

INFECTION AND ENVIRONMENTAL CONTAMINATION
IN A GENERAL HOSPITAL
AND
IN A DERMATOLOGY DEPARTMENT

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"Infirmaries, or hospitals, in all countries, are for the most part unclean and infectious places, and tho' every precaution is taken to purify them, such as washing with vinegar, burning brimstone, gunpowder, or resinous substances, scouring the boards, and such like; yet a perfectly safe purification, in some cases, can never be fully effected the seeds of infection once sown, continue, in some instances, to spread contagious diseases, and to contaminate the house, as much as ever the walls of the Israelites were infected with the filthy leprosy, which is said to have germinated from the walls of their tents or hutts"

(Brocklesby, 1764).

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PREFACE

In the first part of this thesis an attempt has been made to provide a concise account of the history of hospital infection. Neglected early contributions, particularly from the eighteenth and nineteenth centuries, are reviewed; and the survey is continued up to 1966. It is hoped that this section, together with the subsequent discussions, may usefully supplement the review by Williams et al. (1960) which deals almost exclusively with the literature from the end of the Second World War until 1960.

The investigations embodied in the second and third parts of the thesis began in 1960. During the first year of the work, a study was made of all clinically-apparent infections which developed in the maternity department and in the majority of medical and surgical wards of a general hospital. To the broad picture of hospital infection which emerged, were added the results of a systematic bacteriological examination of the hospital environment.

Following this general study, a detailed enquiry was made into the mechanism of cross-infection in a dermatology department. The conditions encountered in such a department offered unique opportunities for the study of the bacteriological interaction of patients and environment. This investigation occupied a period of four years. It was mainly concerned with the dispersal of pathogenic bacteria by patients, and with the effects of specific counter-measures on both the incidence of cross-infection and of bacterial contamination of the environment.

PART I.

INTRODUCTORY REVIEW

(1) THE EARLY HISTORY OF HOSPITAL INFECTION

The subject of hospital cross-infection still awaits a historian. His task will be considerable for it must encompass more than 4,000 years of man's social history, and deal with the numerous institutions which were the forerunners of the modern hospital.

The Hygienic Standards of Early Hospitals

Before the beginning of the Fifth Century B.C. organized hospitals for the care of the sick existed throughout the civilized world, and notably in India, Egypt, Palestine and Greece. The hygienic conditions which prevailed seem to have been greatly superior to those that were tolerated less than one hundred years ago in the hospitals of Western Europe.

Detailed advice on hospital construction and hygiene

is contained in the Charaka-Samhita, a Sanskrit textbook of medicine which was probably written in the Fourth Century B.C., although based on writings of the Second Millenium B.C. The following extract from the work lays down sound principles for the prevention of hospital infection:

'In the first place a mansion must be constructed under the supervision of an engineer well-conversant with the science of building mansions and houses. It shall be spacious and roomy One portion at least should be open to the currents of wind. It should not be exposed to smoke, or dust, or injurious sound or touch or taste or form or scent After this should be secured a body of attendants of good behaviour, distinguished for purity and cleanliness of habits'.

The successful avoidance of hospital infection is evident from the remarkable range of operations described in the Sushruta-Samhita, an ancient surgical treatise which forms a companion to the Charaka-Samhita.

The Greeks of the Fifth Century B.C., though not as resourceful in surgery as their Indian contemporaries, provided admirable hospitals adjacent to the temples of Asklepios. The ward excavated at Epidauros is probably the oldest extant in the world.

'The abaton (ward) was a lofty and airy sleeping chamber, its southern side being an open colonnade ... This provision of abundance of pure fresh air for the sick by day and night, which is so beneficial now, was undoubtedly so then also, and probably brought much credit to the god and his shrine ... the precinct was as beautiful as the noblest works of Greek art could make it'. (Caton, 1899).

A reconstruction of part of the temple is reproduced in Figure 1.

In the small hospitals provided by the Ancient Jews at this time, the spread of infection was prevented by an

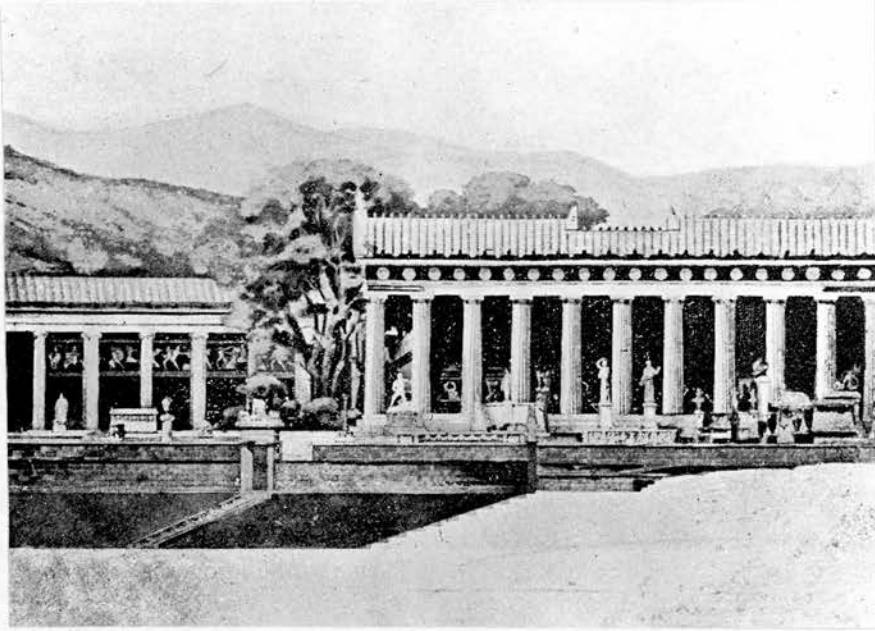


FIGURE 1. A RECONSTRUCTION OF THE ABATON (HOSPITAL WARD) AT THE
TEMPLE OF ASKLEPIOS NEAR EPIDAUROS - 5th.CENTURY B.C. (Caton,1899)

inflexible application of the laws of Leviticus. These deal not only with general hygiene, but also with the diagnosis of skin infections and other 'uncleanness', the isolation of the infected, and the destruction of fomites. In the Jewish Talmud, too, there are instructions for the prevention of air-borne infection, and the surgeon is warned that he must not touch a wound because 'the hands cause inflammation' (Snowman, 1935).

While it is likely that these high standards were maintained in the Roman valetudinaria, there was a general deterioration in European hygiene after the fall of the Roman Empire.

The Hospitals of Mediaeval and Renaissance Europe

The historian of hospital infection will find rich source material in the scattered references of mediaeval chroniclers to pestilence and 'visitations' in the monastic infirmaries, the leprosaria and the larger pre-Renaissance hospitals of Western Europe (Figures 2 and 3).

The early hospital reformers met with little success. In the Thirteenth Century, Theodoric of Bologna deplored the current teaching that 'laudable pus' was a prerequisite for sound wound healing. He carefully cleansed all wounds, and then sutured them to avoid contamination from the air. By these means he prevented suppuration in most of his cases (Major, 1954). As a result of his pioneer work on aseptic surgery Theodoric was persecuted by his colleagues and denounced



FIGURE 2. A WARD IN THE HÔTEL-DIEU, PARIS. (From a 15th. Century engraving — Tollet, 1892)

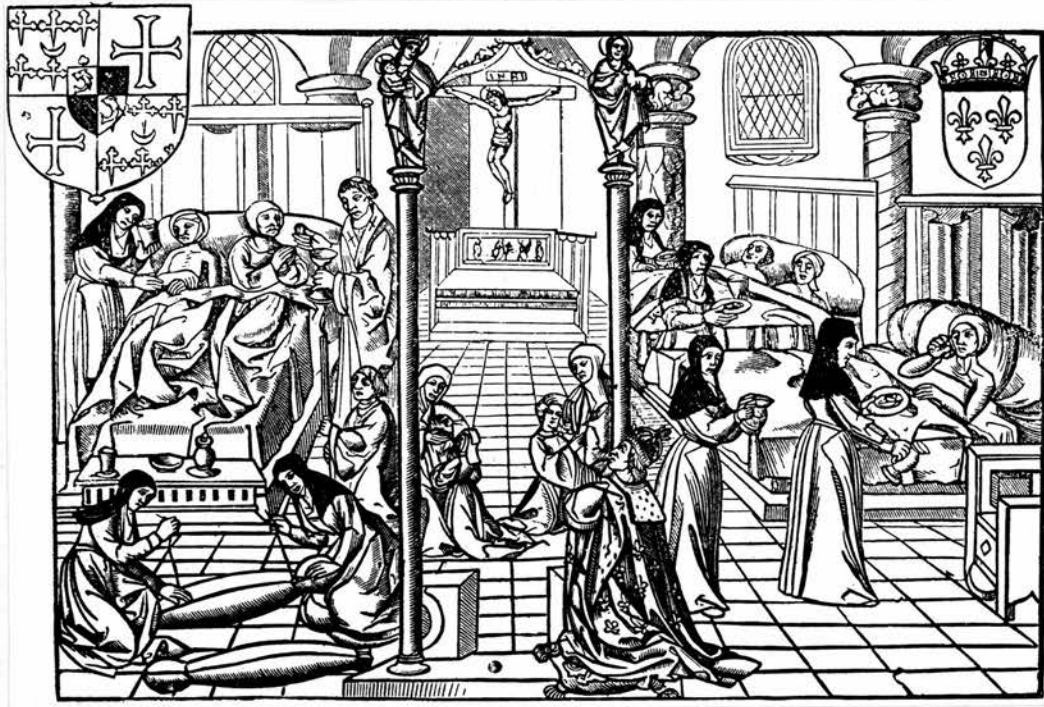


FIGURE 3. A WARD IN THE HÔTEL-DIEU, PARIS. (From a 16th.Century engraving — Tollet, 1892)

as a heretic by the Church. His pupil, Henri de Mondeville, also taught that suppuration hindered wound healing, but the belief in 'laudable pus' remained.

The following sixteenth-century comment upon surgical practice at the great Hôtel-Dieu in Paris is quoted by Bell (1801):

'A young surgeon who is bred in the Hôtel-Dieu, may learn the various forms of incisions, operations too, and the manner of dressing wounds; but the way of curing wounds he cannot learn. Every patient he takes in hand must die of gangrene'.

A typical surgical ward of this period is depicted in Figure 4.

Severe overcrowding in hospitals persisted for two centuries after the death of Ambroise Paré, as is shown in Figures 5 and 6 - which undoubtedly flatter their subjects. 'The possibility of nursing the sick in single beds' which Madame Necker suggested towards the end of the Eighteenth Century was considered very remarkable at a time when patients at the Hôtel-Dieu were still being nursed six or even eight in a bed amidst appalling squalor (Tenon, 1788). Madame Necker's innovation had been long anticipated, however, by the founders of the Edinburgh Royal Infirmary. A visitor to the new hospital wrote in 1739:

'the Beds are designed only to hold one Person ... the House is kept clean and sweet; you find nothing in it to offend either your Smell or your Eye; the Patients are used with great tenderness, and the Order established in the House, gives great satisfaction' (Maitland, 1753).

Very great interest was taken in each patient and detailed records were carefully kept as can be seen from the



FIGURE 4. A 16th-CENTURY SURGICAL WARD. (Paracelsus, 1565)

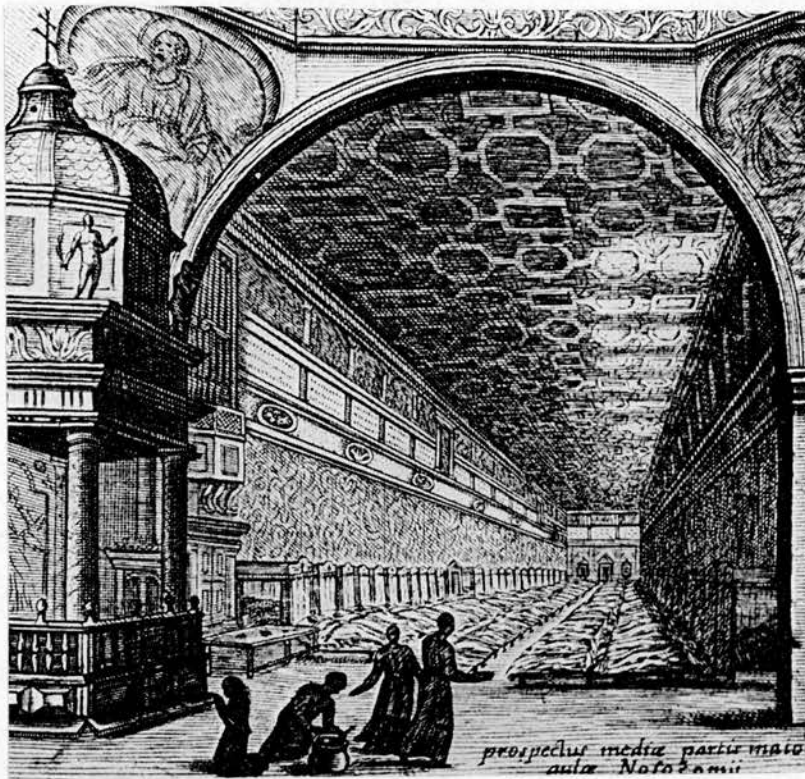


FIGURE 5. A MEDICAL WARD IN THE 17th. CENTURY.
(San Spirito, Rome — from Castiglioni, 1947)



FIGURE 6. A WARD IN THE HÔTEL-DIEU, PARIS. (From an early 18th. Century engraving — Tollet, 1892)

contemporary account quoted in the Appendix (p.383.). Unfortunately the early promise of this hospital proved to be illusory, as was shown by the observations first of Howard, then of Bell, and finally of Simpson (reviewed on p.23 et seq.).

Early Investigations of Hospital Cross-infection

The scientific study of hospital cross-infection began during the first half of the Eighteenth Century; and from that time until the beginning of the 'Bacteriological Era' many of the most notable contributions originated in Scotland. (See accompanying Table).

Hospital Fever. Sir John Pringle (1750, 1752) made the first important observations while he was both physician to the British Army overseas and Professor of Pneumatical and Ethical Philosophy at Edinburgh. In his efforts to improve the health of the expeditionary forces, Pringle introduced great sanitary reforms into his military hospitals to remedy the evils of overcrowding and poor ventilation. Pringle's insistence on adequate ventilation and spacing of patients, as expressed in the following passage, now appears unremarkable, but his views were revolutionary at the time:

'As to the disposition of hospitals, with regard to preserving the purity of the air, the best rule is, to admit so few patients into each ward, that a person unacquainted with the danger of bad air, might imagine there was room to take in double or triple the number. It will also be found a good expedient, when the ceilings (sic) are low, to remove some part of them, and to open the garret story (sic) to the tiles. It is surprising in how few days the air will be corrupted in close and crowded wards; and,

EARLY SCOTTISH PIONEERS AGAINST HOSPITAL INFECTION

	FLOURISHED	MAIN RELEVANT ACHIEVEMENTS
JOHN PRINGLE	1735-80	'Antiseptics'; reformed military hospitals
JAMES LIND	1745-90	Reformed naval hospitals; isolation wards
FRANCIS HOME & } THOMAS YOUNG }	c.1750-80	Appreciated contagious nature of puerperal fever
ALEXANDER HAMILTON	1760-1800	Valuable observations on puerperal fever
ALEXANDER GORDON	c.1795	Established contagious nature of puerperal fever
(MENZIES & PATERSON)	c.1795	Trials of air disinfection in hospital ships
JOHN BELL	1790-1820	Valuable observations on surgical sepsis
JAMES Y. SIMPSON	1830-70	Investigated hospital infection in its entirety
(JOSEPH LISTER)	(1860-1900)	(Antiseptic and aseptic surgery)
ALEXANDER OGSTON	1875-1920	'Staphylococcus'; elucidated bacteriology of suppuration
WATSON CHEYNE	1875-1925	First hospital bacteriological laboratory (Edinburgh, 1876)
JOHN CHIENE	1880-1909	Created interest in hospital bacteriological services

what makes it hard to remedy the evil, is the difficulty of convincing either the nurses or the sick themselves, of the necessity of opening the doors or windows at any time for air. I have generally found those wards the most healthful, when by broken windows, and other wants of repair, the air could not be excluded'.

