a higher age and length of stay group was chosen to represent the maximum carriage rate, such a boundary value would not represent the majority of normal patient's age and length of stay maxima.

When the above boundary condition ($X=70, T=70, P=.25$) was used, V values larger than 0.0001 made the exponential go beyond the calculable range. The model was plotted three-dimensionally using the computer graph plotting package (GINO-F). Figures 26 - 28 show the carriage rate profiles produced by different V values. The effect of the constant V was prominent in the short stay groups, and in fact for very long stay groups variations in the constant V did not alter the shape of the surface significantly. The age curves in different length of stay groups increase with age in a quadratic manner, and the length of stay curves increase linearly in different age groups. These individual age and length of stay curves are similar to the average age and average length of stay curves shown in Chapter 6. This model

FIGURE 26

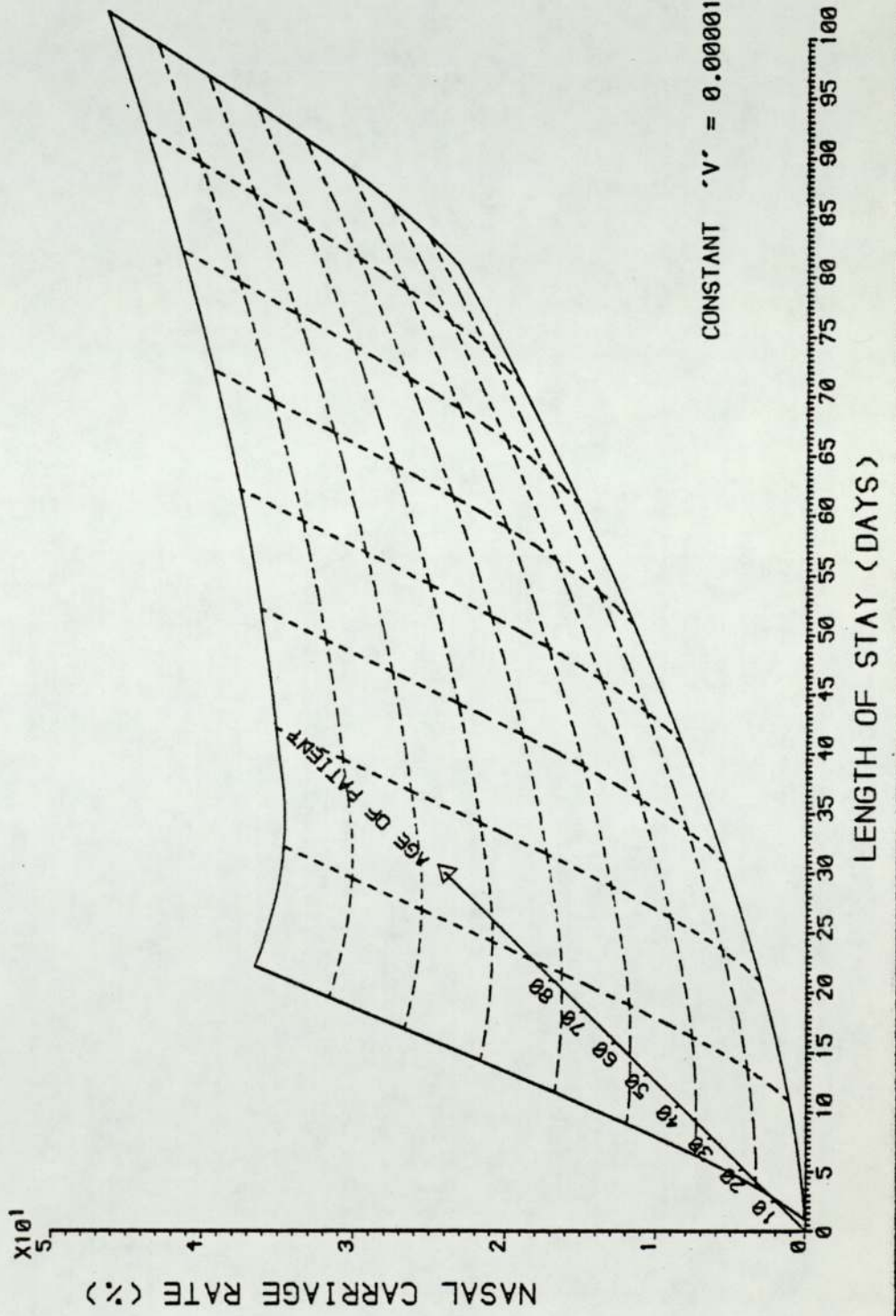
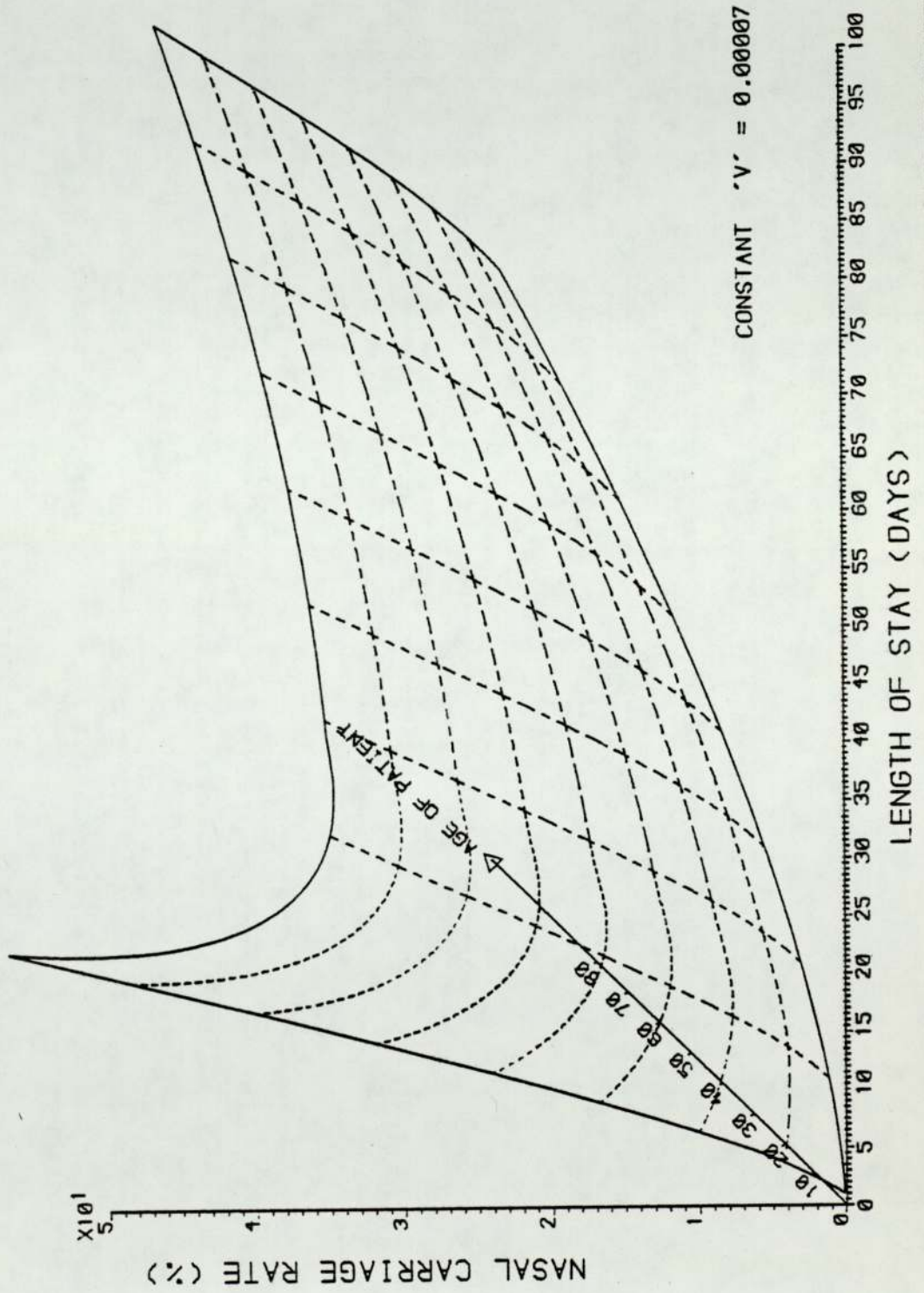