Pringle's general sanitary improvements resulted from his careful studies of the epidemiology of 'hospital-fever', dysentery and 'the itch' amongst his patients. 'Hospital-fever' itself was first shown by Pringle (1750) to be the same disease as 'Jayl-fever' (typhus). His principal work which was published in 1752 embodies not only Pringle's observations on hospital infection but includes also his descriptions of 'Experiments on Septic and Antiseptic Substances', and here the term 'antiseptic' makes its first appearance in the literature. Moreover, in the fourth edition of his book Pringle (1764) favours the role of animate contagion rather than miasma in the spread of infection in hospitals, and he was thus one of the earliest to appreciate the wider medical implications of the discoveries of Leeuwenhoek and Kircher which he cites.

Pringle's observation that the hospitals were 'among the chief causes of sickness and death in an army' stimulated his military successor, Richard Brocklesby (1764) to bring about further improvements in hospital conditions. Brocklesby's book 'Oeconomical and Medical Observations ...' contains excellent accounts of the epidemiology and prevention of 'the malignant sore throat', 'spotted fever' and 'the dangerous putrid fever' in his hospitals. Brocklesby's trenchant statement on the dangers of hospitals is still relevant at the present day:

'Infirmaries, or hospitals, in all countries, are for the most part unclean and infectious places, and tho' every precaution is taken to purify them, such as washing with vinegar, burning brimstone, gunpowder, or resinous substances, scouring the boards, and such like; yet a perfectly safe purification, in some cases, can never be fully effected the seeds of infection once sown, continue, in some instances, to spread contagious diseases, and to contaminate the house, as much as ever the walls of the Israelites were infected with the filthy leprosy, which is said to have germinated from the walls of their tents or hutts '

Similar work to improve naval hospitals was carried out at this time by the Edinburgh physician, James Lind (1757). He recommended that wards should be reserved for different diseases to reduce cross-infection, and he gave detailed instructions for the disinfection of clothes and other fomites, the destruction of vermin and the filtration of water.

Towards the end of the Eighteenth Century, when many important hospitals were being founded both in Britain and abroad, the hygienic conditions of civilian hospitals also began to receive attention.

It was in the British navy, too, that the first planned trials of air disinfection were carried out. Outbreaks of 'ship fever' and respiratory infection on board British hospital ships in 1795 stimulated the Scottish naval surgeons Archibald Menzies and David Paterson to study the effects of nitrous acid fumes (Smyth, 1799). They observed very beneficial results following fumigation, although the great reduction in the incidence of 'ship fever' (typhus) must have been mainly due to their assiduous disinfection of clothes and their careful adherence to Lind's general hygienic regimen.

Of interest also at this time is the report by Smyth (1795) of 'an acid water drawn from tar' used as a disinfectant in hospitals by 'Mr. J. Bell', 'Mr. W. Farquharson' and others who were apparently naval surgeons too. Unfortunately nothing was to be heard of carbolic acid as a disinfectant for more than half a century, until the work of Lemaire (1863).

The first substantial attack on the condition of surgical wards was made by Alanson (1782) in his book 'On Amputations'. In this work the surgeon is warned of the increased danger of wound sepsis in crowded, city hospitals which

'are so tainted by unwholesome effluvia, that they are rather a pest, than a relief, to the objects they contain.'

Alanson gives detailed instructions for cleansing and ventilating the wards, for recognising infected individuals at the time of admission to avoid 'importing infection', for isolating those infected while in hospital, and for disinfecting personal clothing and bedclothes by baking 'in an oven constructed for the purpose'.

Shortly after Alanson's work civilian medical wards also came under very detailed scrutiny. Thus, Tenon (1788) made a thorough survey of the Parisian hospitals, and uncovered truly appalling conditions, particularly in the great Hôtel-Dieu. The philanthropist, John Howard (1789) also conducted a comprehensive enquiry into the state of the lazarettos, hospitals and prisons of Western Europe. Most of the British hospitals proved to be 'offensive beyond

description'; and the Edinburgh Royal Infirmary was not spared Howard's censure.

Then, in 1795, the French Council of Health drew up a very comprehensive series of instructions for the prevention of hospital infection (Transcript, 1804). These mainly consist of sensible rules 'for maintaining the salubrity and purifying the air of the wards of hospitals' together with interesting methods for the disinfection of selected articles used in hospitals. Unfortunately these recommendations resulted in no very obvious improvements. Robert (1806) described a formidable variety of diseases which were frequently contracted by patients in the principal French hospitals. His list of infections amongst medical patients includes

'érysipèle, la fièvre scarlatine, les ophtalmies, les rhumatismes aigus ... les synoques simples et putrides, les fièvres intermittentes, quelque typhus, quelques dyssenteries, et des fièvres erysipilateuses'.

Apart from these studies of infection in medical wards, the most valuable work on cross-infection during the Eighteenth Century was carried out in the field of obstetrics.

Puerperal Fever. Charles White (1773) and two Edinburgh professors, Francis Home and Thomas Young, seem to have been the first to consider puerperal fever an infectious disease (Thomas, 1819). Young's successor, William Hamilton, also had very advanced views on the communicability of both puerperal fever and surgical sepsis in hospital. Hamilton's remarkable insight into these conditions is evident in the

following passage:

"In hospital practice there is no doubt but that the disease (puerperal fever) is produced by specific contagion from the air of the wards. It is particularly observed in surgical wards that there is such a state of the air sometimes as produces almost in every wound, even the slightest symptoms of erysipelas and even mortification. In the Edinburgh Infirmary, when such a state of the air was present puerperal fever raged violently, but at no other time."
(Hamilton, 1781).

This observation on the relationship between surgical erysipelas and puerperal fever is very interesting, and has been fully confirmed by modern bacteriology.

It was not, however, until the publication of the masterly, but neglected monograph of an Aberdeen physician, Alexander Gordon (1795), that the infectious nature of puerperal fever was fully established. Although Gordon's observations on the Aberdeen epidemic were made in domiciliary practice they were of great relevance to hospitals. Of special value was the emphasis placed by Gordon on the transmission of infection on the hands and clothing of attendants. This was a more helpful approach than the one current at that time, derived during the Seventeenth Century from Sydenham and during the Eighteenth Century from Mead. Both of these revered medical men had held that diseases became epidemic owing to the interaction of 'Miasmata' and an 'Epidemick Constitution' of the atmosphere. But Gordon stated emphatically

'That the cause of the epidemic puerperal fever under consideration was not owing to a noxious constitution of the atmosphere, I had sufficient evidence; for, if it had been owing to that cause,

it would have seized women in a more promiscuous and indiscriminate manner. But this disease seized such women only as were visited or delivered by a practitioner or taken care of by a nurse, who had previously attended patients affected with the disease.

In short, I had evident proofs of its infectious nature, and that the infection was as readily communicated as that of smallpox or measles and operated more speedily than any other infection with which I am acquainted.

With respect to the physical qualities of the infection ... I had evident proofs that every person who had been with a patient in the puerperal fever, became charged with an atmosphere of infection, which was communicated to every pregnant woman who happened to come within its sphere. This is not an assertion, but a fact, admitting of demonstration...'

On the prevention of the disease, Gordon admits

"I must speak with great uncertainty, because in this matter I have not experience for my guide

Whether the infection of the puerperal fever is capable of being destroyed by the same means as that of other fevers, I cannot confirm with certainty but think it very probably and that they ought to be tried.

That fresh air and cleanliness are insufficient for the destruction of contagion and that there is no certain antidote but fire and smoke has been demonstrated by the ingenious Dr. Lind. This excellent author has proved that fire and smoke are the most powerful agents for annihilating infection; and, as he thinks, even the plague itself.

The methods which he recommends for the purification of infected chambers and for the fumigation of infected apparel may be seen by perusing his ingenious papers on fevers and infections to which I refer the reader.

The same means ought to be practised for preventing the infection of puerperal fever. The patient's apparel and bedclothes ought to be burnt or thoroughly purified; and the nurses and physicians who have attended patients affected with the puerperal fever, ought carefully to wash themselves and to get their apparel properly fumigated before it be put on again."

Near the end of his "Treatise", Gordon gives more details of the manner in which some patients receive the infection:

"That putrid matter is capable of producing an inflammatory disease is a position which perhaps will be

questioned by many readers. Be that as it will, its truth is proved both by dissection and inoculation for the smallpox; for if the matter be taken from the most malignant smallpox and applied to the arm of a person who never had the disease; it produces inflammation in the part to which it is applied and afterwards (provided the patient has been properly prepared) a distinct smallpox of the mildest kind.

And if in the dissection of a putrid body a surgeon scratch his finger, the part festers, that is inflames and suppurates; and if a fever should be the consequence it is inflammatory in the beginning and only ultimately putrid

In like manner, if putrid matter be applied to the uterus it inflames that organ and the contiguous viscera; that is, it gives rise to puerperal fever, which is ushered in with a cold stage, and succeeded by a very rapid pulse and acute pain in the abdomen."

Because of his scrupulous honesty in naming those attendants who had spread the infection, Gordon suffered a fate which foreshadowed that of Semmelweis.

Fifty years later, the celebrated paper 'on the contagiousness of puerperal fever' by Oliver Wendell Holmes (1843) merely re-emphasised Gordon's findings. Semmelweis (1847; 1849) carried the work one stage further, and obtained a marked reduction in the incidence of puerperal fever in hospital by using a solution of chlorinated lime for the disinfection of attendants' hands. Several years before either Holmes or Semmelweis, however, James Young Simpson in Edinburgh was lecturing persuasively on the contagiousness of puerperal fever. Simpson in this way began the battle against hospital cross-infection which he was to fight during the remainder of his life. (Selwyn, 1965).

Surgical Gangrene and Surgical Fever. Simpson (1850; 1859)

then proceeded to make a special study of the epidemiology and prevention of 'surgical fever', which was, he believed, frequently due to cross-infection, and was closely analogous in other respects to puerperal fever. On the aetiology of puerperal fever, he had already extended the observation of Hamilton (1781) by noting in 1836 that

'the same focus of contagion producing puerperal fever in puerperal patients (caused) erysipelas, inflammatory sore throat, etc., in patients who were not in the puerperal state'. (Simpson, 1851).

In his Clinical Lectures, which were not published until 1859, Simpson declared that the subject of surgical fever had been completely neglected by surgeons, while

'every patient placed upon an operating table (in hospital) is in ... greater danger than a soldier entering one of the bloodiest and most fatal battle fields'.

In a passage on 'Communication by contagious inoculation' Simpson described transmission of infection by the surgeon, his attendants and nurses, adding

'I believe that surgical fever is often enough propagated in this way, just as puerperal fever is, ... perhaps ... to a degree that is at present not yet dreamt of'.

Deaths from surgical sepsis were not due to 'mortification' of the wound alone but rather

'were engendered by some morbid material circulating in the blood producing a special toxæmic state'.

In these papers, Simpson anticipated his later views on hospital reform, but in addition he made two very remarkable observations. Patients were to be operated upon soon after their admission to hospital to minimise their exposure 'to

the vitiated air of an hospital before being subjected to the surgeon's knife'. This is fully in accordance with modern views on the acquisition of pathogenic 'hospital' bacteria. He also recommended that 'in the prophylaxis of surgical fever' fresh wounds could be treated with 'acid, chlorinated or other antiseptic applications' (Simpson, 1859).

In the mid-Nineteenth Century, death from post-operative wound infection - as described so vividly by Brown (1858) in 'Rab and his Friends' - occurred in more than 50 per cent of cases in many of the major hospitals. The surgeon, however, rarely sought for the cause in his own techniques (Figure 7) or in the condition of the hospitals in which he worked. Yet at the beginning of the century, the Edinburgh surgeon, John Bell (1801) in despair had written of 'the Hospital Gangrene',

'... in great hospitals especially, it prevails at all times ... let (the surgeon) bear in mind that this is a hospital disease; that without the circle of the infected walls the men are safe; let him, therefore, hurry them out of this house of death ... let him lay them in a schoolroom, a church, on a dunghill or in a stable ... let him carry them anywhere but to their graves'.

Bell's observations formed the basis of further work by Ollivier (1822). This French surgeon gave a detailed account of 'typhus traumatique', and 'gangrène ou pourriture des hôpitaux'. He considered at some length 'le virus gangreneux traumatique' describing experiments in which he inoculated himself with septic material with and without the addition of antiseptics. In this and in other ways he proved the efficacy of the various antiseptics which Pringle (1752) had originally described, and which Ollivier recommended for the



FIGURE 7. THE FIRST SURGICAL OPERATION UNDER ETHER ANAESTHESIA,
BOSTON, 1846.

prevention and treatment of wound sepsis. In the prophylaxis of wound sepsis he also advised strict cleanliness of the clothes of the surgeon and patient, of the surgeon's hands and his instruments as well as of the rooms, beds, blankets and dressings. In particular a dressing was not to be used repeatedly for different patients as it became 'imprégnée de miasmes septiques' but such was the practice 'de la charpie conservée depuis plusieurs années dans L'Hôtel-Dieu de Paris'.

He described how on one occasion the material for dressings

'à portée des salles, fut distribuée aux blessés de l'une des journées sanglantes de la révolution; chez la plupart, elle envenima les plaies, et y attire la pourriture dite des hôpitaux'.

Nevertheless, the majority of surgeons agreed with Guy (1863) that the continued high mortality was due to intrinsic defects in the patient, in view of the 'sanitary excellence our ... hospitals have now attained'. This complacent attitude was undermined as a result of Simpson's detailed enquiry into the mortality following amputations in hospitals of differing sizes, and in country practice. Simpson showed that the mortality was proportional to the size of the hospital and the degree of overcrowding. His main findings, together with detailed suggestions for hospital reforms, were published within a year of his death in a series of papers on 'Hospitalism' (Simpson, 1869; 1870). These remain as models for the epidemiologist. The results of the investigation supported his earlier statement (Simpson, 1867) that

'although the establishment of hospitals is a necessity the bringing together within a confined area of

many sick persons is perilous. The risks of contamination of the air and of impregnation of the materials of the building with morbid substances, are so greatly increased, that the greatest care is necessary that hospitals should not become pesthouses, and do more harm than good. There is indeed a continual sacrifice of life from diseases caught in or aggravated by hospitals. The risk ... is least in the best ventilated hospitals. A great supply of air, by immediately diluting and rapidly carrying away the morbid substances evolved in such quantities from the bodies and excretions of the sick, reduces the risk to its minimum'.

Inevitably, Simpson's work became the centre of bitter controversy. His chief opponent was the surgeon, Timothy Holmes (1869) who, several years earlier, had been co-author of an official report on the state of British hospitals (Bristowe and Holmes, 1863). Despite the abundant evidence of cross-infection presented in this report, its authors concluded that most of the hospitals examined were in themselves satisfactory - thus agreeing with Guy.

The case for hospital reform, however, had already been ably promoted by Florence Nightingale (1858) following her experiences in military hospitals during the Crimean War (Figure 8), and her subsequent examination of British civilian hospitals. Miss Nightingale argued her case persuasively and undoubtedly brought about great improvements in hospital conditions; though, unlike Simpson, she showed no interest in the work of the pioneer bacteriologists and students of air hygiene. Moreover, she was hostile to the "Germ Theory" of disease for the remainder of her life.



FIGURE 8. THE HOSPITAL AT SCUTARI, CRIMEA. (From a lithograph published in 1856)

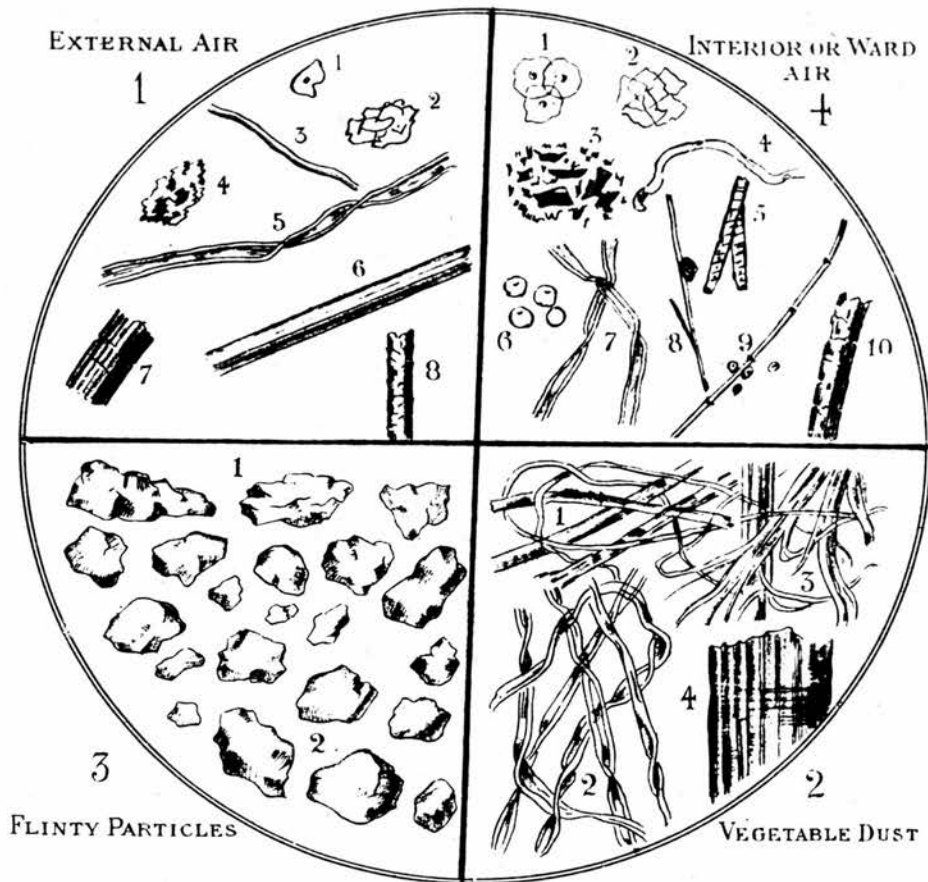
Studies of the Mechanism of Cross-infection in the Nineteenth
Century

Much of the early experimental work on the transmission of infection in hospital is cited by Simpson (1869). He was particularly impressed by the observations of Pasteur, Gratiolet and Lemaire

'that the atmosphere is full of living spores and germs of various infusoria, etc., which, when they find a proper nidus, lead on by their development to fermentations, putrefactions, suppurations, etc.'

Of great interest also at this time were the reports of Thomson (1855), Rainy (1855) and Elisel (1861) on the presence of skin scales, 'pus globules' and other possible vehicles of infection in the air, and on the walls and floors of hospital wards. These findings were confirmed and extended by a number of medical officers in the British army, notably Hewlett, Stanley and Baynes (1861), de Chaumont (1867) and Temple-Wright (1869). Towards the end of this period, further valuable information resulted from the study of air-borne dust by Tyndall (1881), and from similar investigations carried out in Edinburgh by Andrew Smart (1883) who, 18 years earlier, had been one of the first exponents of the 'germ theory' of disease. Figure 9 reproduces Smart's diagram of the microscopical appearance of suspended dust.

The ancient concept of infection from the environment thus obtained scientific support before the birth of medical bacteriology. The earlier findings of Gordon, Simpson and Semmelweis on the transmission of infection by indirect



*Microscopical Examination of Dust suspended in the Air.**

INTERNAL (OR WARD) AIR.

1. Epithelium from the Mouth. 2. Ditto from the Skin. 3. Mineral Dust. 4. Flax Fibre. 5. Striped Muscular Fibre. 6. Animal Cells. 7. Cotton Fibre. 8. Unstriped Muscular Fibre with Fat Globule adherent. 9. Fungi and Spores. 10. Woollen Fibre.

EXTERNAL AIR.

1. Epithelium Cell from the Mouth. 2. Ditto Scales from Skin. 3. Linen Fibre. 4. Mineral Dust. 5. Cotton Fibre. 6. Hair. 7. Woody Fibrous Tissue. 8. Woollen Fibre.

VEGETABLE DUST.

1. Linen Fibre. 2. Hemp. 3. Cotton. 4. Pine Wood.

MINERAL DUST.

1. Flinty Granules with sharp edges. 2. The same with edges rounded off.

* The examinations of the Ward and External Air were, at the author's request, kindly made by Dr Wood, House Physician, Old Royal Infirmary; to whom he is also indebted for the accompanying Sketch.

FIGURE 9. MICROSCOPIC "DUST" IN THE AIR BOTH INSIDE AND OUTSIDE
THE OLD EDINBURGH ROYAL INFIRMARY, ABOUT THE YEAR 1870. (Smart, 1883).

contact, together with the initial observations on environmental contamination provided a foundation for the further study of hospital infection.

The accumulating knowledge achieved its first practical expression in the work of Joseph Lister (1867; 1875). While his prophylactic use of carbolic acid in wounds had been anticipated by others, especially in France and Germany - indeed Simpson (1859) had previously advocated similar measures - Lister's unique contribution lay in his early insight into the role of bacteria in surgical sepsis, and his demonstration that sepsis can be avoided by excluding bacteria from a surgical wound.

During the remainder of the Nineteenth Century, the principles of antiseptic, and later, aseptic surgery were successfully disseminated by Lister and his students; and Simpson's ideas on hospital reform gained gradual acceptance, aided by the advocacy of Erichsen (1874), Hutchinson (1874), Bradley (1876) and others. Meanwhile, a firm aetiological basis for the study of hospital infection was provided by the new bacteriological discoveries - such as those of the Aberdeen surgeon, Alexander Ogston (1881), who classified the principal pyogenic cocci as streptococci, and those that he termed 'staphylococci'. However, even earlier than Ogston, Watson Cheyne in Edinburgh had investigated the bacteriology of wound infections. In 1876, during his period as Lister's house-surgeon, Cheyne started what was probably the first clinical bacteriological laboratory in Britain 'in a little

passage behind the operating theatre in the old Edinburgh Infirmary (Cheyne, 1925). The further development of hospital bacteriology in Britain also received its impetus from Edinburgh. In 1884, the Professor of Surgery at Edinburgh, John Chiene, read a memorable paper at the Annual Meeting of the British Medical Association on 'The desirability of establishing bacteriological laboratories in connection with hospital wards' (Report, 1884); and in 1887, the Edinburgh Royal College of Physicians founded a clinical laboratory for research and for 'the examination of specimens met with in practice' (Ritchie, 1953).

A better understanding of the indirect routes of hospital cross-infection resulted from the work of Nepveu (1877), Cornet (1889) and Flügge (1897). Nepveu reported the discovery of

'des micrococcus en très-grande quantité (50 à 60 par champ du microscope), quelque microbactéries; de plus des cellules épithéliales en petit nombre, quelques globules de pus...'

on walls and other solid surfaces in hospital. Though the bacteria seen were probably saprophytes, Nepveu's findings, nevertheless, gave tangible form to the mystical and ubiquitous 'poison nosocomial'. Cornet and Flügge who were both concerned principally with the transmission of tuberculosis in the air, stressed the importance, respectively, of dust and of droplets derived from the respiratory tract as the vehicles of air-borne infection.

As a result of this intensive activity in the study of infection and hospital hygiene, the art of hospital construction rapidly developed into an exact science - notably in the work of Galton (1893).

At the close of the Nineteenth Century, therefore,

the triumphs of asepsis and hospital reform seemed to herald the final victory over hospital cross-infection.

(ii) HOSPITAL INFECTION IN THE TWENTIETH CENTURY

Any undue optimism which may have been current at the turn of the century in relation to hospital infection was soon found to be unjustified. Whereas during the previous century the interest in cross-infection had been focused on obstetrical and surgical problems, there was at the beginning of the Twentieth Century a renewal of interest in cross-infection amongst medical patients. The stimulus was provided by the opening of a large number of hospitals for infectious diseases.

Infectious Diseases Hospitals

The relevant work at this time consisted mainly of clinical observations on the acquisition of specific infectious fevers by patients during their stay in hospital. Measles, chickenpox, scarlet fever, whooping cough and diphtheria were frequently seen to spread in the fever wards. Observations made on the transmission of these diseases have provided valuable information on hospital infection in general, and air-borne infection in particular. Thus Biernacki (1908) observed that cross-infection with whooping cough was largely prevented by spacing beds twelve feet apart, and similar findings were later reported in connection with cerebro-spinal fever (Glover, 1920).

A reasonable inference from these results is that both the whooping cough bacillus and the meningococcus rarely survive the processes involved in the formation of droplet nuclei and dust.

The importance of air-borne infection was not, however, accepted by all who worked in infectious diseases hospitals. Rundle (1912) strenuously denied the relevance of the more recent air studies, including those of Gordon (1902-3), Harrington (1904) and Robb (1909). Rundle freely treated different infectious diseases in the same ward, and claimed a surprisingly low incidence of cross-infection as a result of what he termed 'medical asepsis'. Nevertheless his system of barrier nursing failed if he admitted to his wards patients with scarlet fever, and especially those with septic complications such as otorrhoea. Harries (1935) in a detailed review of cross-infection in children's fever wards also minimised the importance of air-borne infection. He noted, however, that efficient barrier nursing failed to prevent the spread of measles and chickenpox.

Streptococcal Cross-infection

Although the epidemiology of scarlet fever in mixed wards could be partially investigated without the aid of the laboratory, purely clinical observations were of very limited value in wards devoted to scarlet fever. Nevertheless, it was suspected that many of the 'relapses' which occurred during convalescence from scarlet fever were due to re-infection from other patients. This impression was supported by a study of the 'return cases' seen in the families of patients who had been

discharged from hospital (Cameron, 1905; Parsons, 1927). The incidence of return cases was found to be proportional to the length of stay in hospital and the degree of overcrowding in the ward. The rate was particularly high in those patients who had chronic diseases of the ear, nose or throat, or who had been nursed in the same ward as 'septic' cases of scarlet fever.

The dissemination of Streptococcus pyogenes by scarlet fever patients in a hospital ward was demonstrated by Deicher (1927); but it was not until the advent of serological typing of Strep. pyogenes that the high incidence of cross-infection in scarlet fever wards was confirmed (Gunn and Griffith, 1928; Brown and Allison, 1935).

The epidemiology of puerperal fever due to Strep. pyogenes was also further elucidated by means of serological typing (Smith, 1931; Colebrook, 1935). This work fully established the importance of nasal and throat carriers in the transmission of streptococcal disease.

It was also shown that streptococcal cross-infection of burns occurred readily in hospital leading to serious local and general complications; and the causative organism was present in unusually large numbers in the air and dust of a burns ward (Cruickshank, 1935). The detailed studies by White (1936) and Cruickshank and Godber (1939) on streptococcal contamination in maternity wards, and also in a diphtheria ward in the second investigation, further emphasised the role of air-borne dust in the spread of infection.

Abundant evidence of streptococcal cross-infection was

found in other branches of hospital practice. Thus Okell and Elliot (1936), working in a general hospital, showed that such infection was especially prevalent amongst patients in wards which dealt with diseases of the ear, nose and throat. Cross-infection with haemolytic streptococci was also found to occur readily amongst measles and diphtheria patients (Allison, 1938), in paediatric medical and surgical wards (Wright, 1940), and amongst patients convalescing after influenza (Cruickshank and Muir, 1940).

At about this time, the observations of Wright, Shone and Tucker (1941) and Crosbie and Wright (1941) on the spread of diphtheria in hospital, helped to elucidate further the general problem of dust-borne infection. This work emphasised the danger of traditional methods of sweeping: and though hospital epidemics of wound diphtheria were probably never common, their study had already provided valuable information on the general epidemiology of surgical sepsis (Bensted, 1936). Likewise, the observations of Del Mundo and McKhann (1941) on the prevention of chickenpox in hospital wards were of interest in the general context of air disinfection by ultra-violet irradiation.

The importance of dust-borne infection was further demonstrated by the reduced incidence of streptococcal infection and of aerial contamination which followed the oiling of floors and bedclothes in a measles ward (Wright, Cruickshank and Gunn, 1944). Although these results appeared to confirm the significance of the earlier observations on infected dust in hospital wards, Begg, Smellie and Wright (1947), carried out a similar

experiment in a measles ward where there was already a relatively low rate of streptococcal cross-infection, and were unable to obtain any further reduction in the incidence by oiling floors and bedding.

During World War II, the application of serological typing to the study of streptococcal wound infections confirmed the early impression of Fleming and Porteous (1919) that streptococcal wound sepsis was often the result of cross-infection (Miles *et al.*, 1940). Another important finding made at this time was the recognition of the nasal carrier of Strep. pyogenes as a dangerous disperser of infection (Hare, 1941; Hamburger, Green and Hamburger, 1945).

The period from 1935 to 1950 which was marked by intensive enquiry into streptococcal cross-infection, saw also a great decline in the importance of this type of hospital infection. While much of the decline can be accounted for by the introduction of sulphonamides and penicillin, by improved hygiene in hospitals, and possibly by the use of chloroxylenol antiseptics in midwifery (Colebrook, 1936), the haemolytic streptococcus itself was probably undergoing a spontaneous decrease in virulence during this period. The trend apparently started in 1866 when, in the absence of improved therapy, there began to occur a steady fall in the mortality from scarlet fever and rheumatic fever (Rolleston, 1928), as well as from erysipelas and puerperal fever (Gale, 1959).

Nevertheless, hospital infection with Strep. pyogenes is still reported from time to time. Among the more serious of

the recent outbreaks of puerperal fever were those recorded by Gibson and Calman (1953) and Gray (1956). In neither incident was the primary source of infection discovered, although infected nurses may have been important secondary sources. Endemic infection has continued to be troublesome in burns wards (Lowbury, 1960a), occasionally in general surgical wards (Rountree, 1955) and also amongst medical patients (Markham, 1959). Moreover, though Strep. pyogenes remains uniformly sensitive to penicillin, treatment with this antibiotic may be relatively ineffective if there is a concurrent infection with penicillinase-producing organisms, for example Staphylococcus aureus (Rountree, 1955). Similar difficulties may be encountered in eliminating the carrier state (Gray, 1956), and possibly in antibiotic prophylaxis against streptococcal infection. Resistance to sulphonamides has been frequently observed (e.g. Francis, 1942; Report, 1945), and more recently the treatment of streptococcal infections has suffered a further setback with reports of increasing resistance to the tetracyclines (Robertson, 1965; Parker, Maxted and Fraser, 1962) and erythromycin (Lowbury, 1960b).