FIGURE 28



is hence representative of the observations made in Part I.

Further, for certain values of $V(0.00001)$, the resulting carriage rate profile produced by this model was quite similar to the surface derived from the multiple regression analysis on nasal carriage in 8.4. This further emphasises the representativeness of the model.

CHAPTER 11

DISCUSSION ON THE MODELLING APPROACHES IN PART II

11.1 Multiple Regression Models

There were three major objectives in carrying out the multiple regression analysis. Firstly it was used to investigate the possibility of bias arising from correlations between different parameters; secondly, to establish the relative significance of each parameter in determining infection and nasal carriage rates, and finally to represent the regression as a model which can be used to correct any observed infection and carriage rates for differences in patient parameters within the samples. As demonstrated in Chapter 8, all three of these objectives were achieved.

The correlation matrix on parameters related to wound infection showed that the correlations between the parameters age, sex, wound drainage and wound description (clean, contaminated or clean-contaminated) are not significant. Hence, the possibility of any bias arising from interactions (correlations) between the patient parameters can be excluded. However, since age was considered as a linear variable, it may be possible that extremely high age when considered separately as a variable is correlated with contaminated wounds.

Previous regression analyses carried out by others (44, 96) on wound infection, have failed to report the results of any correlation analysis, particularly in this type of study where statistically viable experiments are difficult to design. Correlation analyses must always be carried out to investigate the possibility of interacting variables. For example in LIDWELL's (44) analysis "duration of operation

over 60 minutes" and "incision over 6 inches long" may be correlated and further, certain types of operations may correlate with wound drains. Also in the analysis reported by DAVIDSON et al.(96) "potentially dirty operations" and "bacteria in wound at end of operation" may be correlated. Further, these studies have not reported the multiple correlation for the regression, and whether group size was used as a weighting factor in the analyses. When the group size is used as a weighting factor, it increases the representativeness of the resulting multiple regression, because the regression attaches more weight to data based on large samples than for data based on small samples (larger the sample more representative the data will be).

The analysis confirmed that age, sex, wound drainage and wound description are significant parameters related to the risk of post-operative wound infection. All the coefficients in the regression were significant, and the correlation coefficient in the regression was considerably high. These significant parameters are similar to some of the parameters obtained through multiple regression by LIDWELL (44) (age over 60, male sex, drainage) and DAVIDSON et al. (96) (age and wound contamination). The regression equation showed that wound contamination is the most important parameter determining the risk of infection, followed by drainage and clean-contamination. These observations are not surprising because they determine the complexity of the operation. Male sex increases the risk of infection by about 3 per cent. The least important factor appeared to be the age, because even at age 70, the risk of infection due to age is less than half that for drainage, contaminated wounds or clean-contaminated

wounds. It is possible that when age is divided into over 60 and under 60, the coefficient for age over 60 would be much higher than even for sex. However, such a division has one weakness; for example, a patient aged 59 years will not have a risk coefficient attached due to the patient's age, whereas when he turns 60, the risk coefficient will be attached. This anomaly is excluded when age is considered as a linear variable, as was the case in this analysis.

The regression model can be used to measure the probability of a patient becoming infected. Once the patient's age, sex and operative conditions are known the model will predict the probability of the patient becoming infected. This knowledge can be used to apply prophylactic antibiotics to high risk patients and further, isolation policies and the degree of nursing care needed can be evaluated from the calculated risk factor. Further, the model can be used to correct experimental results for differences in patient parameters, when investigating the significance of some factors related to operations or operating theatre practices.

The correlation analysis on parameters related to nasal carriage confirmed that the correlations between age, sex, length of stay in hospital and antibiotic therapy are not significant. Hence, the possibility of a bias arising from interactions (correlations) between these parameters can be excluded. The multiple regression coefficients for the four parameters were statistically significant, and the resulting correlation coefficient was also considerably high. A previous regression analysis reported by LIDWELL et. al. (24) indicated that age and exposure to antibiotics are associated with the risk of nasal carriage. It was logical to introduce

the constant and the age-square term to the regression, and although the resulting coefficients for age, age-square and constant are not significant, it is probable that when these three terms are considered jointly, their contribution to the regression may become significant. The regression confirmed that age, sex, length of stay and antibiotic therapy are the patient parameters related to the risk of nasal carriage. From the coefficients of the regression it is apparent that exposure to antibiotics contributes the most risk of carriage but this may be overshadowed by high age and extreme length of stay.

The regression model on nasal carriage can be used to determine the probability of becoming a nasal carrier. Further, the model can effectively be used to correct experimental results for differences in the distribution of patient parameters. The application of the model in this manner would help to establish the significance of ward and environmental parameters on nasal carriage, free from any bias arising from patient parameters. Hence, the multiple regression models achieved the major objective of this study.

The graphical representation of the regression model is useful in demonstrating the logic of the model. The description of a surface derived from the significance of age and length of stay being shifted up or down depending on the presence of the other two parameters, sex and antibiotics, is easy to understand. However, there is one weakness in the model, because it assumes that the effects of sex and antibiotics are constant over the whole range of age and length of stay groups. It may just be possible that for example, the significance of antibiotics on nasal carriage

is more profound in the elderly than the young, in which case the assumption of a constant antibiotic effect is invalid. In other words, although the correlation matrix confirmed that there are not any high correlations between these parameters, slight interactions between these parameters may still prevail. The graphical representation can be used to simulate this aspect. In the presence of these interactions the surface in the graphical representation will tilt (rather than shifting in parallel) in different directions depending on the interactions of parameters. Therefore the graphical representation of the regression is an effective tool in explaining the relationship between nasal carriage and patient parameters.

The constant in the graphical representation may be interpreted as the contribution made by the ward parameters to the level of nasal carriage. This constant due to the ward parameters is independent of any patient parameters, and would change from ward to ward. Although the ward parameters are represented as a singular constant, it is likely that the constant is made up of the addition of a multitude of different ward parameters. The model can be used to determine the relative significance of ward parameters. The graphical representation is particularly useful because it recognises the significance of both the patient and ward parameters, and in this sense it is unique.

The method of applying the regression models in correcting the infection and nasal carriage rates related to ward parameters for differences in patient parameters, was discussed in 8.5. Although such methods of correction are perfectly feasible when applied to studies based on limited

differences in ward parameters, it is not suited for application in this cross-sectional survey for two main reasons. First, the very nature of cross-sectional surveys will introduce a bias into the observations due to the possibility of correlations between ward parameters. If a significant ward factor is correlated with a non-significant ward factor, the non-significant factor would also appear to be significant. Further, when a ward factor related to low carriage rates is correlated with a factor related to high carriage rates, the result may be to show that both carriage rates are nearer the average carriage rate. Secondly, even after carrying out correlation analysis, conclusions made on so vast a number of ward parameters (over 200 parameters in which there are many sub-divisions) would be bound to contain many spurious results. Therefore, although the model is useful in correcting infection and carriage rates for differences in patient parameters, the use of the model in determining the significance of ward parameters must be limited to controlled studies on a few ward parameters at a time.

II.2 Preliminary Modelling Approach

The modelling approach in Chapter 9 was aimed at developing a modelling concept capable of explaining the underlying trend behind the age and length of stay curves. Since there are many other factors apart from age (such as type of operation) that are related to the risk of wound infection, the models are mainly to explain the relationship between nasal carriage and age and length of stay.

It was specifically stated that the age and susceptibility functions discussed were for the total patient population, as opposed to referring to the behaviour of individual

patients. This was because the age and length of stay curves were derived as the average of the total patient population. The graphical model postulated to depict the relationship between age and nasal carriage rate was purely a hypothetical one. However, the two phenomena incorporated in the model, the notion of ageing and acquiring resistance, are generally accepted to be true on their own. Therefore, there is sufficient basis for proposing this model. The application of the log model confirmed the existence of the ageing function. The age curves for nasal carriage, wound infection and those from the N.R.C. study, when plotted on double logarithmic scales, followed the log model derived for age specific incidence rates of cancer. This implied that just as in the case for the incidence of cancer, wound infection and nasal carriage rates are also dependent on the ageing phenomenon.

The increase in carriage rate with length of stay is most likely to be the result of the increased exposure to the micro-organisms. Exposure may also be interpreted as the rate of interaction between susceptibles and nasal carriers. Deterministic models based on this basic epidemiological concept can be modified to suit the epidemiology of staphylococcal nasal carriage. The only assumption made in the development of the model was that there is a proportion of patients who will not normally be carriers, or in other words, there is a proportion of patients who are not susceptible. The literature survey in fact confirmed that this assumption was true.

The association between length of stay and nasal carriage derived from the modified deterministic model was very similar to the curves experienced in Chapter 6,

where the nasal carriage rate increased linearly upto the 30 - 40 day group and reached a stabilised state. The linear increase was clear in all graphs described in Chapter 6 (when the influence of age, sex and operation were considered), but the stabilised state in each graph varied. This is probably due to the distribution of patient numbers in different length of stay groups. If this variation in the stabilised state can be attributed to the difference in the distribution in numbers, then the model described here is representative in determining the association between nasal carriage and length of stay in hospital. The rate of interaction 'r' can be assumed to be both a measure of physical interaction between carriers and susceptibles, and a measure of susceptibility. Therefore the value 'r' would change when sex, age and operative conditions change in a patient community, as well as when changes in the ward structures affecting physical interaction are introduced. In effect, the parameter 'r' may be made up of many independent parameters related to physical interaction (ward parameters) and susceptibility (patient parameters). It is also known that the carriage rate increases rapidly when there are heavy dispersers present in the ward. This in effect is a factor related to the rate of dispersion which could easily be incorporated into the parameter 'r'. The presence of heavy dispersers would increase the value of 'r'. This emphasises the versatility of the variable 'r', which in a modelling sense can be incorporated to refer to many other parameters affecting the relationship between length of stay and nasal carriage rate.

This deterministic model is based on the assumption

of a closed interacting patient population, quite contrary to the type of patient populations represented in a cross-sectional survey of this nature. Patients in a cross-sectional survey are derived from a diverse population in many different wards. Hence a group of patients in a length of stay group may be formed from many different wards, which makes the assumption of a closed interacting patient population somewhat invalid. However, as discussed in Chapter 7, large cross-sectional surveys are representative of continuous surveys (where the assumption is valid), and further, nasal carriage and length of stay curves reported by others (24,28,45,48,55,63,64,99) from continuous surveys are similar to the curves experienced in this study. Therefore, even though the assumption of a closed interacting patient population (when interpreted literally) is invalid in the cross-sectional survey, the curves produced by the model were remarkably similar to the curves experienced in this study as well as other continuous studies. This similarity is a further indication of the usefulness of cross-sectional surveys in mimicking continuous surveys, and the representativeness of this model both in cross-sectional and continuous applications.

The two models on age and length of stay are useful in explaining the underlying reason for the observed relationships. They are individual models designed to explain a single phenomenon at a time. The age model is only valid when the length of stay is constant and similarly, the length of stay model is valid only for a constant age group. Therefore these models have limited practical use. Ideally we must have a model capable of predicting the carriage rate at any age or

length of stay group. However, the contribution of these models as an initial attempt cannot be neglected. For the first time in this area of study, attempts were made to explain the significance of age and length of stay on nasal carriage using modelling concepts.

11.3 The Comprehensive Model

The objective in formulating the comprehensive model was to establish a model incorporating all the parameters and capable of illustrating the underlying behaviour of the variables. The regression model incorporated all the variables, but does not offer any explanation; whereas the initial models were capable of offering explanations on the behaviour of certain variables taken in isolation. In defining this comprehensive model on nasal carriage, the effect of sex and antibiotics were considered to be step functions. This assumption left age and length of stay as the major variables in defining the model.

Before formulating the model a further variable, the distribution of number of patients in age and length of stay groups, was introduced. This is a parameter neglected by all the previous researchers in this area. If one is comparing the carriage rates reported in two countries, it must first be established that the distribution of the total number of patients in age and length of stay groups are similar. If the distributions are not similar, a method must be found to correct the difference. For example, in one population, the majority of the patients may be long stay elderly patients, which would for now obvious reasons, have a high carriage rate.

If the distribution of the number of patients are incorporated in the model as a variable, it would enable us to overcome this problem.

In order to introduce the distribution of number of patients as a parameter, it was first necessary to define the distribution. Since there were a few data points on the distribution which would have been unrepresentative due to the cross-sectional nature of the survey, and also would have made the task of curve fitting impossible, a series of geometric progressions were fitted to the data. As was shown in Table 34, this modified data was strikingly similar to the actual data. The numbers surface curve generated from this data would be an accurate estimate to the actual data.

The model was formulated using the total differentials of the relationship between carriage rate, age, length of stay and the numbers distribution. A further assumption was made on the relationship between the number of carriers and total patients. Since there was not an established relationship between age and length of stay, the difficulty of obtaining such a relationship to solve the differential equation was overcome using a geometric technique. The t plane established a relationship between age and length of stay, and when the t plane sweeps the X and T plane, it covers the whole spectrum of values for age and length of stay. Without the aid of this geometric conversion, it would have been impossible to solve the differential equation.