Therefore, despite the optimism which followed the introduction of penicillin, streptococcal cross-infection may still present problems in hospital but has become relatively unimportant in comparison with infections due to other organisms. Coinciding with the decline of the haemolytic streptococcus as a hospital pathogen, Staph. aureus emerged, after World War II, as the principal cause of cross-infection in hospital.

The Emergence of Staphylococcus Aureus

Hospital cross-infection due to Staph. aureus was of some importance before the end of the period which the streptococcus dominated, as was shown for example by Smith (1935), Poole and Whittle (1935), Hart (1937), Devenish and Miles (1939) and Miles (1941). Nevertheless, the reported increase in the incidence of staphylococcal hospital infection during the past 20 years is undoubtedly real and cannot be ascribed to improved diagnostic facilities, or to the greater interest shown in such infections following the decline in the importance of streptococcal infections (Hassall and Rountree, 1959). The general increase in non-streptococcal hospital infection, and of staphylococcal infection in particular, is the result of changes affecting both the host and the pathogen.

Serious and persistent staphylococcal disease is not infrequently found in otherwise healthy young adults (Colbeck, 1962). However, factors which have tended in recent years to increase the susceptibility of hospital patients to severe infection include the higher average age of the hospital population, the prolongation of life in cases of malignant disease and in advanced systemic diseases, the greater scope of modern surgery, the wider use of antimetabolic drugs, cortico-steroids and irradiation, and the uncontrolled use of antibiotics which can seriously disturb the normal bacterial flora of the body. Indeed McDermott (1956) held that increased host susceptibility alone could be responsible for the observed increase in staphylococcal hospital infection.

The ecological position of the pathogen has, nevertheless, undergone important changes as a result of the use of specific anti-bacterial drugs. Not only have these drugs acted as a selective force favouring the survival of resistant and possibly more virulent strains of bacteria, but the availability of such powerful prophylactic and therapeutic agents has tended to encourage a complacent attitude towards infection, with a consequent deterioration in the standards of aseptic technique (Barber, 1961).

Although excellent initial results were obtained with penicillin in the treatment of infections due to Staph. aureus as well as Strep. pyogenes, early failures were reported in the case of staphylococcal infection (Rammelkamp and Maxon, 1942). After being generally available for only a few years, penicillin began to prove ineffective against an increasingly large proportion of pathogenic staphylococci in hospitals (Barber, 1947; Barber and Rozwadowska - Dowzenko, 1948). Similar disappointments were experienced in the case of streptomycin (Buggs et al., 1946), the tetracyclines and chloramphenicol (Schneierson, 1952), and erythromycin (Lepper et al., 1953). Moreover, the reliance placed upon the newer antibiotics in cases of severe, drug-resistant infections is no longer justified, for there have been alarming reports of naturally-occurring hospital strains of Staph. aureus that are resistant to fusidic acid (Crosbie, 1963) and to the penicillinase-insensitive synthetic penicillins, such as methicillin (Parker and Jevons, 1964).

There has thus been established a vicious circle in

which cross-infection with resistant strains necessitates the use of newer antibiotics which, in their turn, selectively eliminate sensitive organisms; and this exposure of bacteria to antibiotics may occur in the environment as well as in the patient (Gould, 1958). A steady accumulation in the total numbers of multiple-resistant 'hospital staphylococci' is favoured by the remarkable ability of these organisms to survive desiccation for long periods in the environment (Rountree, 1963). Of relevance also is the demonstration that some multiple-resistant strains are of enhanced virulence, possibly due to their repeated passage in hospital patients (Barber et al., 1960).

The Laboratory Investigation of Staphylococcal Infections.

For more than 50 years after Ogston's first description of the staphylococcus, laboratory studies were hampered by the lack of a reliable test to distinguish pathogenic from non-pathogenic strains. Biochemical tests based on the fermentation of mannitol and liquefaction of gelatin were found to be of limited value in the identification of pathogenic staphylococci, and most bacteriologists continued to recognise pathogens on the basis of pigmentation alone, as originally described by Rosenbach (1884).

An important advance was made by Darányi (1925) who confirmed an earlier observation that pathogenic staphylococci have the ability to coagulate plasma. However, the general acceptance of coagulase production as a reliable criterion of pathogenicity awaited further detailed studies (Cruickshank, 1937).

The growing interest in staphylococcal infections led also to the introduction of special indicator and selective media. One of the simplest and most useful of the indicator media was developed by Fujita and Yoshioka (1938), and consists of one part of milk to two parts of nutrient agar. The milk greatly enhances staphylococcal pigmentation. Equally simple selective media which contain excess sodium chloride have also proved to be very satisfactory. These are based on the work of Koch (1943) and consist of nutrient broth with 10 per cent sodium chloride, or either nutrient agar or milk agar with 7.5 per cent sodium chloride. Ludlam (1949) devised a more complex selective medium for the isolation of Staph. aureus from material which is heavily contaminated with other bacteria. This medium which has been widely used contains lithium chloride, potassium tellurite and mannitol in a nutrient agar base. Two other special media are also worthy of mention. The first, an indicator medium developed by Barber and Kuper (1951) allows the identification of Staph. aureus in mixed cultures on the basis of phosphatase production. Because of the high correlation between phosphatase and coagulase production the demonstration of free phenolphthalein in staphylococcal colonies which are growing on phenolphthalein-diphosphate agar is regarded as evidence of pathogenicity. More recently a combined selective and indicator medium containing potassium tellurite and egg-yolk in nutrient agar (Alder, Gillespie and Waller, 1962) has proved to be useful in the study of staphylococcal contamination of the environment; but unfortunately colonies on this medium cannot be examined directly by the slide

coagulase test.

After the adoption of coagulase production as the criterion of pathogenicity, methods of sub-dividing the pathogenic staphylococci were sought to meet the needs of the epidemiologist. Serological procedures were developed for this purpose, notably by Cowan (1939) but, despite further refinements in technique, serological typing of Staph. aureus proved to be less useful than the comparable techniques already available for Strep. pyogenes. The finer differentiation of individual strains of Staph. aureus was made possible by the work of Fisk (1942). He observed that the bacteriophages liberated by lysogenic strains of Staph. aureus caused the selective lysis of other strains. Unlike most earlier investigators, Fisk was able to demonstrate distinctive patterns of lysis when different strains of Staph. aureus were exposed to the action of a set of bacteriophages. Current techniques for bacteriophage typing, such as these developed by Blair and Williams (1961), allow the bacteriologist to characterize individual strains of Staph. aureus with great precision; and the information thus obtained is usually supplemented by the antibiotic sensitivity pattern of the organism.

By these means it has proved possible not only to elucidate individual problems of epidemic and endemic infection but also to recognise broad differences in the biological properties and pathogenic abilities of different bacteriophage 'types'. Of the four main bacteriophage groups, staphylococci in group II are rarely resistant to antibiotics other than penicillin,

and are not often involved in epidemics of hospital infection. In the occasional outbreaks reported (e.g. Bowers and Rose, 1961), minor skin infections are the rule. The rare conditions of Ritter's disease and pemphigus neonatorum are more serious manifestations of infection with types '55/71' and '71' (Benson, Rankin and Rippey, 1962). Group II strains are, however, among the commonest causes of sporadic minor sepsis. Type '71', in particular, has been isolated from the majority of acute cases of impetigo (Parker and Williams, 1961). On the other hand, a limited number of strains in group I have been responsible for major epidemics of severe hospital infection throughout the world. The strain which is lysed only by bacteriophages '80' and '81' was resistant to penicillin but sensitive to tetracyclines when it was first recognised in 1953 in Australia (Isbister *et al.*, 1954); but it soon appeared in serious outbreaks of hospital infection in Europe, America and Africa, and was often tetracycline-resistant *ab initio* (Williams, 1959). The related type '52/52A/80/81' has more recently shown similar pandemic tendencies (Parker and Jevons, 1963).

In recent years staphylococci in group III - especially strains lysed by bacteriophages '47', '75' and '77' - have begun to rival the notorious Group I strains in their epidemic propensities (Parker and Jevons, 1963), and they develop antibiotic resistance with remarkable facility (Jackson, Lepper and Dowling, 1954). Another feature of epidemiological importance in this group is its implication in most of the fully elucidated cases of staphylococcal food poisoning (Anderson and Williams, 1956;

Munch-Petersen, 1963).

Bacteriophage '83A', which was added to the typing set in 1957, has allowed the recognition of yet another important 'hospital' staphylococcus. In 1963, Temple and Blackburn in Glasgow described an epidemic strain ('Type A') which is not lysed by bacteriophage 83A but which in other respects resembles type 83A. In particular, both strains show 'inhibition reactions' but not true lysis with many of the group III bacteriophages, and both are resistant to most of the available antibiotics. It seems likely that Type A evolved from type 83A by lysogenization and the acquisition of a 'blocking phage' (Jevons and Parker, 1964). This mode of origin is comparable with the lysogenic conversion of Type 80/81 to 52/52A/80/81 postulated by Rountree and Asheshov (1961). If such processes occur in nature they may be an important factor in the continuous evolution of epidemic strains. In this connection, the report by Ritz and Baldwin (1958) that sensitive strains of Staph. aureus can acquire penicillin-resistance by transduction is of great interest. Similar observations were made by Morse (1959) on resistance to streptomycin, by Pattee and Baldwin (1961) on resistance to erythromycin, novobiocin, oleandomycin and spiramycin, and by Collins and McDonald (1962) on tetracycline-resistance.

Bacteriophage typing has thus provided extensive evidence that only a few homogeneous types of Staph. aureus have been responsible for most of the staphylococcal disease which has occurred in hospitals during the past ten years. This concept of a limited number of potentially dangerous staphylococci has

stimulated the search for simple in vitro tests of virulence.

As 'markers' of virulence, leucocidin activity (Valentine, 1936) and alpha toxin production (Christie, North and Parkin, 1946) have not proved to be superior to coagulase production. A reaction which appeared to be more closely related to virulence was reported by Gillespie and Alder (1952). They found that a high proportion of strains of coagulase positive staphylococci which were derived from closed lesions produced opacity in egg-yolk media; but most strains from carriers and other sources did not produce this effect. Further work confirmed these results (Alder, Gillespie and Herdan, 1953). More recently, however, Jessen et al. (1959) reported the paradoxical finding that strains of Staph. aureus which produced no opacity in egg-yolk broth were responsible for the majority of deaths from staphylococcal bacteraemia. A further report from these investigators (Faber et al., 1960) supported their earlier observation.

The correlation of virulence with relative resistance to mercuric chloride has also been investigated recently (Moore, 1960). Although it is still controversial as an indicator of virulence, mercuric chloride resistance has been helpful in the preliminary identification of epidemic 'hospital' strains of staphylococcus. A comparable but technically simpler screening test for epidemic staphylococci is the determination of tetracycline sensitivity. Whereas tetracycline-sensitive staphylococci are no longer responsible for hospital epidemics (Williams, 1959), strains found to be tetracycline-resistant must be regarded as



virulent hospital pathogens until the results of epidemiological investigations - including bacteriophage typing - are available. The value of excluding tetracycline-resistant strains from surgical wards was shown in an investigation in which all patients with clinical infection due to resistant organisms, as well as all nasal carriers of these organisms were isolated wherever possible (Williams et al., 1962). Despite the incompleteness of the isolation policy it was concluded that the sepsis rate had been reduced by about one-half as a result of these measures.

On a similar basis, neomycin-resistance has recently been used to allow rapid identification of a new epidemic strain which was first reported in Southern Scotland (Robertson, 1963; Mitchell, 1964). This particular strain is apparently a variant of 'Type A' to which reference has already been made in relation to lysogenization.

Another marker of virulence has been investigated by Willis and Turner (1962) who have re-examined the significance of pigmentation. These investigators standardised the conditions for pigment production by using a nutrient agar indicator medium containing 1 per cent glycerol monoacetate. Cultures were incubated at 37°C. for 48 hours and then examined immediately. Using this technique, consistent differences in pigmentation were observed within the species Staph. aureus. In particular, epidemic hospital strains, including Type A, were characterised by 'yellow' pigment, while other strains usually produced orange or cream pigment (Willis and Turner, 1963). The enhanced pigmentation observed is comparable to that found on milk agar (p.47.),

although glycerol monoacetate agar is more readily standardised.

Nevertheless, despite the numerous attempts to correlate the virulence of Staph. aureus with in vitro properties, little real progress seems to have been made (Elek, 1965).

Hospital Infections Due to Gram-negative Bacilli.

The importance of the Gram-negative bacilli as a cause of hospital infection is still not widely appreciated. Nevertheless, the reasons which underlie the increase in staphylococcal cross-infection apply also to the undoubted increase which has occurred in hospital infections due to Gram-negative bacilli.

Members of Escherichia, Klebsiella, Proteus, Pseudomonas and related genera possess very limited pathogenic abilities in the healthy host, but are peculiarly suited to their increasing role in hospital infection. They are endowed with considerable innate powers of resistance to antibiotics and antiseptics, and can survive well and even multiply under varied environmental conditions. The modern hospital with its aggregation of susceptible patients, and its increasingly bold diagnostic and therapeutic techniques offers excellent scope for the opportunist pathogens which abound beneath its roof.

Early concern was expressed by Miles (1944) about a possible rise in the incidence of drug-resistant coliform infections as a result of the wider use of sulphonamides and penicillin. Strong support for this view was provided by Florey, Ross and Turton (1947). They found that 50% of traumatic wounds treated in hospital were rapidly colonised by coliform bacilli in

patients who had received prophylactic penicillin injections. Many of the infected wounds and a large number of non-infected wounds were later invaded by Proteus species and by Pseudomonas pyocyanea. Shortly after this report, Colebrook, Duncan and Ross (1948) demonstrated the great importance of Ps. pyocyanea as a pathogen in burns. The prevalence of Ps. pyocyanea in burns units, and the serious consequences of infection with this organism were confirmed by Jackson, Lowbury and Topley (1951), and by later investigators including Markley et al. (1957).

The introduction of the broad-spectrum antibiotics was followed, in medical as well as surgical wards, by a further rise in the incidence of severe infections due to Gram-negative bacilli. The relatively drug-resistant Proteus species and Ps. pyocyanea have become especially prominent as causes of serious systemic infections (Yow, 1952; Finland, Jones and Barnes, 1959; McHenry, Martin and Wellman, 1962).

The emergence of Ps. pyocyanea as one of the most important pathogens in the modern hospital is of particular interest. The host factors which have been discussed in connection with staphylococcal hospital infections play an even greater part in Pseudomonas infections. In medical patients who develop Pseudomonas bacteraemia following cross-infection, obvious predisposing factors are always present, and they include neoplastic diseases - notably leukaemia, advanced diabetes mellitus, post-radiation therapy and prolonged treatment with antibiotics or cortico-steroids (Forkner et al., 1958; Williams, Williams and Hyams, 1960; Curtin, Petersdorf and Bennet, 1961); and the

susceptibility of patients with burns to overwhelming Pseudomonas infections has already been noted. Despite advances in the treatment of 'bacteraemic shock' (Annotation, 1963a) most of the reported cases of bacteraemia with Ps. pyocyanea have been fatal.