The model was formed from the solution to the differential equation. The constant of integration W was calculated using the boundary conditions while carrying out the computation in plotting the surface. Therefore, it was not

necessary to calculate this constant separately. Age 70 years, length of stay 70 days and a carriage rate of 25 per cent was used as a boundary condition, mainly because this is the highest carriage rate normally experienced and which generally corresponds to extreme age and length of stay groups. The surface changed its shape for different values of V (the constant assumed to be the relationship between the number of carriers and the total number of patients). The significance of the changes in V was predominant mainly in the early length of stay groups, and for the very long stay patients, the changes in V did not have much impact. This implies that the changes in the relationship between the number of carriers and the total would only influence short stay patients. It may well be that over-crowding is a function of V (the relationship between the number of carriers and the total), in which case it is highly probable that changes in the degree of over-crowding would mainly influence the short stay patients as opposed to the long stay patients.

It was interesting to note that the resulting carriage rate surface for some values of V (e.g. 0.00001) was strikingly similar to the regression surface on nasal carriage developed in Chapter 8. When the sex and antibiotic variables are incorporated in to this mathematical model as step functions, the result would be four surfaces shifted in parallel upwards or downwards depending on the presence of the 4 sex and antibiotic states. The capability of the model based on mathematical concepts in producing a model similar to the regression model, confirms the accuracy and the usefulness of this approach. The model incorporates all the variables and is capable of offering an explanation on the behaviour of variables

The model has many practical and theoretical applications. Foremost, it can be used to compare carriage rates in different patient populations. For example, the numbers distribution for two different hospitals can be derived from admissions records, and once these distribution are established the model can be used to compare carriage rates. Differences in the carriage rate profiles of the two hospitals may indicate the differences in ward or theatre practices. The constant V which defines the relationship between the number of carriers and the total number of patients, is likely to represent ward parameters. For example, the value of V will be different in an open ward when compared to an isolation ward.

The model can be applied as a simulation device, in a theoretical sense. We can observe how the carriage rate will change when certain parameters are changed. For example, population trends such as an increase (or decrease) in the proportion of elderly people in the population, will effect the nasal carriage rate. Similarly, any changes in the hospitals' policy on the normal duration of hospitalisation for certain diseases will affect the nasal carriage rate. The effect of these changes on the nasal carriage rate can be simulated using the model. The change in the population trend or the duration of hospitalisation will result in a different number, age and length of stay distribution. This new hypothetical numbers distribution will be used to simulate the expected carriage rate resulting from the change in the parameters.

Finally, it must be noted that although this is an

elementary model, for the first time, we are able to use a mathematical model which could predict the relationship between nasal carriage and the patient parameters. This modelling concept can be extended to the epidemiology of other organisms such as the gram-negative bacilli in the gastro-intestinal tract.

CHAPTER 12

CONCLUSIONS

The rather extensive literature survey carried out indicated that there are many contradictory views on the significance of certain parameters on wound infection and nasal carriage. The confusion arose primarily due to the somewhat uncontrolled nature of the experiments carried out and the failure in recognising the need to make allowances for the significance of patient parameters. The cross-sectional survey was intended to isolate the patient parameters and to develop a model capable of correcting patient samples for differences in patient parameters.

The primary analysis of the data established that age, sex, wound drainage and wound description are associated with post-operative wound infection. The correlation analysis confirmed that these parameters are not correlated, and hence, these observations are free from bias arising from interaction between parameters. The multiple regression indicated that wound contamination is the most significant parameter followed by drainage and male sex in determining the risk of infection.

On nasal carriage, age, sex, length of stay and exposure to antibiotics appeared to be the significant parameters. The correlation analysis confirmed that these parameters are not correlated, which excluded the possibility of a bias arising from interaction between parameters. The multiple regression indicated that exposure to antibiotics and male sex are more predominant in determining the risk of nasal carriage, but for extremes of age and length of stay, age

and length of stay can be more predominant.

The patient parameters shown in this cross-sectional study is similar to observations made in continuous studies. Further, the age and length of stay curves derived in this study were similar to curves derived from other sources based on continuous studies. It was not possible to compare the age and nasal carriage curves from other sources at the beginning of this study, but recent work by my colleagues (I25) based on the analysis of a continuous survey, produced age and nasal carriage curves decidedly similar to the curves reported in this cross-sectional study. Hence, confirming that large scale cross-sectional studies are useful and also representative of continuous studies, as a tool of epidemiology.

The major objective of the study was to develop a model capable of correcting experimental results for differences in patient parameters. This was achieved primarily through the multiple regression models on wound infection and nasal carriage. This is one of the first (if not the first) multiple regression studies carried out on the patient parameters related to nasal carriage. The resulting graphical representation was extremely useful in demonstrating both the significance of patient parameters and environmental (ward) parameters.

The primary modelling approach was useful in explaining the behaviour of the variables, age and length of stay. The log model confirmed the significance of the ageing phenomenon, and the modified deterministic model confirmed that the relationship between nasal carriage and length of stay follow basic epidemiological concepts. The rate of interaction between susceptibles and carriers, as defined in the

model is capable of representing variations in both patient and ward parameters.

In the process of developing the comprehensive mathematical model, the significance of a further variable so far neglected by everyone was established. This is the distribution of number of patients in different age and length of stay groups. This distribution of numbers is very important when comparing carriage rates reported on different patient samples. Using total differentials, a model based on age, length of stay and the numbers distribution was formulated which can be used to determine the expected carriage rate. This mathematical model was very versatile and quite similar to the regression surface on nasal carriage. This study hence confirmed the usefulness of modelling techniques, applied to the epidemiology of staphylococcal nasal carriage.

CHAPTER 13

FURTHER WORK

- I. This study laid the foundation for the modelling approach to the study of cross-infection. The models are still at their infancy stage and can be expanded using some of the concepts developed in this thesis. These concepts can equally be applied to different organisms in different sites, such as gram-negative bacilli in the gastro - intestinal tract.

2. In the multiple regression analysis the variables were only considered as singular variables. It is possible that products of some factors such as age and length of stay, if included in the regression could improve the multiple correlation.

3. The correlation analysis and the correction of ward parameters using the regression models should be followed through, using the existing data, and if possible with the aid of further experiments.

4. The association between exposure to antibiotics and nasal carriage established here was based on the assumption that antibiotics are in the majority administered before the patients became carriers. Although this assumption may be valid, it is worthwhile investigating this aspect further using a controlled study.

5. The association between nasal carriage of resistant Staphylococci and the risk of post-operative wound

infection was not adequately established in the literature survey. Since, this study was based on a cross-sectional survey, this association could not be tested here. Therefore this must be carried out based on an independent controlled study.

6. Many conclusions have been made in the past on the significance of many parameters on nasal carriage and cross-infection, without correcting the experimental results for differences in patient parameters. Most of these conclusions can now be re-examined with the aid of the models developed here.

A P P E N D I X .A.