An increase in the frequency of less serious infections due to Ps. pyocyanea is reported by Barber (1961) and Gould (1963). The commonest sites involved are operation wounds, the chest and the urinary tract. As in the case of similar lesions infected with Proteus and coliform bacilli, these may be important sources of further hospital cross-infection. Reservoirs of Pseudomonas infection revealed by studies of the hospital environment include antiseptic solutions and lotions (Anderson and Keynes, 1958), cork-stoppered bottles in general (Lowbury, 1951), transfusion fluids (Gilat, Hertz and Altmann, 1958), urinals and bedpans (McLeod, 1958), the humidifier of an operating theatre ventilation system (Anderson, 1959), and contaminated resuscitation equipment (Bassett, Thompson and Page, 1965). But although, in contrast to Staph. aureus, the survival of Ps. pyocyanea is favoured by moist conditions, as is also the case with Proteus and coliform bacilli, air-borne infection may occur in burns units (Lowbury, 1954) and in wards where there are patients with Pseudomonas chest infections (Williams, Williams and Hyams, 1960; Gould, 1963).

Various 'non-pathogenic' Gram-negative bacilli have recently been implicated in serious hospital infections. Thus, a species of Achromobacter was responsible for an outbreak of neonatal septicaemia (Foley et al., 1961); and there have been

several reports of outbreaks of neonatal meningitis due to group C flavobacteria (e.g. Cabrera and Davis, 1961; George, Cochran and Wheeler, 1961). Recently, flavobacteria were also found to have caused a hospital outbreak of bacteraemia in adults, and the infection appeared to have been transmitted by intravenous injections of anaesthetics stored in contaminated vials (Olsen, Fredericksen and Siboni, 1965). There are reports, too, of hospital infection due to Serratia marcescens. This organism has been responsible for an outbreak of urinary tract infection after catheterization (Taylor and Keane, 1962), and the same organism has been involved in a number of cases of severe infection following peritoneal dialysis (McCracken and Lipscomb, 1965). The environmental reservoirs of infection, where these have been identified, have proved to be similar to those found in the case of Ps. pyocyanea (Editorial, 1961).

In contrast to the Gram-negative infections already discussed, the incidence and severity of hospital infections due to intestinal pathogens have shown no tendency to rise in recent years.

Hospital epidemics of neonatal and infantile diarrhoea due to specific enteropathogenic types of Escherichia coli were frequently recognised following the report by Bray (1945), and the case mortality was often more than 40 per cent (e.g. Kirby, Hall and Coackley, 1950). Since 1955, however, outbreaks have become less frequent and have tended to be milder. This improvement resembles the decline in streptococcal hospital infections since advances in prevention and treatment are not the only factors

responsible; in addition a decrease in the virulence of specific serotypes of Esch. coli seems to have taken place (Rogers, 1963).

The incidence of Salmonella infections in hospital may also have fallen in recent years (Taylor, 1963). In outbreaks ascribed to hospital cross-infection rather than to food-poisoning, children have generally been involved in the spread of infection. Such outbreaks have usually been well circumscribed, although temporary closure of a maternity hospital was necessary in the outbreak of infection with Salm. paratyphi B reported by Jones and Pantin (1956). In Britain, food-poisoning, especially due to salmonellae, still occurs more commonly in hospitals than elsewhere (Report, 1964a).

Shigellae, like salmonellae, tend to spread in children's wards due to poor personal hygiene, and similar factors maintain endemic infection in mental hospitals (Geller, Eymann and Dingman, 1964). But despite the steady increase in the incidence of Sonne dysentery in the general population of Britain, there has apparently been no corresponding increase in the number of infections occurring in general hospitals (Williams et al., 1960).

The detailed investigation of hospital infection due to Gram-negative bacilli has become possible only relatively recently. Even now, bacteriological 'typing' methods are not entirely satisfactory, notably in the case of Proteus species where reliance is placed upon the mutual interaction of swarming bacilli - a phenomenon which was first described by Dienes (1946). Moreover, because of the technical difficulties encountered when using more specific procedures, many investigators still rely

upon differences in antibiotic sensitivity patterns when tracing hospital infections due to Escherichia and Klebsiella species (Gillespie et al., 1964). Standardised techniques are, however, available for the serological investigation of infections due to klebsiellae (Ørskov, 1952) and Esch. coli (Rogers, Dowse and Hall, 1959); while in the case of Ps. pyocyanea precise epidemiological work has proved possible by the combined use of bacteriophage and serological typing (Gould and McLeod, 1960), and, more recently by means of 'pyocine' typing (Wahba, 1965). Bacteriocines have also been used successfully in the epidemiology of infections due to Esch. coli (Linton, 1960) and Shigella sonnei (Gillies, 1964).

Miscellaneous Infections in Hospital

While cross-infection due to Strep. pyogenes, Staph. aureus and the Gram-negative bacilli has generally followed an endemic pattern in hospital, with superimposed periods of epidemic activity, many other micro-organisms have been involved in isolated outbreaks of hospital infection. A brief review of this group of infections indicates the range of problems with which a hospital may be faced at any time.

Amongst the less common bacterial infections which are acquired in hospital, the most serious are due to clostridia. In cases of post-operative tetanus (e.g. Robinson, McLeod and Downie, 1946), and in Clostridium welchii wound infections, it is rarely possible to determine the source of infection with

certainty because of the frequent occurrence and wide distribution of spores - both on normal skin and in the general environment (Lowbury and Lilly, 1958a, 1958b; Lowbury, 1963a). However, the available evidence suggests that the occasional outbreaks of anaerobic wound infections which occur in hospital are probably not the result of true cross-infection but are more likely to be due to inadequate sterilisation of surgical materials or to contamination of the operating theatre from extraneous sources (Report, 1959a). The use of tourniquets and tight bandages may be an important predisposing factor (Rubbo, 1958).

The acquisition of tuberculosis in a British hospital must now be uncommon, consequently the recent report of Heycock and Noble (1961) which described an outbreak of syringe-transmitted infection is of great interest. The incident occurred in a paediatric ward, and the source was a nurse with a positive sputum; as a result, two of the infected children died. Other outbreaks due to contaminated syringes have been reported in recent years (Debré et al., 1951; Tamura et al., 1955).

Reference has already been made to cross-infection in wards devoted to specific infectious diseases, but in general paediatric wards, too, there is always the risk of an outbreak of infection following the admission of an undiagnosed case of whooping cough, measles or chickenpox. A member of staff who is in the prodromal stage or is suffering from an atypical illness may also be a source of these childhood infections, as shown in the recent outbreak of chickenpox in the Maternity Department of a London hospital (Newman, 1965). This disease

which is particularly dangerous in the newborn can spread with relative ease among patients and staff, and may even be transmitted by 'immune' individuals. Likewise, atypical cases of smallpox - though fortunately rare in Britain - are a serious hazard in hospital (Tainsh, 1962; Dixon, 1962).

Amongst the commoner virus infections, herpes simplex, viral hepatitis and diseases due to enteroviruses may be of particular importance in hospital. The most serious outbreaks of cross-infection with the herpes virus have occurred in newborn infants, leading to systemic infection (Zuelzer and Stulberg, 1952), and in patients suffering from eczema who may develop Kaposi's varicelliform eruption (Dudgeon, 1958). These manifestations of primary infection with the herpes virus are believed to be the result of droplet infection derived from attendants in most cases. A more unusual mode of infection which operates in the reverse direction was described by Stern et al. (1959), and, more recently by Ward and Clark (1961). The primary lesions were observed on the fingers of nurses who had apparently been infected by direct contact with the respiratory tract secretions of unconscious patients while manipulating endotracheal tubes. Super-infection of the lesions with hospital strains of staphylococci occurred in a number of cases, usually following incision of the whitlow.

Although there have been several reports of hospital infection with other viruses of the respiratory tract, notably the respiratory syncytial and para-influenza viruses, and adenoviruses, such episodes seem to be relatively uncommon

(Dudgeon, 1963). In this connection, the description by Eichenwald (1958) of an outbreak of 'stuffy-nose syndrome' amongst the newborn is of great interest. The syndrome was ascribed to synergism between adenovirus type 1 and Staph. aureus in a mixed infection. In later work, Eichenwald, Kotsevalov and Fasso (1960) showed that infants with sub-clinical infection may be of great epidemiological importance as prolific dispersers ('cloud babies') of Staph. aureus in a maternity nursery.

Paediatric wards provide very favourable opportunities for cross-infection with 'enteric' viruses. A typical epidemic of infectious hepatitis in a children's ward was reported by Noordsij (1959), but endemic infection may be just as common (Capps, Bennett and Stokes, 1952). The closely related condition of serum hepatitis is readily transmitted in hospital not only by transfusion procedures but also from patient to patient on contaminated stylets and needles. This form of hospital infection still carries a high mortality (Dougherty and Altman, 1962). Recently an outbreak of viral hepatitis in a British hospital was traced to cross-infection during renal dialysis. Six members of staff became infected, and one died (Annotation, 1965). In another incident, 28 members of staff were infected (Ringertz and Melén, 1966).

Enterovirus infections acquired in hospital have also received some attention recently, notably the very serious condition of epidemic myocarditis of the newborn due to Coxsackie viruses of group B (Jack and Townley, 1961; Voláková et al., 1964). The unusual susceptibility of the newborn to

group B Coxsackie viruses may be partly explained by the finding that antibody titres against these viruses - ~~apparently~~ in contrast to those against polio viruses - are much lower in cord blood than in maternal blood (Steigman and Lipton, 1961). Echovirus and Coxsackie viruses have also been implicated in hospital outbreaks of aseptic meningitis (Macrae, 1959) and infantile diarrhoea (Eichenwald and Shinefield, 1962).

Although often overlooked, the spread of disease due to fungi and even larger parasites is an established hospital hazard. Thrush is familiar in maternity nurseries both as epidemic and endemic infection (Ludlam and Henderson, 1942; Dunn, 1962). Feeding-bottle teats and other fomites have usually been implicated in the spread of infection, but Shrand (1961) held that infection occurred more commonly from the mother's vagina during delivery. Cross-infection with dermatophytes also is an acknowledged risk in hospital, particularly in dermatological wards; and as early as 1886, Crookshank reported that 'spores of Trichophyton have been discovered in the air of hospitals for diseases of the skin, and achorion in wards with cases of favus.'

Cross-infection due to a protozoon has very recently been reported from Germany (Truckenbrodt et al., 1965). These investigators described a serious outbreak of pneumocystis carinii pneumonia amongst children in hospital. The infection, though highly communicable, usually produces disease only in debilitated individuals. Of the diseases due to larger members of the animal kingdom, scabies can be extremely troublesome in

hospital, as was the experience of Pringle (1752). More recently, large outbreaks of cross-infestation have been described in medical wards by several investigators including Ingram (1951), Wells (1952) and Herridge (1963). These outbreaks are not only of interest as curiosities but they may also throw some light on the spread of skin infections in general.

Healthy Carriers of Hospital Pathogens

Each of the important hospital pathogens may be harboured for prolonged periods without producing disease. The concept of the healthy carrier, although first centred upon the typhoid bacillus and the meningococcus, was developed principally in relation to Strep. pyogenes, which can be isolated from the throats of between 2 and 20 per cent of normal individuals (Wilson and Miles, 1964). There is evidence to suggest that strains of Strep. pyogenes when carried for long periods tend to lose the type specific M antigen, and undergo loss of virulence (Griffith, 1934; Rothbard and Watson, 1948). Nevertheless, chronic carriers have not infrequently been the apparent source of outbreaks of infection in institutions (e.g. Boissard and Fry, 1944; Gray, 1956).

The nasal carrier rate for Strep. pyogenes is usually lower than the throat carrier rate, but reference has already been made to the finding that nasal carriers are more dangerous dispersers of infection than throat carriers. This is explained by the ease with which nasal carriers heavily contaminate their

handkerchiefs, hands, clothing and ultimately their general surroundings (Hamburger and Green, 1946; Hare and McKenzie, 1946). The demonstration of the important part played by healthy carriers in the spread of streptococcal infection, and particularly the more recent work on streptococcal nasal carriage stimulated considerable interest in the epidemiological role of staphylococcal carriers.

In recent surveys, approximately 40 per cent of adults have been found to be healthy nasal carriers of Staph. aureus (Williams et al., 1959; McDonald et al., 1960). Williams and his colleagues found that 58 per cent of patients were nasal carriers after staying in hospital for four weeks. Following a more detailed analysis of their accumulated results, Noble et al. (1964) reported that the acquisition of nasal staphylococci by hospital patients was influenced by antibiotic treatment and by the development of sepsis, as well as by the length of stay in hospital. More than 73 per cent of patients who received antibiotics and whose stay in hospital exceeded 40 days acquired Staph. aureus in the anterior nares. This incidence may be compared with that in the newborn, 100 per cent of whom have been found to be nasal carriers of Staph. aureus by their twelfth day in hospital (Cook, Parrish and Shooter, 1958).

Other sites at which healthy individuals may harbour Staph. aureus include the throat, the nasopharynx, the alimentary tract and the skin; but the normal carrier rates at these sites tend to be lower than in the anterior nares (Williams, 1963). Of particular interest is the wide variability of staphylococcal

skin carriage. With the exception of the perineum for which a carrier rate of 13 per cent was demonstrated in both sexes by Bøe *et al.* (1964), covered areas of normal skin rarely carry a permanent population of Staph. aureus. In contrast, from 5 to 30 per cent of tests on the exposed areas of the body have yielded Staph. aureus in different surveys, but most of these positive cultures, probably represent contamination from sites such as the anterior nares at which bacterial multiplication is occurring. Duguid and Wallace (1948) and Hare and Thomas (1956) showed that nasal carriers of Staph. aureus - although quantitatively less important - resemble nasal carriers of Strep. pyogenes in producing contamination of their surroundings. The marked variation found in the amount of bacterial dispersal produced by individual carriers is of great epidemiological importance. Such differences may be associated with secondary colonisation of particular areas of skin - notably the perineum - from which dispersal may more readily occur (Ridley, 1959); and reference has already been made to the enhanced dispersal of Staph. aureus reported in infants who had a subclinical adenovirus infection of the respiratory tract (Eichenwald, Kotsevalov and Fasso, 1960).

The wide variations in the ability to disperse bacteria may be the explanation for the discordant results obtained following the suppression of nasal carriage in hospital. The apparent importance of nasal carriers as a source of hospital infection was demonstrated by Gould and Allan (1954) in a general hospital, and by Gillespie *et al.* (1961) in surgical wards. These,

and other investigators found that the treatment of nasal carriers with topical antibacterial agents resulted in a reduction in staphylococcal cross-infection, although the interpretation of the results of Gillespie and his colleagues, is complicated by their simultaneous use of other counter-measures.

Less equivocal evidence of the importance of nasal carriers in cross-infection has been obtained in maternity hospitals where outbreaks of staphylococcal infection have been controlled by nasal disinfection (e.g. Gillespie and Alder, 1957; Klein and Rogers, 1959; Baker and Christie, 1959). These investigations appeared to provide support for the view of Elek and Fleming (1960) that in staphylococcal cross-infection 'the crux of the problem lies in nasal carriage'. Nevertheless, Ulstrup and Ødegaard (1961) found that adequate nasal disinfection in a maternity nursery produced no significant change in the incidence of cross-infection, and similar results were obtained in surgical wards by Henderson and Williams (1961). Rountree et al. (1962) have also reported that nasal disinfection is of doubtful value in preventing cross-infection amongst surgical patients. Moreover, Forfar and Maccabe (1958) found that the careful use of face masks did not bring about a reduction in staphylococcal infections of the newborn.

Although opinions still differ, therefore, as to the part played by staphylococcal nasal carriers in hospital cross-infection, the danger of autogenous infection in nasal carriers seems to be well established. The emphasis placed by Dolman (1935) on 'auto-inoculation of staphylococci carried in the

nose' has been justified by later work. Valentine and Hall-Smith (1952), Tulloch (1954) and Gould and Cruickshank (1957) confirmed that the strains in the anterior nares and in the lesions of carriers were usually identical. Moreover, these investigators were able to reduce the incidence of recurrent staphylococcal disease amongst their patients by means of nasal disinfection.

While most of the earlier work was concerned with superficial lesions in patients outside hospital, the role of autogenous infection in surgical sepsis has received attention more recently. Colbeck et al. (1959) found that patients who were staphylococcal nasal carriers had an incidence of wound sepsis which was seven times as high as that in non-carriers. A considerable excess of surgical sepsis in nasal carriers was also reported by Williams et al. (1959) and by McNeill, Porter and Green (1961). Of particular interest is the observation that patients who became nasal carriers during their stay in hospital had a staphylococcal sepsis rate that was ten times higher than in non-carriers, and four times higher than in 'permanent' carriers who retained their own strain in hospital (Williams et al., 1962). Similarly, the colonization of the nose by Staph. aureus is often a precursor of sepsis in newborn infants. The aetiological role of endogenous nasal staphylococci in sepsis was demonstrated by Shinefield et al. (1965). They inoculated the anterior nares of infants with an apparently avirulent strain of Staph. aureus. This prevented the colonization of the nose by epidemic strains, and, in a series

of outbreaks of hospital cross-infection, the infants who were treated in this way obtained substantial protection against infection. Evidence of the importance of autogenous infection in newborn infants was also presented by Cope et al. (1961) and by Jennison and Komkrower (1961) who noted a significantly higher sepsis rate in infants who became nasal carriers as compared with infants in whom nasal colonization had been prevented by the use of antibacterial creams.

Recently, however, the importance of autogenous infection in surgical patients has been questioned by Henderson and Williams (1963) and by Bassett et al. (1963). Both groups of investigators reported that the incidence of staphylococcal sepsis in nasal carriers was not significantly different from that in non-carriers. Indeed, in a similar investigation, Moore and Gardner (1963) found that patients who were staphylococcal nasal carriers on admission to hospital actually had a lower sepsis rate than non-carriers.

Relatively little attention has been paid to healthy carriers of important hospital pathogens other than Strep. pyogenes and Staph. aureus. The available data indicate that normal carrier rates may range from an alleged 90 per cent for the herpes virus in and around the mouth (Blank and Rake, 1955) to 3 per cent for Ps. pyocyanea in faeces (Lowbury and Fox, 1954). The healthy carrier rate for Proteus species in patients who had recently entered hospital was found by Edebo and Laurell (1958) to be 10 per cent on direct culture of faeces, and 20 per cent when enrichment media were used. In this investigation

the faeces of almost all patients who had been in hospital for three weeks or more yielded Proteus, due apparently to cross-infection from other patients via rectal thermometers.

The substantial carrier rates of these and probably of other hospital pathogens underline the need for sensitive typing methods. These are essential not only for the detailed investigation of the routes of cross-infection, but also to enable autogenous infection to be differentiated from hospital-acquired infection.

The Present Extent of the Clinical Problem

Reports of cross-infection have, in recent year, come from almost every branch of hospital practice. The frequent communications from obstetrical and surgical departments in particular indicate the extent of the problem in these fields.

Maternity Wards. Hospital infection in maternity wards now rarely endangers the mother's life as it did during the era of the haemolytic streptococcus; nevertheless, careful prospective studies have shown that puerperal mastitis due to endemic cross-infection occurs in from 2.5 to 7 per cent of mothers (Lindau and Löfkvist, 1958; Plueckhahn and Banks, 1964). During epidemics, 50 per cent or more of mothers may develop mastitis with abscess formation (Gibberd, 1953). Although the lesions are usually diagnosed following discharge from hospital, the causative organism is almost always a 'hospital' staphylococcus

which is probably acquired from the infant. The evidence for this view includes the report by Plueckhahn and Banks (1964) that disinfection of the infants' carrier sites was followed by a marked decrease in the incidence of puerperal breast abscess.

The central problem in maternity units is therefore staphylococcal infection of the infant. It has already been noted that most infants are nasal carriers of Staph. aureus before they are discharged from a maternity hospital. Recent reports of the incidence of clinical infection in infants range from 40 per cent recorded by Plueckhahn and Banks (1961) to 10 per cent recorded by Cope et al. (1961). During epidemics also the incidence of disease rarely exceeds the level of almost 40 per cent reported by Wilkinson (1959), though at such times staphylococcal disease tends to be of increased severity and may be associated with a high mortality, as in the outbreaks reported by Beaven and Burry (1956), and Timbury et al. (1958).

Endemic staphylococcal sepsis of the newborn generally takes the form of purulent conjunctivitis or small, multiple pustules. The more serious skin conditions of pemphigus neonatorum and Ritter's disease are now fortunately uncommon, though they were encountered not infrequently before World War II (e.g. Poole and Whittle, 1935). Likewise, severe outbreaks of intestinal infection in newborn nurseries are now also becoming rare, and the apparent decline in the virulence of enteropathogenic types of Esch. coli has already received special mention. But attention has also been drawn to the possible

increase in the incidence of other neonatal infections due to Gram-negative bacilli and viruses.

The relatively minor staphylococcal infections which are now prevalent in maternity departments may appear to be of no importance. Nevertheless, this form of sepsis usually necessitates an additional stay in hospital of at least two days in each case. An increased burden is thus placed on the already overcrowded maternity department. The standard of nursing care may fall as a result, and this in turn will favour the spread of infection. Furthermore, the infants and mothers who develop minor sepsis or who become healthy carriers of hospital staphylococci are not only sources of further cross-infection in hospital, but they may also suffer severe autogenous staphylococcal disease after leaving hospital, and, moreover, they may introduce virulent hospital pathogens into the general community (e.g. Hurst and Grossman, 1960; Ravenholt and Ogden, 1963).

Surgical Wards. The general pattern of endemic and epidemic infection of the newborn applies equally to surgical wound sepsis. Just as in the case of neonatal endemic sepsis the incidence of more than 40 per cent recorded by Plueckhahn and Banks (1964) is unusually high, so also is the total endemic sepsis rate of more than 40 per cent observed by Jeffrey and Sklaroff (1958) in one surgical ward of an Edinburgh hospital. Nevertheless, the results of the Edinburgh investigation dispelled some of the complacency which had existed in relation to post-operative sepsis. More recent surveys have

shown that in the absence of epidemics of wound infection, sepsis rates of approximately 10 per cent are common (Public Health Laboratory Service, 1960; Moore and Gardner, 1963), but rates of about 20 per cent are not exceptional (e.g. Rountree et al., 1960; McNeill, Porter and Green, 1961). In contrast, a few investigations have indicated a relatively low incidence of wound sepsis, such as the rate of 2 per cent which Ljungqvist (1964) recorded after 'clean' operations. It is interesting therefore that in the majority of recent enquiries into endemic infection of surgical wounds, sepsis rates have been as high as those recorded in epidemics of infection, such as that described by Shooter et al. (1958) which was associated with a sepsis rate of 14.5 per cent, and the epidemic reported by Mitchell et al. (1959) in which a similar sepsis rate was observed.

When the statistics of wound infection are examined in greater detail, the sepsis rate is found to be dependant on certain host factors, and to increase with the age of the patient, the duration of operation, the length of incision and the use of drainage-tubes (Lidwell, 1961). The incidence tends to be higher also in cases dealt with later on the operating list (Douglas, 1963). These and other factors, such as the care taken to secure accurate apposition of tissues during wound closure, help to explain the observed differences in sepsis rates in the various types of operation; and all of these factors must be taken into account when evaluating measures designed to reduce the incidence of wound infection (Moore and Gardner, 1963).

While wound infections - particularly those due to Staph. aureus - have been the subject of much investigation, other important forms of sepsis amongst surgical patients have received relatively little attention. This is especially true of post-operative chest infections which may often be the result of cross-infection (Shooter et al., 1958). In the experience of Gillespie et al. (1961) the most serious effects of staphylococcal cross-infection were seen in sepsis which did not involve the patients' wounds. The important post-operative complications which were encountered included pneumonia, urinary tract infection, enterocolitis and fungunculosis. Enterocolitis is probably the most dangerous of these conditions. It may occur sporadically, as in the Bristol investigation, or in outbreaks such as that described by Cook et al. (1957). Although its pathogenesis has not been fully elucidated, this complication is usually seen in patients receiving antibiotics and is often due to super-infection of the bowel with a hospital staphylococcus (Hummel, Altemeier and Hill, 1964). The case-mortality is still in the region of 50 per cent.

The recent reports from various surgical specialties indicate that cross-infection continues to pose complex problems in each field. Thus a high incidence of sepsis is often encountered in thoracic surgical units, (Laurell and Lindbom, 1961; Goldfarb and James, 1963), and amongst urological patients treated by conventional methods (Mitchell and Gillespie, 1964). Similarly, in the absence of specific countermeasures almost all gynaecological patients treated by bladder drainage develop

urinary tract infections (Gillespie et al., 1964). Sepsis is still very frequent, too, in burns wards and gives rise to problems which continue to occupy the attention of Lowbury and his colleagues (e.g. Lowbury, Kidson and Lilly, 1964). The recent incident in which post-operative eye infections with Ps. pyocyanea produced blindness in six patients (Editorial, 1964) and the subsequent outbreak of staphylococcal sepsis in the same ophthalmic surgical department, demonstrate that the most meticulous operative technique performed under modern conditions is unsafe in the presence of bacterial contamination of the environment.

Although it is extremely difficult to assess the cost of surgical sepsis in terms of morbidity, mortality and increased hospital expenditure, a partial estimate was given in the report of the Public Health Laboratory Service (1960). When wound infection alone was considered and when the enquiry was restricted to England and Wales, it seemed likely that in each year 75,000 patients remain in hospital an extra week or more, and 500 die as a result of sepsis. The annual monetary cost of this single type of hospital infection in England and Wales may be more than £5 million.

Medical Wards. Relatively few recent reports deal with hospital infection outside the fields of obstetrics and surgery. This might indicate that cross-infection is of no importance in medical wards. In favour of this conclusion, the results of a clinical survey carried out by Florey (1958) in a New York hospital

suggested that staphylococcal infection was of little significance amongst medical patients. Infections due to other organisms were not investigated. However, while no attempt was made in this study to assess the incidence of cross-infection, the author conceded that there was 'presumptive evidence of added infection within the hospital'. Likewise, in a more recent investigation of staphylococcal sepsis in a medical ward of 26 beds there was no evidence of disease due to cross-infection, although nasal swabs from 27 per cent of the patients yielded a staphylococcus which had not been present on admission (Shooter et al., 1960).

Several other investigators accord a greater importance to staphylococcal infection in medical wards. Thus, following a brief clinical study in a general hospital, Godfrey and Smith (1958) reported significant infections due to Staph. aureus in 12 per cent of medical patients, and although bacteriological evidence was not obtained, most of the sepsis was ascribed to cross-infection. In a more thorough investigation, Farrer and Macleod (1960) reached a similar conclusion. However, in a recent Report (1965b) of the Public Health Laboratory Service the recorded incidence of staphylococcal infections developing in medical wards was only 2.2 per cent (vide p.199). The infection rate due to other pathogens was similar, but many of the cases were not examined bacteriologically. In a companion study based on necropsies, staphylococcal infection, mainly of the lungs, was apparently the immediate cause of death in 8.6 per cent of patients dying in hospital

(Report, 1966).

The possible importance of staphylococcal infections in mental hospitals was recently emphasised by Reza (1964), who presented evidence that infections of the lungs, with Staph. aureus, acquired in hospital, were a leading cause of death among long-term psychiatric patients.

Serious epidemics of staphylococcal infection in medical wards are dealt with in two other reports. The first of these describes outbreaks of severe infection amongst patients with chronic respiratory diseases (Maccabe, 1959). The second report contains details of a large outbreak which resulted in the death of 14 patients and the spread of infection from the hospital into the surrounding community (Vogel, et al., 1959). Further evidence for the spread of hospital staphylococci into the community is presented by Bashe, Miller and Wentworth (1962).

Follow-up studies of patients discharged from maternity and other departments have thus shown that hospital infection can extend far beyond the confines of the ward. The hospital, which was formerly an important source of virulent streptococci for the general population, has now become a reservoir of Staph. aureus; but other pathogenic organisms may be derived from this source, particularly if the carrier state is a consequence of infection. Salmonellae have been transmitted in this way (Leeder, 1956; Poole and Ardley, 1958). Also, for many years, there have been claims that diseases such as diphtheria and smallpox may spread from hospitals via the air, and recently further circumstantial evidence of the transmission of smallpox by this route was presented by Peirce et al. (1958).

The extent of the ramifications of hospital-derived infection is evident from the recent report that hospital staphylococci can spread not only in the human population at large, but also amongst domestic and farm animals (Moeller et al., 1963).

Environmental Studies in Hospital

Most of the work on hospital cross-infection which has been reviewed consists of clinical and bacteriological observations on the infected patient. Environmental aspects of the problem have been relatively neglected, even though satisfactory methods of study have been available for more than 20 years. Indeed, 80 years ago Crookshank (1886) described a number of simple but effective bacteriological air samplers which had been devised a few years earlier. The reasons for the present neglect include the widespread notion that the bacteriological examination of the environment is unduly difficult, but there is also a general belief that infection from the environment, and air-borne infection in particular, is of little or no practical importance.

The initial enthusiasm for the theory of air-borne infection, described earlier, was largely dispelled at the beginning of the present century by bacteriological studies which indicated that almost all the micro-organisms present in the air are non-pathogenic. This finding received support from Lister who had discarded his carbolic acid air-spray and was

able to maintain a relatively low rate of wound sepsis by concentrating upon the avoidance of contact infection. Flügge's concept of droplet-borne infection also fell into disfavour when it was shown that most droplets settled to the ground after travelling a very short distance. The general view, which is still held widely but often uncritically, was expressed by Chapin (1912). He wrote

'most infectious diseases are not likely to be dust-borne, and they are spray-borne only for two or three feet, a phenomenon which after all resembles contact infection more than it does aerial infection ...'

The similar views of Rundle (1912) have already been cited in connection with cross-infection in fever hospitals.

During the years immediately before World War II there was, however, renewed interest in air hygiene as a result of the work on dust-borne streptococcal infection described earlier. Moreover, Wells (1934) reinstated the concept of droplet-borne infection by showing that ejected droplets smaller than about 100 microns in diameter may rapidly evaporate to form air-borne 'droplet nuclei'. Wells and his colleagues demonstrated the survival of a wide range of bacteria and also of the influenza virus in droplet nuclei, and they introduced quantitative techniques for air sampling - notably the use of the air centrifuge.

The crowded conditions of war time air-raid shelters and barracks acted as a further stimulus to the investigation of airborne infection. Additional information was obtained on the survival of pathogenic bacteria and viruses in dust, and valuable quantitative methods were developed for studying

air hygiene. Indeed, the techniques in current use are mainly those which were employed at that time by Bourdillon and his colleagues (Bourdillon, Lidwell and Thomas, 1941; Bourdillon, Lidwell and Lovelock, 1948).