APPENDIX A.I

CROSS INFECTION SURVEY REGIONAL SURVEY

PATIENT'S INFORMATION RECORD

HOSPITAL

				1
				4

WARD

Month and year }
 Day } of admission

								7
--	--	--	--	--	--	--	--	---

side ward number

				11
--	--	--	--	----

Type of patient

				13
--	--	--	--	----

Sex 1. Male 2. Female

				15
--	--	--	--	----

Age

				17
--	--	--	--	----

Hospital Unit number

				18
--	--	--	--	----

Date of discharge (B4) or date of survey

										20
--	--	--	--	--	--	--	--	--	--	----

Days in hospital

				26
--	--	--	--	----

Diagnosis 1.

								28
--	--	--	--	--	--	--	--	----

2.

								32
--	--	--	--	--	--	--	--	----

Operation

								36
--	--	--	--	--	--	--	--	----

Date Days after admission

				39
--	--	--	--	----

WOUND

- 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
--	--	--	--	----

TYPE OF DRAIN

- 1. Redivac 2. Corrugated 3. Large tube 4. Wick
- 5. Small tube 6. More than one drain (of different types)

				42
--	--	--	--	----

DESCRIPTION

- 0. Not infected 1. Margin red with serous discharge
- 2. Purulent 3. Sinuses or fistulae 4. Wound break down
- 5. Deep abscess 6. Cellulitis 7. Previously Infected (now clean or healed)
- 8. Haematoma 9. Slough

				43
--	--	--	--	----

				44
--	--	--	--	----

				45
--	--	--	--	----

				46
--	--	--	--	----

SEVERITY OF INFECTION

- 1. Doubtful 2. Mild 3. Moderate 4. Severe 5. Drain wound only - mild

				47
--	--	--	--	----

SOURCE OF INFECTION

- 1. Ward 2. Theatre 3. Ward or Theatre 4. Self 5. Unknown

				48
--	--	--	--	----

PYREXIA

- 0. No 1. Yes >100°F 2. Not known

				49
--	--	--	--	----

Onset of infection (days after operation)

				50
--	--	--	--	----

				51
--	--	--	--	----

OTHER INFECTIONS

- A.
- B.
- C.

		52
		54
		56

ACQUIRED 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
--	--	----

BACTERIOLOGY

- 1. Site
- Organisms
- 2. Site
- Organisms

		59
		60
		62
		63

Antibiotic sensitivity of staph. aureus.

- 0. Not applicable 1. Sensitive 2. Resistant to penicillin only
- 3. Resistant to 1 antibiotic other than penicillin 4. Resistant to 2 or more antibiotics (No staph. aureus - leave blank)

Site 1		65
Site 2		66

CHEMOTHERAPY

- 0. None 1. Penicillin 2. Amp 3. Clox 4. Sulphon
- 5. Strep 6. Tetra 7. Neo 8. Nitrofurantoin 9. Meth
- A. Eryth B. Novo C. Poly D. Kana E. Ceph F. Fuc
- G. Linco H. Topical Antibiotic K. Chloramphenicol L. Gentamycin
- M. Carbenicillin

		67
		68
		69
		70

ASSOCIATED FACTORS

- 1. Immuno-suppressive drugs 2. Irradiation 3. Steroids
- 4. Diabetes 5. Uraemia 6. Obesity 7. Malnutrition
- 8. Agammaglobulinaemia 9. others specify

		71
		72

Haemoglobin

		73
--	--	----

Procedures

		74
		75

Isolation (Regional Survey) 0. Nil 1. Side-ward 2. Ventilated side-ward
3. Barrier-nursing in main ward

		76
--	--	----

Other information

		77
--	--	----

RECORD NO.

2	B	79
---	---	----

APPENDIX A.2

WARD PRACTICES

(Where information not recorded code H)
(Where information not known code K)

Hospital	<input type="checkbox"/>	<input type="checkbox"/>	1
Ward	<input type="checkbox"/>	<input type="checkbox"/>	4
Year	<input type="checkbox"/>	<input type="checkbox"/>	6
Month	<input type="checkbox"/>	<input type="checkbox"/>	8
Day	<input type="checkbox"/>	<input type="checkbox"/>	10
Total Nursing Staff	<input type="checkbox"/>	<input type="checkbox"/>	12
S.R.N. Day staff	<input type="checkbox"/>	<input type="checkbox"/>	14
S.R.N. Night staff	<input type="checkbox"/>	<input type="checkbox"/>	15
S.E.N. Day staff	<input type="checkbox"/>	<input type="checkbox"/>	16
S.E.N. Night staff	<input type="checkbox"/>	<input type="checkbox"/>	17
Orderlies	<input type="checkbox"/>	<input type="checkbox"/>	18
Domestics	<input type="checkbox"/>	<input type="checkbox"/>	19

FLOORS

Frequency of cleaning

1. More than twice daily 2. Twice daily 3. Daily
4. Alternate days 5. Less frequently 20

Dry cleaning

1. Nil 2. Vacuum cleaner with filter 3. Vacuum cleaner without filter 21
4. Broom 5. Polish - hand 6. Polish - machine 7. Kex type mop
8. Other (specify) 22

Wet cleaning

1. Nil 2. Mop - string 3. Mop - sponge
4. Mop with two-compartment bucket 5. Hand scrubbing
6. Scrubbing machine 7. Combined scrubbing and vacuum machine
8. Other (specify)
- Routine 23
Special 24

Storage of Mops

0. No special technique 1. Dried 2. Disinfectant 3. Other 25

WALLS AND SURFACES

Frequency of cleaning

1. Daily 2. 2-3 times per week 3. Weekly 4. Fortnightly 5. Monthly
6. 2-4 months 7. 5-6 months 8. Less frequently 9. Irregularly
- Complete ward 26
Whole wall routine 27
Whole wall special 28
Lower wall 29
Surfaces 30

Method

- 1. Dry dusting 2. Damp dusting 3. Kex-type mop 4. Washing
- 5. Spraying 6. Others

- Walls routine 31
- Walls special 32
- Surfaces 33

SPECIAL RISK SITES

Frequency of cleaning

- 0. Not used 1. After use always 2. After use sometimes
- 3. After use by infected patients and daily 4. After use and daily
- 5. Daily 6. Less frequently 7. Disposable 8. Other

- Urinals 34
- Bed pans 35
- Pots (children) 36
- Toilet 37
- Toilet seat 38
- Bath 39
- Wash basin 40
- Wash bowl 41

Method

- 0. Not used 1. Washed only, no further treatment 2. Hot water
- 3. Boiled 4. Steam treatment 5. Disinfectant 6. Disposal unit

- Urinals 42
- Bed pans 43
- Pots (children) 44
- Toilet 45
- Toilet seat 46
- Bath 47
- Wash basin 48
- Wash bowl 49

Covers

Disposable toilet seat covers

- 1. Yes 2. No 3. Sometimes

50

Bed pan covers

- 0. Not used 1. Linen 2. Disposable 3. Other

51

BLANKETS - MATERIAL

- 1. Wool 2. Cotton cellular 3. Synthetic fibre
- 4. Mixed 5. Other - specify

52

Frequency of changing

- 1. Weekly 2. Twice weekly or more frequently 3. Every 2-4 weeks
- 4. Less frequently 5. After discharge of patient 6. Irregularly
- 7. Other