These investigators devised the 'slit-sampler' in which almost all the bacteria-carrying particles in a known volume of air are collected by impaction on to a solid nutrient medium in a standard Petri dish. To collect mainly the heavier particles which fall relatively quickly, Bourdillon and his co-workers exposed settle plates in the manner originally described by Koch (1881). By the application of Stokes' Law the mean diameter of the bacteria-carrying particles in air could be calculated from the ratio of bacterial counts obtained with the slit-sampler and the settle plate. A more direct method of estimating the diameters of air-borne infected particles has recently been developed by Lidwell (1959) using a size-grading slit-sampler.

The 'sieve-sampler' of DuBuy and Crisp (1944) has also been used in a number of investigations. It consists of a cylindrical vacuum cleaner modified to hold a Petri dish at the air intake duct. This apparatus although robust and capable of sampling a relatively large volume of air in a short time, gives only semi-quantitative results - especially with the smaller particles (Wells, 1955a).

Convenient and standardised techniques are now also available for the bacteriological sampling of textiles and solid surfaces. The sweep-plate method of Blowers and Wallace

(1955) has been widely used in the examination of textiles, but is less accurate than the percussion technique of Puck et al. (1946) or the more recent contact-plate technique of Rubbo and Dixon (1960). The surfaces of solid objects are generally examined by simple swabbing procedures.

Careful air sampling has shown that infection from droplets and droplet nuclei is of limited importance in relation to Strep. pyogenes and Staph. aureus (Hare and MacKenzie, 1946; Duguid, 1946). Instead, the importance of dust from self-contaminated clothing has become evident as a source of air-borne infection (Green, Challinor and Duguid, 1945; Duguid and Wallace, 1948; Hare and Thomas, 1956).

Apart from its theoretical interest, the detailed study of the hospital environment can lead to improvements in clinical practice. This was shown for example by Bourdillon and Colebrook (1946) whose detailed environmental studies formed the basis for greatly improved air hygiene in a room used for dressing burns. As a result of this work, a sustained reduction in the incidence of sepsis was obtained (Lowbury, 1954).

The importance of air-borne infection in surgical operating theatres has been demonstrated in a number of investigations. Thus Blowers et al. (1955) found that improved ventilation and the avoidance of dust-raising activities in operating theatres led to reductions not only in the bacterial air counts but also in the rates of wound sepsis. Similar results were reported by Shooter et al. (1956). The work of Hart has provided additional evidence of air-borne

infection in operating theatres. Reviewing his investigations which extended over a period of 30 years, Hart (1960) concluded that the use of ultra-violet radiation in operating rooms caused a marked reduction in the incidence of surgical sepsis.

More recently Shooter and his colleagues have provided evidence for the view that staphylococcal wound sepsis is often the result ^{of} infection from the ward environment. Following their work on the isolation of patients infected with tetracycline-resistant staphylococci (referred to on pages 52 and 337) these investigators observed the effects of segregating pre-operative and post-operative patients. Although the segregation was not complete and the same nurses served both parts of the ward, encouraging results were nevertheless obtained in relation both to nasal colonization and wound sepsis (Shooter et al., 1963).

In non-surgical wards the importance of air-borne infection has been recognised for at least two centuries, and some of the observations made in fever wards, maternity units and general hospitals have already been noted. To these findings may be added the evidence obtained from work on the disinfection of hospital air. Thus Harris and Stokes (1946) reported a striking reduction in respiratory tract infections following the use of propylene and tri-ethylene glycol vapour in children's wards. Similar clinical results were obtained by Rosenstern (1948) who employed ultra-violet irradiation in an infant nursery; and a further report on the successful use of this method in preventing chicken pox cross-infection has recently been given

by McMath and Hussain (1960).

Other applications of the science of air hygiene to the problem of hospital infection have been reviewed by Wells (1955b), and examples of the use of environmental studies in tracing obscure reservoirs and routes of infection in hospital have already been given. Mention has also been made of the possible significance in hospital of individuals who heavily contaminate the environment with pathogenic organisms. Yet, despite the undoubted importance of environmental infection, the systematic examination of the hospital environment is at present either an emergency measure taken during an epidemic or is restricted to special investigations, many of which are only indirectly concerned with clinical problems, and the results of which are not always accessible to clinicians.

Part II

STUDIES IN A GENERAL HOSPITAL

(i) FOREWORD

(ii) MATERIALS AND METHODS

(i) FOREWORD

Shortly after the present work had been planned, Williams et al. (1960) emphasised the need for comprehensive information on hospital infection. Their views were summarised in the following passage:

'During the last few years practically all the emphasis in the research and writing on hospital infection has been concentrated on the coccal infection in surgical and maternity departments, and on the intestinal infections, especially in children's wards. But these by no means complete the tally of infections acquired in hospitals, although there are, unfortunately, very few reports that give a total picture of cross-infection in a general hospital.'

These authors were able to cite four British reports which are concerned with non-staphylococcal as well as staphylococcal infection in hospital. Two of these accounts deal only with children's hospitals, and the third is limited to a consideration of respiratory tract cross-infection. The fourth survey cited had been carried out in 1950 by Goodall (1952). This work was based on data collected by a large number of different observers, and cross-infection was distinguished from pre-existing infection on purely clinical grounds. Furthermore, bacteriological evidence was not presented to support the author's criticisms of the standards of hygiene in the wards. Nevertheless, the report was the only one up to 1960 that dealt with the problem of hospital infection as a whole.

The short-term clinical investigations carried out more recently by Florey (1958) and Godfrey and Smith (1958), which have already been reviewed (p. 75.), were confined to

staphylococcal infections occurring throughout the hospital, as was the more detailed study by Farrer and MacLeod (1960). Moreover, in none of these American investigations was attention paid to environmental contamination. Similar limitations exist in more recent surveys, including those reported by Minchew and Cluff (1961) and Frohman et al. (1964). On the other hand, Siboni (1960), who also considered only the staphylococcus, studied bacterial contamination of the environment in detail, but paid little attention to clinical infection.

The purpose of the present investigation was to obtain over a period of one year a reliable record of environmental contamination by pathogenic bacteria and the acquisition of significant bacterial infection of all types throughout a general hospital. One of the central themes of the work was a comparison of the pathogens found in the environment with those isolated from lesions. It was hoped that it would thus be possible in a wide range of clinical conditions to assess the extent of bacterial dispersal by infected patients. In order to evaluate the role of the 'active disperser' in the general context of hospital infection, a correlation was also sought between the exposure of patients to pathogenic bacteria in the environment and the development of clinical infection.

(ii) MATERIALS AND METHODS

Ward Accommodation

The hospital consists of a central block of three storeys built in 1867 as a municipal workhouse. Connected with the main block is a group of wards of the pavilion type which was built later in the Nineteenth Century for the specific purpose of housing the sick. Since World War II the in-patient accommodation has been increased by the construction of regional centres for radiotherapy and neuro-surgery adjoining the original buildings.

The nominal capacity of the hospital is 509, but in 1960 and 1961 up to 525 patients were accommodated on several occasions. The beds are distributed amongst 12 in-patient departments, and the present investigation was carried out in eight of these, namely, General Surgery, Gastro-enterology, Urology, Paediatric Medicine, Paediatric Surgery, Gynaecology, Obstetrics and one of the two general medical departments. Excluded from the study were the second medical department (61 beds), the neurosurgical and radiotherapy units (60 and 107 beds respectively), the orthopaedic unit (12 beds) and five beds which are occupied by private patients.

Three of the eight units investigated are situated in the two-storey pavilion group. These are General Surgery, Gastro-enterology and Urology. The gastro-enterological and general surgical units occupy the ground floors and first floors,

respectively, of two pavilions. Both units consist of two identical wards 69 ft. 6 in. long and 23 ft. wide, each containing 16 beds.* The ground floor wards are 11 ft. 6 in. high, and those on the first floor are 13 ft. 6 in. high. The general surgical unit also possesses a third ward of six beds in an attic storey; it is 32 ft. long, 22 ft. wide and 15 ft. high.

The ground floor and first floor of the third pavilion contain, respectively, the female and male urological wards. The female ward has ten beds and is 48 ft. long, 26 ft. wide and 11 ft. 6 in. high; the male ward of 18 beds is 64 ft. long, 26 ft. wide and 13 ft. 6 in. high. A small sterilising room (8 ft. 6 in. by 8 ft.) opens into the male ward.

All three units are connected by radiating corridors which have an average width of 4 ft.

The remaining five units consist of relatively small wards situated in the main block. The general medical unit is on the ground floor and contains five wards with a ceiling height of 12 ft. Two of these - for female patients - have nine beds each. Both wards are 35 ft. 6 in. long and 20 ft. wide. A small four-bedded ward is also for female patients. Male patients are housed in two wards of six and eight beds respectively. The larger room is 35 ft. long and 17 ft. 6 in. wide. The duty room in the unit is 18 ft. 6 in. long by 7 ft. wide. The rooms are connected by a corridor, the main section of which measures 41 ft. by 5 ft. 3 in.

* Dimensions are given of all the rooms which were examined in detail.

The obstetrical and paediatric units are situated on the first floor (which also has a ceiling height of 12 ft.). The antenatal section of the obstetrical unit contains 19 beds distributed amongst eight small rooms, the largest of which has five beds and measures 23 ft. by 16 ft. 6 in. The adjoining small labour ward and forceps theatre were not examined in detail. The postnatal section contains up to 33 beds housed in four wards. Two of these have the same dimensions as the main female medical wards, and each provides accommodation for 12 mothers - although designed to hold nine or ten beds only. The remaining two wards are each intended to house four patients. In the adjoining nursery section 45 infants - and occasionally more - are accommodated. The two main nurseries measure 25 ft. by 17 ft. 6 in. and each holds approximately 19 bassinets. A room for premature infants leads off one of the main nurseries and measures 17 ft. 6 in. by 10 ft.

The paediatric medical unit which accommodates up to 29 children is adjacent to the maternity department and shares a common corridor. The main ward contains 13 cots and measures 34 ft. 6 in. by 18 ft. In addition there are five single cubicles and two rooms for six and four children, respectively. The duty room is 17 ft. 6 in. long and 8 ft. 6 in. wide. The adjoining paediatric surgical unit accommodates 26 children. Two identical wards (36 ft. by 20 ft.) hold nine and eleven children, respectively. In addition there are two cubicles each for two children, and two single cubicles. The milk kitchen (17 ft. by 10 ft.) is shared by both paediatric units.

The gynaecological unit is situated on the second floor, above the paediatric surgical unit. It contains two main wards (36 ft. by 20 ft.) each of nine beds. A third ward (20 ft. 6 in. by 20 ft.) accommodates four patients. The unit's combined duty room and sterilizing room is 21 ft. 6 in. long and 12 ft. 6 in. wide. All the rooms are 12 ft. 6 in. high.

Throughout the hospital a spacing of 6 ft. between bed centres was thought to be desirable, but in practice bed centres were generally between 4 ft. 6 in. and 5 ft. apart.

The main surgical operating theatres were built in 1958, and at the time of the investigation only two of the four theatres were in use. These consist of a double theatre which shares common 'scrub-up', sterilizing and changing facilities. Both theatres are 25 ft. long, 20 ft. wide and 11 ft. high. The 'clean' corridor running through the theatre suite is 60 ft. long, 5 ft. wide and 8 ft. 6 in. high. The plenum ventilation which is installed in the theatres is of the displacement type, and it provides 12 changes of air per hour.

The Bacteriological Examination of the Environment

Detailed sampling was carried out in the duty rooms and in each of the wards in the gynaecological, general surgical, gastro-enterological and urological wards, as well as in the urological sterilizing room. The larger of the male wards and one of the two main female wards were examined in the general medical unit, together with the duty room and the main corridor.

In the paediatric department sampling was carried out in the large medical ward, the medical duty room, one of the two large surgical wards and the communal milk kitchen. The rooms examined in the obstetrical department consisted of one of the two large post-natal wards, the largest of the antenatal wards and the main nursery, together with the adjoining room for premature infants.

Intensive examinations of the environment were conducted during three two-monthly periods, each of which was divided into fortnightly 'tours' of the hospital. The sampling days were Monday, Tuesday, Wednesday and Thursday in the first, third, fifth and seventh weeks; Tuesday, Wednesday and Thursday in the second and fourth weeks, and Monday, Wednesday and Thursday in the sixth and eighth weeks. A timetable was drawn up to enable the same observer to examine each of the departments for a complete day in the course of a fortnight. The examination of individual departments was, however, spread over the two weeks. Moreover, the timetable (Table I) was arranged so that sampling in each department was repeated only once at the same time on any particular day during the two-monthly period. In this way the possible sampling errors associated with a fixed weekly timetable were minimised.

The operating theatres were examined on several occasions during the year, at irregular intervals.

Air Sampling. Each day was divided into four two-hourly periods; 9 a.m. to 11 a.m., 11 a.m. to 1 p.m., 1 p.m. to 3 p.m., and 3 p.m.

TABLE I - TIMETABLE FOR THE EXAMINATIONS OF THE ENVIRONMENT

Week	Time	Monday	Tuesday	Wednesday	Thursday
1,3	9a.m.-1p.m.	General Medicine	Paediatrics	General Surgery	Obstetrics
	1p.m.-5p.m.	Obstetrics	Urology	Gastro- enterology	Gynaecology
2,4	9a.m.-1p.m.		Gastro- enterology	Gynaecology	Urology
	1p.m.-5p.m.		General Medicine	Paediatrics	General Surgery
5,7	9a.m.-1p.m.	Urology	General Surgery	Obstetrics	Paediatrics
	1p.m.-5p.m.	Paediatrics	Gynaecology	General Medicine	Gastro- enterology
6,8	9a.m.-1p.m.	Gynaecology		Gastro- enterology	General Medicine
	1p.m.-5p.m.	General Surgery		Urology	Obstetrics

to 5 p.m. Air sampling was performed in each period at the fixed sites, using 'settle plates', the slit sampler and the sieve sampler (vide p. 79.). A pair of settle plates was exposed for the whole two-hour period at approximately 3 ft. above floor level, and where possible the centre of the room was chosen as the fixed site. The Petri dishes used had a diameter of $3\frac{1}{2}$ in. and contained blood agar and salt-milk agar, respectively (p. 99). Similar plates were inserted into a 'Casella' slit sampler which was operated at an air intake of 1 cu. ft. per minute. During each period a blood agar plate was exposed for two minutes in the machine, and a salt-milk agar plate was exposed for ten minutes. In addition, a salt-milk agar plate was inserted for two minutes into the sieve sampler which had an air intake of approximately 20 cu. ft. per minute.

Solid Surfaces. Moist surfaces were tested with dry cotton wool swabs which were then plated on to blood agar without delay. Each swab was rubbed over about 4 in. of the test surface - representing an area of approximately 2 sq. in. Table tops, window ledges and all other dry surfaces were examined by pressing a strip of self-adhesive cellulose tape ('Sellotape') on to the area to be tested. The tape was held at its ends, and the area in contact with the surface was approximately 2 sq. in. After maintaining contact for a few seconds, the tape was stripped off and pressed gently for several seconds on to blood agar or salt-milk agar (usually the two media were used in parallel).

Before using the method routinely, preliminary

experiments were performed to test its validity. Strips were detached from numerous rolls of tape in this Department and elsewhere. The adhesive surface was in each case tested for the presence of aerobic organisms by pressing the strips on to blood agar for two minutes and then detaching. No growth was obtained in any of the tests. The possibility that the adhesive had an adverse effect on bacteria was then explored. The surfaces of clean ceramic tiles were artificially contaminated with Staph. aureus (propagating strain '75'), and Esch. coli recently isolated from a wound. The contaminated tiles were then sampled with strips of tape which were detached and pressed on to blood agar after varying intervals of time. No significant reductions in bacterial counts were observed over a period of six hours.