Routine

53

54

Infected patients

55

56

CURTAINS AND SCREENS

- 0. No curtains or screens 1. Curtains only 2. Screens only
- 3. Curtains and screens

57

Material

- 1. Cotton 2. Plastic 3. Fibreglass 4. Material 5. Other - specify

Curtains

58

Screens

59

Changed or Disinfected

- 1. Weekly 2. Fortnightly 3. Monthly 4. 2-3 monthly 5. 4-6 monthly
- 6. Over 6 months 7. Irregularly 8. Other - specify

Curtains

60

Screens

61

TOWELS - type for hand washing

- 1. Linen 2. Roller 3. Roll-c-mat 4. Paper 5. Others - specify

62

MATRESSES AND PILLOWS

- 0. Not used 1. Not covered 2. Linen covers 3. Waterproof covers
- 4. Waterproof cover special cases only 5. Variable

Pillows

63

Mattresses

64

Treatment of Mattresses and Pillows

- 0. Not used 1. Not treated 2. Treated after all infectious patients
- 3. Treated after some infected patients 4. Treated after each patient
- 5. Irregularly 6. After death only 7. Other - specify

Pillows

65

Mattresses

66

Method of Treatment

- 0. Low temperature wash only 1. Water 80°C-99°C 2. Water 100°C
- 3. Autoclave 4. Low tem. steam 5. Phenolic - specify 6. Q.A.C. specify
- 7. Formaldehyde 8. Fresh air 9. Other - specify

Blankets

67

Mattresses (routine)

68

" (contaminated)

69

Pillows (routine)

70

" (contaminated)

71

Sorting of linen

1. In ward 2. Sometimes in ward 3. Never in ward
4. Other arrangements 72

Disposal of linen

1. Special sack at bedside 2. Ordinary sack at bedside
3. Special sack in sluice room 4. Ordinary sack in sluice room
5. Other arrangements
- Routine 73
- Contaminated 74

Material of sack

1. Canvas 2. Plastic 3. Synthetic fibre 4. Other cloth
5. Paper 6. Other
- Routine 75
- Contaminated 76

DISINFECTION OF THERMOMETERS

1. Individual thermometers in disinfectant 77
2. All treated together after temperature round
3. Individually disinfected only on patients' discharge
4. Wiped with disinfectant after each patient 78
5. Individual thermometers in disinfectant (not labelled)
- Record No. B B 79

Card 2 Repeat columns 1-5 as Card 1

PRE-OPERATIVE PREPARATION IN WARD (Cold surgery only)

1. Day of operation 2. Previous day 3. Two days of treatment
4. Three days of treatment 5. Other 6

Method

1. Plain soap 2. Hexachlorophane soap or detergent 3. Chlorhexidine
4. Iodine 5. Iodophor 6. 70% Alcohol 7
7. Hexachlorophane soap and chlorhexidine 8. Others - specify 8

TREATMENT OF SHAVING EQUIPMENT (Ward)

0. Not used 1. Boiled or autoclaved after use
2. Boiled or autoclaved daily 3. Disinfected after use
4. Disinfected daily 5. Stored in disinfectant 6. Washed only
7. Disposable 8. Other - specify
- Brush 9
- Razor 10
- Electric razor heads 11

WOUND DRESSING

Wound dressing site

1. Ward 2. Dressing room, non-ventilated 3. Dressing room - ventilated
4. Bathroom 5. Sterilising room 6. Other - specify
- Main site 12
- Other site 13

Use of wound dressing room

0. Not applicable 1. All patients 2. Clean operations only
3. Septic operations only 4. All patients (excluding side-wards) 14
5. Clean operations (excluding side-wards)
6. Septic operations (excluding side-wards)

Number of staff in dressing team

1. One 2. Two 3. Sometimes two usually one 15

Dress

0. No special dress 1. Mask 2. Gown 3. Gown & Mask
4. Gown, mask & cap 5. Gown & cap 6. Cap & mask 7. Other - specify 16

Gloves used

1. Yes 2. No 3. Special wounds only 17

Hand washing

1. Plain soap 2. Hexachlorophane bar soap
3. Hexachlorophane detergent 4. Hexachlorophane liquid soap
5. Iodophor e.g. betadine 6. Other - specify

General 18

Dressings 19

Special techniques 20

Scrubbing

1. Yes 2. No 3. Special cases or technique only
4. At beginning of dressing round only 21
5. Beginning of round and special cases

TREATMENT OF NAIL BRUSHES

0. No nail brushes 1. No treatment 2. Autoclaved or boiled daily
3. Autoclaved or boiled daily and stored in disinfectant 22
4. Stored in disinfectant 5. Autoclaved after each use
6. Periodic treatment only 7. Other - specify

USE OF HAND CREAM IN WARDS

0. Not used 1. Rarely 2. Sometimes 3. Usually 4. Always 23

Container

1. Individual tube or jar 2. Communal jar 3. Communal tube 24

TREATMENT OF CHEATLE'S FORCEPS

0. Not used 1. Boiled or autoclaved before use
2. Boiled or autoclaved daily and stored in disinfectant 25
3. Stored in disinfectant 4. C.S.S.D.

DRESSING TECHNIQUE

1. Not no touch 2. No touch - pre-packed set
3. No touch - drum or box 4. Other procedure - specify 26

Number pairs of forceps used per dressing (usual) 27

CLEANING LOTION FOR WOUNDS

1. Saline 2. Eusol 3. Savlon 4. Cetrinide 5. 70% Alcohol
6. Chlorhexidine 7. Other - specify

Clean 28

Dirty or septic 29

ANTI-BACTERIAL SPRAY

0. Never used 1. Always used 2. Sometimes used

Name of spray Clean 30
Dirty or septic 31

TYPE OF DRESSING

0. Nil 1. Nil + Norbecutane 2 Gauze & cotton wool
3. Gauze & elastoplast sealed 4. Other - specify

Clean undrained 32
Drained 33
Dirty or septic 34

HANDLING OF CONTAMINATED DRESSINGS

1. Ungloved fingers 2. Gloved fingers 3. Forceps
4. Forceps, sometimes fingers

35

DISPOSAL OF CONTAMINATED DRESSINGS & INSTRUMENTS

1. Paper or plastic bag 2. Open receiver 3. Closed bucket
5. Open bucket 5. Paper bag and bucket 6. Container with disinfectant
7. Other - specify

Dressings & Disposables 36
Instruments (metal) 37

USE OF SIDE ROOMS

0. No side room 1. Very ill patients 2. Private patients
3. Infected patients 4. Any patients 5. Any combination

38
 39

Isolation facilities

1. Inadequate 2. Satisfactory
3. Satisfactory but not used for infections

40

Isolation of infections

0. Never 1. Rarely 2. Sometimes 3. Usually 4. Always
5. Hospital acquired only 6. Serious infections only 7. Not applicable

Wound infections 41
Enteric " 42
Other notifiable diseases 43
Infections due to Staph.aureus 44
" " " Ps.Pyocyanea 45
Other organisms - specify 46

Other Indications for isolation

1. Patients with suspected infection on admission
2. Patients transferred from other hospitals
3. Patients with suspected infection and transferred from
other hospitals

47

Barrier Nursing

1. Not done 2. In side-ward 3. Side-ward if available or main ward
4. Main ward only 5. Not applicable

- Notifiable diseases 48
Other infections, non-hospital acquired 49
" " , hospital acquired 50

Disposal of infected cases

1. Not transferred 2. Special isolation unit
3. Infectious diseases hospital or ward 4. Not applicable
5. Other - specify

- Notifiable diseases 51
Other infections - non-hospital acquired 52
" " - hospital acquired 53

Terminal disinfection of Isolation areas

1. Never 2. Rarely 3. Sometimes 4. Usually 5. Always
6. Not applicable or known

- Notifiable diseases 54
Other infections - non-hospital acquired 55
" " - hospital acquired 56

Treatment of Isolation areas

1. Routine treatment only 2. Washing with soap or detergent only
3. Washing with disinfectant 4. Formaldehyde fumigation
5. Sulphur fumigation 6. Fogging or spraying
7. Not applicable or known

- Notifiable diseases 57
Other infections - non-hospital acquired 58
Other infections - hospital acquired 59

Time of occupation after treatment

1. Within 6 hours 2. 6-24 hours 3. Over 24 hours
4. Normally 24 hours (less in emergency)
5. Normally over 24 hours (less in emergency)

60

TREATMENT OF WARD EQUIPMENT

0. Not used 1. Not treated 2. Boiled 3. Autoclaved 4. Hot air oven
5. Disinfectant 6. Disposable 7. C.S.S.D. 8 Other - specify
Syringes

61

62

General Instruments 63

64

Cutting Instruments 65

66

Drainage bottles 67

Suction tubing 68

Suction bottles 69

Tracheotomy tubes 70

L.P. sets 71
Aspiration sets 72
Oxygen masks 73

Crockery and Cutlery

Washing

1. Hand washed 2. Machine washed 3. Machine washed - heated over 80°C 74
4. Hand washed and heated over 90°C 5. Disinfectant 6. Other

Drying

1. Heat 2. Drainage only 3. Linen towel 4. Drainage + towel 75
5. Paper towel 6. Other - specify

76

Record No.

C B 79

ANTIBIOTIC PROPHYLAXIS

Specify type of case and antibiotic used.

Card 3 Repeat columns 1-5 as Card 1

DISINFECTANTS

1. Phenolic (Carbolic
(Lysol/Sudoal
(Izal type
(Hycolin/Printol
(Dettol
2. Tego 3. Q.A.C. 4. Chlorhexidine 5. Savlon 6. Alcohol
7. Iodophor e.g. Betadine 8. Chlorine Compound 9. Other

Name of Disinfectant Concentration

Floors - Main ward	6
" Annexes	7
Whole wall routine	8
" " special	9
Lower wall	10
Surfaces	11
Storage of mops	12
Bed pans	13
Urinals	14
Pots - children	15
Toilet	16
Toilet seat	17
Toilet brush	18
Bath	19
Wash basin	20
Wash bowl	21
Nail brushes - storage	22
Thermometers	23
Shaving brush 1. Ward	24
2. Barber	25
Razor 1. Ward	26
2. Barber	27
Razor head	28
Hand cream	29
Contaminated instruments	30
Isolation area	31
Crockery and Cutlery	32
Syringes	33
Chester forceps	34
Instruments general	35
Instruments cutting	36
Drainage bottles	37
L.F. & Aspiration needles	38
Suction equipment	39
Tracheotomy tubes	40
Oxygen masks	41
Respirator	42

APPENDIX A.3

WARD STRUCTURES AND FACILITIES

- Hospital 1
- Ward 4
- Year 6
- Month 8
- Day 10

AGE OF WARD (years)

- 1. 2 2. 2-5 3. 5-9 4. 10-19 5. 20-49 6. 50-99 7. 100- 12

TYPE OF PATIENTS

- 1. General surgical 2. General medical 3. Gynaecological
 - 4. Obstetric 5. Paediatric (medical) 6. Surgical & Medical
 - 7. Surgical & Gynaecological 8. Geriatric (medical)
 - 9. Orthopaedic 10. Others - see separate code.
- 13

Sex of patient

- 1. Male 2. Female 3. Male & Female in same ward
 - 4. Male & Female in different sections
- 15

STRUCTURAL FEATURES

General layout - grade

- 16

Position of ward

- 1. Lower ground floor. 2. Ground floor 3. First floor 4. Floors 2-3
 - 5. Floors 4-5 6. Higher floors 7. On more than one floor
- 17

Ward 1. Number of beds

- " 2. " " " 18
- " 3. " " " 20
- " 4. " " " 22
- " 5. " " " 23
- " 6. " " " 24
- " 6. " " " 25

Shape of Ward 1

- 1. Rectangular 2. Square 3. Round or oval 4. L. shaped
 - 5. Polygonal 6. Triangular 7. Other (specify)
- 26

Floor area Ward 1 (Sq.ft.)

- 1. <125 2. 125-249 3. 250-499 4. 500-999 5. 1000-1999
 - 6. 2000-4000 7. >4000
- 27

Height of Ward

- 1. < 10 ft. 2. 10-15 ft. 3. >15 ft.
- 28

Division of Ward 1

- 0. Not divided 1. Cubicles 2. Bays
- 29

No. of divisions Ward 1

- Single beds 30
- 2-4 beds 31
- 5-8 beds 32
- over 8 beds 33

No. of occupied beds, Ward 1 34

No. of extra beds, Ward 1 36

Balcony

0. No balcony 1. Balcony no beds 2. 1-2 beds 3. 3-5 beds 4. 6-8 beds 5. Over 8 beds 6. Balcony, no beds - dry room 37

Day room - number (in addition or instead of balcony) 38

Average distance between bed centres - all wards with more than 6 beds

1. <5 ft. 2. 5'-5'11" 3. 6'-6'11" 4. 7'-7'11" 5. 8'-8'11" 6. 9' + 39

No. of bed spaces less than 6 ft. all wards. 40

No. of bed spaces measured 42

Windows all wards more than 6 beds

1. Bright daylight 2. Moderate daylight 3. Restricted 4. variable in different wards 44

Type of floor, Ward 1

1. Wooden boards 2. Wooden blocks 3. Terrazzo 4. Plastic tiles 5. Plastic sheet 6. Tiles non-plastic 7. Lino 8. Other - specify 45

Condition of floor Ward 1

1. Good 2. Above average 3. Average 4. Below average 5. Poor 6. Average with areas of localised damage 46

Condition of walls, Ward 1

1. Good 2. Above average 3. Average 4. Below average 5. Poor 6. Average with areas of localised damage 47

WOUND DRESSING ROOM

0. None 1. Mechanically ventilated with air lock 2. Mechanically ventilated without air lock. 3. Not ventilated 48

Type of ventilation

SLUICE ROOM

0. None 1. One less than 50 ft. 2. One 50 ft.-100 ft. 3. One over 100 ft. 4. Two less than 50 ft. 5. Two 50 ft.-100 ft. 6. Two over 100 ft. 7. Two of different sizes 8. More than two 49

Type of floor of Sluice room

1. Wooden boards. 2. Wooden blocks 3. Terrazzo 4. Plastic tiles 5. Plastic sheet 6. Tile non-plastic 7. Lino 8. Other, specify 50

Size and design of Sluice room

1. Good 2. Adequate 3. Inadequate 4. Poor 51

General condition

1. Good 2. Above average 3. Average 4. Below average 5. Poor

52

Position

1. Opening on to main ward 2. Annexe adjacent to ward
3. Corridor away from ward 4. Other, specify

53

STERILISING OR PREPARATION ROOM

1. Good 2. Adequate 3. Inadequate 4. Poor 5. None

54

KITCHEN

1. Good 2. Adequate 3. Inadequate 4. Poor 5. None

55

STORAGE OF LINEN

1. In ward area 2. Special room 3. Sister's office 4. Other, specify

56

FACILITIES

Number of baths (excluding side wards)

57

" " showers " " "

58

" " wash-basins - patients' (excluding side wards)

59

" " " " - staff private

60

" " " " - Ward 1

61

Taps

1. Elbow operated Ward staff

62

2. Hand " Private staff

63

3. Foot " Washroom patients'

64

4. Elbow or hand operated Side ward "

65

Sterilising room

66

Wash basins in side wards

1. Yes 2. No 3. Variable

67

TOILETS

Number patients (Main ward)

68

Total

69

Separate for staff 1. Yes 2. No

70

Type

1. Hand flush high level 2. Hand flush low level 3. Foot flushing
4. Non-flushing hand 5. Non-flushing foot 6. Mixed

71

Toilet wash basins - site

1. In toilet 2. Adjacent to toilet 3. Not adjacent to toilet

72

STERILISING IN WARD

0. None 1. Boiler 2. Autoclave 3. Autoclave & boiler 4. Others

73

Use of Sterilisers

0. Not used 1. Used rarely 2. Used frequently

74

MULTIPLE USE OF FACILITIES

0. Not used for any other purpose

1. Dressings

2. Examinations and/or admissions

3. " " " and dressings

4. Disinfection of bed pans and/or urinals

5. " " contaminated linen

6. " " bed pans and contaminated linen

7. Preparation and storage of flowers

8. Other, specify

1. Bath room

75

2. Bath

76

3. Sterilising room

77

Same room for bath and toilet

1. Yes 2. No

78

Record No.

A B 79

A P P E N D I X .B.

APPENDIX B.1

CLASSIFICATION OF OPERATIONS
CLEAN-CONTAMINATED OPERATIONS

	<u>Computer Code</u>
Gastrectomy ..	423) If drained code 8
Cholecystectomy ..	521) If not drained code 7
Appendicectomy ..	441) If known to be pre- viously infected eg. Abscess
Pyloroplasty ..	431) Gangrene code 4
Perineal urethostomy	664
Prostatectomy suprapubic	672
Block dissection ..	923
Amputation for gangrene	
B.K.	894
Foot	895
Toes	896
Thoracotomy ..	331
Lobectomy ..	344
Cystotomy ..	640

EXCLUDED FROM SURVEY

Haemorrhoidectomy ..	483
Vaginal repair (Colporaphy)	743
Vaginal hysterectomy	724
Dilation - Curettage	732
Tonsillectomy ..	261

CONTAMINATED

Excision pilonidol	935
Colectomy ..	452
Colestomy ..	457
Caecostomy ..	458
Abdo-perineal excision	471
Mastoidectomy ..	206

CLEAN OPERATIONS

Hernia inguinal ..	560
Hernia repair ..	402
Varicose veins ..	460
Stripping of varicose veins	919
Ligature veins ..	916
Hydrocele ..	613
Excision of Hydrocele	690
Circumcision ..	682
Umbilical hernia ..	5602
Repair ..	404
Cystoscopy ..	649
Laparotomy (unspecified)	400
Vagotomy ..	433
Prostatectomy retro ..	673
Nephrectomy ..	606
Mastectomy ..	382
Biopsy of breast ..	386
Abdominal hysterectomy	722
Cataract Extrac.(Iridectomy)	151
Bunionectomy ..	838
Menisectomy ..	829
Caesarian section ..	765
Endartrectomy ..	902
Amputation (Clean contaminated if for gangrene)	894
Skin graft ..	942
Lumbar sympathectomy	041
Orchioplasty (Torek)	694
Pinning or plating ..	806

CLEAN OPERATIONS (CONTINUED)

Traction of fracture	..	804
Arthrodesis	..	836
Exc. Carpel Tunnel	..	851
Tonsils - enlarged	..	5100 medical diagnosis
Excision - abscess (boils, ulcers, carbuncles, cysts)		930

APPENDIX B.2

TYPE OF PATIENTS IN THE SURVEY

				%
1. General Surgical	..	2785	..	23.70
2. General Medical	..	2178	..	18.54
3. Gynaecological	..	575	..	4.89
4. Obstetric	..	1379	..	11.74
5. Paediatric (Medical)	..	221	..	1.88
6. Surgical and Medical	..	239	..	2.03
7. Surgical and Gynaecological		3	..	0.03
8. Geriatric Medical	..	390	..	3.32
9. Orthopaedic	..	835	..	7.11
10. Geriatric Surgical	..	106	..	0.90
11. Ophthalmic	..	183	..	1.56
12. General Surgical & Orthopaedic		295	..	2.51
13. Medical & Ophthalmic	..	23	..	0.20
14. Trauma	..	416	..	3.54
15. Paediatric (Medical & Surgical)		277	..	2.36
16. Medical Chests	..	122	..	1.04
17. Surgical (Thoracic)	..	145	..	1.23
18. Metabolic	..	38	..	0.32
19. Isolation (Adults)	..	113	..	0.96
20. Paediatric (Surgical)	..	162	..	1.38
21. Isolation (Children)	..	98	..	0.83
22. E.N.T.	..	294	..	2.50
23. Urological	..	112	..	0.95
24. Isolation (Babies under 1 year)		47	..	0.40
25. T.B.	..	22	..	0.19
26. Medical & Thoracic Surgery		2	..	0.02
27. Premature or Special Baby Unit		147	..	1.25
28. Burns	..	47	..	0.40

TYPE OF PATIENTS IN THE SURVEY (CONTD.)

				%
29. Radiotherapy	..	106	..	0.90
30. Neurosurgical & Ophthalmic		26	..	0.22
31. Intensive care	..	43	..	0.37
32. Neurosurgical	..	36	..	0.31
33. Neurosurgical (Medical)		18	..	0.15
34. Neurosurgical (Medical & Surgical Children)		9	..	0.08
35. Medical & Orthopaedic		55	..	0.47
36. Gynaecological or Orthopaedic		43	..	0.37
37. Dermatology & Dental	..	58	..	0.49
38. Diabetes	..	20	..	0.17
39. Surgical & E.N.T.	..	9	..	0.08
40. Unknown	..	72	..	0.61
		Total		<u>11749</u>

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