After the procedure had been in use for several months, Mair Thomas (1961) described a similar technique which she had used mainly for 'swabbing' skin.

Fabrics. Bedclothes and other fabrics were examined by a direct impression technique. In this procedure, a ground glass stopper with a flat top of $2\frac{1}{4}$ in. diameter was pressed against the back of the stretched fabric. The surface of the material to be tested was then held firmly in contact with blood agar or salt-milk agar for several seconds. The method is similar to that described by Rubbo and Dixon (1960), but avoids the need for any special apparatus. The term 'positive cultures' is used to refer to cultures which included two or more colonies of Staph. aureus or other pathogenic bacteria on the impression plates.

Examination of Settled Dust. In addition to the regular environmental testing already described, occasional samples of settled dust were collected into sterile 'bijou' bottles from the various sites. For this purpose a small brush was used after it had been disinfected in boiling water and allowed to dry over a hot water radiator. The samples of dust were sieved through galvanized wire netting (no. 16 standard wire gauge) in order to remove coarse particles. The dust was then examined both for bacterial content and physico-chemical composition.

Semi-quantitative bacterial counts were performed by vigorously shaking 100 mg. amounts of each sample in 10 ml. of nutrient broth. The broth was then clarified by centrifugation at 500 r.p.m. for three minutes, and viable counts were made on the supernatant ('washings') by the method of Miles and Misra (1938). The media used were blood agar and salt milk agar in parallel. Preliminary tests had been carried out on several samples to assess the efficiency of this method of examination. Ten cycles of shaking and centrifugation of the dust were performed. (Quarter-strength Ringer's solution was used as suspending fluid, for over this longer period bacterial growth might have taken place in broth). At each stage the washings were plated out and finally the dust itself was spread over blood agar. In this way it was found that the first cycle removed about 15 per cent of the 'total' bacterial population from each sample of dust.

Dust samples were examined under the microscope after staining by the method of Pressley (1958). For this purpose a

dye mixture was prepared. It contained 3 gm. 'Solar Scarlet RL' (Sandoz), 3 gm. 'Artisil Yellow RGFL' ultra dispersed (Sandoz), 5 gm. 'Brilliant Alizarine Milling Blue RWL' (Sandoz), 10 gm. hydrated sodium sulphate, 10 ml. concentrated sulphuric acid and distilled water to a total volume of 1 litre. Particulate material which is boiled in this mixture for five minutes stains according to its chemical nature: cellulose is pink, cellulose acetate is yellow, animal proteins are blue, nylon is green, while both 'Orlon' and 'Terylene' remain almost colourless. After staining in this way Pressley recommended that the solid material should be recovered in a sintered glass filter. However, it was found that such a filter retained the material firmly and was difficult to clean. In the present work disposable membrane filters ('Oxoid') were used, and proved to be very satisfactory. The stained debris was washed on the filter, and then mounted on a glass slide in glycerol.

During the intervals between the two-monthly periods of intensive sampling, environmental testing was confined to the exposure of settle plates at the various sites from 10 a.m. to 12 a.m. on one day each week.

To reduce the risk of contamination by fungi, the surface of each plate used in the environmental studies was spread with 0.2 ml. of a 0.1 per cent solution of nystatin in 50 per cent methyl alcohol.

The Ascertainment of Clinical Infection

The wards were visited twice each week, independently

of the environmental studies which were in progress at any particular time. Each visit usually took the form of a brief ward round in the company of the house surgeon or house physician, together with the ward sister when possible. During the visit any clinical infections which had not been present on admission were personally ascertained and recorded; in addition, records of clinically-diagnosed infection were kept by each ward sister.

The criteria of clinical infection were those unanimously accepted by the senior medical and surgical staff during discussions before the start of the investigation.

'Infections of the skin and subcutaneous tissues' ranged from small pustules to carbuncles and extensive cellulitis. 'Infected wounds' were those exuding pus or showing unequivocal signs of inflammation around the line of closure; stitch abscesses and infected haematomas were included in this category. Other infections including those of the urinary tract and respiratory tract were diagnosed clinically on the basis of the history and physical signs.

The term 'hospital infection' was used to describe all clinical infections which developed after patients had been admitted to hospital (vide p.185). The British Paediatric Association (1946) while attempting to define 'cross-infection', provided a concise definition of the more broadly based 'hospital infection'. This is:

'... any infection acquired by a patient in the hospital environment. Clinically it is an infection arising during the course of another illness for which the patient was originally admitted to hospital, and may attack the respiratory tract, gastro-intestinal tract,

wound, skin, or mucous membrane, or be manifested as one of the specific fevers'.

On the few occasions when a complete ward 'round' could not be carried out, an examination was made both of the current case notes and charts in the ward, and the lesions of individual patients who had been reported to be 'infected' or 'possibly infected'. At the time of the visit concise information was entered into a notebook concerning all clinically-diagnosed infection which had apparently developed in hospital. In addition, if suitable specimens had not already been submitted for bacteriological examination, these were collected during or immediately after the visit.

A laboratory diagnosis of 'infection' was established by the isolation of pathogenic organisms from pus or inflammatory exudate. In the case of sputum or urine specimens, the results of culture were evaluated in the light of the microscopical findings - particularly the presence of pus cells.

Copies of all the bacteriological reports upon clinical specimens from the wards were collected each week. Positive results from those reports which dealt with the ascertained 'hospital infections' were entered upon index cards. At this stage, also, clinical data on the bacteriologically-confirmed cases of hospital infection were abstracted from the notebooks and entered on index cards.

The Collection of Specimens from Patients and Staff.

Lesions. Pus and other exudates were collected into sterile 1 oz. 'Universal' bottles, or, if only present in small amounts, samples were taken on dry cotton-wool swabs. 'Clean-catch' mid-stream specimens of urine were obtained from patients of both sexes; catheter specimens were not taken unless the patient was undergoing catheterization for other purposes or was unable to provide a mid-stream specimen.

At fortnightly intervals during the periods of intensive sampling of the environment, all healthy surgical wounds that were not more than five days old and were accessible in the various units were swabbed to obtain an index of the extent of bacterial contamination.

Nasal Swabs. Dry cotton-wool swabs were rotated three times in both nostrils. These swabs were collected intermittently from patients and members of staff. No attempt was made to obtain a detailed continuous record of nasal carriage in the large hospital population.

Hand Impressions. These were intended to provide an index of skin contamination throughout the hospital and were taken without prior warning from members of staff and occasionally also from patients. The finger tips and part of the palm of each hand were pressed gently on to a Petri dish containing milk agar (p.99).

Isolation and Identification of Bacteria.

Specimens from clinically-infected lesions were submitted without delay to the hospital bacteriological laboratory and examined by Dr. A.F. Maccabe and his staff. All other material was examined by the author in the University Department of Bacteriology; much of the initial processing was, however, carried out in a laboratory which is attached to the Urology Department of the hospital and contains an incubator set at 37°C. The laboratory was made available by the kindness of Mr. W. Selby Tulloch.

Primary Cultures. The media used were prepared according to the methods described by Cruickshank (1960). Nasal swabs were plated on to 'milk agar' containing two volumes of nutrient agar (with 3 per cent agar) and one volume of sterilized milk. The same medium was used for taking hand impressions. The wound swabs examined by the author were plated on to 10 per cent horse blood agar and milk agar containing 7.5 per cent sodium chloride ('salt-milk agar'); these were the same media as were used for air sampling.

In the clinical laboratory specimens of pus and swabs from surgical wounds, burns, primary skin infections and from the ear and the vagina were inoculated on to blood agar and MacConkey's agar plates for aerobic incubation, and blood agar plates for anaerobic incubation. Sputum was first homogenized by incubating at 37°C. with an equal volume of 1 per cent pancreatin solution; the material was then inoculated on

to blood agar for aerobic incubation and on to 'chocolate' blood agar for incubation in an atmosphere enriched with carbon dioxide. Eye swabs and nasal swabs were examined using the same media as in the case of sputum. Throat swabs were plated on to blood agar and crystal violet blood agar. Deposits from specimens of urine were inoculated on to blood agar and MacConkey plates. Viable counts of bacteria in urine were only performed in special cases. Specimens of faeces from patients who had developed diarrhoea were plated on to desoxycholate-citrate agar, and on to MacConkey's agar in the case of infants and young children. Enrichment cultures of faeces were also prepared in selenite F medium.

Direct Gram-stained films of the specimens were examined in all cases, with the exception of urine and faeces. Wet films were prepared from urine deposits, and faeces were examined microscopically only when this was specifically requested - as in the case of post-operative diarrhoea, when Gram-stained films were examined for direct evidence of staphylococcal superinfection.

Cultures in the clinical laboratory were incubated at 37°C. for approximately 18 hours and then examined at once. The cultures investigated by the author were incubated for between 24 and 36 hours (with the exception of salt-milk agar plates which were incubated for 72 hours). After a preliminary inspection to reveal any plates that required immediate attention (such as those on which there were spreading colonies), the cultures were left on the laboratory bench for about 48 hours to

allow enhancement of staphylococcal pigmentation. This time sequence also made it possible for the initial examination of most of the primary cultures to be performed on days when environmental sampling was not in progress.

Further Laboratory Investigations. Counts of the total number of bacterial colonies and the presumptive number of pathogenic bacteria were made on all plates used in the environmental studies.

Colonies morphologically resembling Staph. aureus were sub-cultured on to sectors of a nutrient agar plate. If the suspected colonies were numerous and appeared to be identical, three were picked at random for subculture. Following overnight incubation, the subcultures were tested for coagulase production by the slide method (Cadness-Graves *et al.* 1943). If the results were equivocal, further tests were performed by the tube method (Fisk, 1940).

Coagulase-positive staphylococci ('Staph. aureus') were subcultured in nutrient broth as a prelude to antibiotic sensitivity testing and bacteriophage typing. The disk technique of Gould and Bowie (1952) was used in the sensitivity tests, and the criteria of sensitivity adopted were, penicillin:- growth inhibited by less than 5 units per ml., streptomycin, tetracycline and erythromycin:- inhibited by less than 2.5 μ g. per ml. in each case, chloramphenicol:- inhibited by less than 7.5 μ g. per ml. Bacteriophage typing was performed using the techniques described by Williams and Rippon (1952). The following

modified set of bacteriophage filtrates was employed: 3A, 3B, 3C, 6, 7, 29, 42E, 42D, 47, 52, 52A, 53, 54, 55, 71, 75, 77, 79, 80, 81, 83A and 187 (in later work - after 1961 - these were arranged on the typing plate according to the conventional groups I, II, III and IV)¹. The bacteriophages were originally obtained from the Staphylococcal Reference Laboratory, Colindale, London, and had subsequently been propagated in The University Bacteriology Department by Dr. J.C. Gould.

Representative strains of Staph. aureus were stored in the freeze-dried state or for short-term purposes as agar slope cultures in 'bijou' bottles. These strains were later tested for methicillin sensitivity by the disk method (criterion of sensitivity: growth inhibited by less than 2.5 μ g per ml.); other tests also carried out on representative strains were of mercuric chloride resistance (Moore, 1960), ability to produce egg-yolk turbidity (Alder and Gillespie, 1952), neomycin sensitivity (Greer and Menard, 1957-58), pigmentation on 1 per cent glycerol monoacetate (Willis and Turner, 1962). Survival tests were also carried out upon several strains that were stored under various conditions. These are described on p.174.

As a preliminary test, Gram-stained films were prepared from cultures morphologically resembling streptococci,

1. Although some phage reactions are shared by different groups, the conventional arrangement is: group I - 29, 52, 52A, 79, 80; group II - 3A, 3B, 3C, 55, 71; group III - 6, 7, 42E, 47, 53, 54, 75, 77, 83A; group IV - 42D; unclassified - 81, 187.

coliform bacilli, Proteus spp. or Ps. pyocyanea that had been obtained from the environment. Streptococci were subcultured on to MacConkey's agar and blood agar; if characteristic growth occurred on the former the organism was described as Strep. faecalis. Strains that failed to grow on MacConkey's agar and produced α -haemolysis on blood agar were tested for optochin sensitivity by the disk method. Resistant organisms were classified as Strep. viridans.

Gram-negative bacilli which grew in subculture on MacConkey's agar were examined for motility in semi-solid agar and were tested for their ability to ferment carbohydrates and to produce indole and urease. Ps. pyocyanea was initially identified on the basis of pigmentation and production of the characteristic odour of trimethylamine; subsequently these strains were typed using bacteriophages as described by Gould and McLeod (1960). As in the case of Staph. aureus disk sensitivity tests were performed on other potentially pathogenic organisms, and, in addition to the antibiotics already listed, sensitivities were determined for sulphonamide (50 μ g. per disk) and, in the case of Ps. pyocyanea, polymyxin B (100 units per disk).

The pathogenic bacteria isolated in the clinical laboratory were identified by methods similar to those already described; bacteriophage typing of Ps. pyocyanea and further tests on Staph. aureus, other than bacteriophage typing, were carried out in the University Bacteriology Department. Representative strains of Staph. aureus on which bacteriophage typing

had already been carried out in the clinical laboratory by Dr. A.F. Maccabe were typed once again in the University to confirm the reproducibility of the results.

The Virological Investigation of 'Sticky Eyes' in Infants

During the first few months of the investigation, cases of purulent conjunctivitis ('sticky eye') among the newborn were encountered from which no significant bacterial growth was obtained in the early stages of the disease. The possibility of a viral aetiology was therefore explored.

Over a two-month period specimens of cord blood were obtained from all infants born in the hospital, and venous blood was collected from the mothers of infants who later developed sticky eye, as well as from the mothers of 30 healthy infants. Early specimens of conjunctival discharge were obtained from all cases of acute conjunctivitis in infants by means of paired cotton wool swabs on wooden sticks. One of the swabs was submitted to the clinical bacteriological laboratory and the second one of each pair was broken off into bijou bottles containing Hanks' balanced saline (supplemented by 2000 μ g. of streptomycin, 10,000 units neomycin and 500 μ g. of nystatin per ml.). In addition, conjunctival scrapings were taken with a platinum loop. Smears of the scrapings were made on glass slides and these were then immersed in methyl alcohol for three minutes. The smears were stained overnight in a 1 in 10 solution of Giemsa stain. Swabs and scrapings were likewise obtained from the cervix uteri of mothers whose infants had developed conjunctivitis.

The yolk sacs of two six-day old chick embryos were each inoculated with 0.2 ml. of the contents of the bijoux bottles. Similar volumes of the fluids were used to inoculate each of two HeLa cell cultures maintained in roller tubes. The culture medium was supplemented by the addition of 50 units of penicillin, and 50 μ g. each of streptomycin and nystatin per ml.

The inoculated eggs were 'candled' daily, and where death of the embryo occurred after three days' incubation, yolk sac impression smears were made from the stalk of the sac, and these were stained in the manner already described for direct smears. If death of the embryo had not already occurred by the nineteenth day of embryonic development, the eggs were chilled and impression smears of the yolk sac were prepared in the same way. All stained smears were examined in particular for basophilic intracytoplasmic inclusion bodies, and for clusters of elementary bodies in the case of the yolk sac material. Material that was apparently negative for virus was passaged blindly through further chick embryos.

HeLa cell cultures were examined daily for cytopathic changes. The cultures were usually discarded after 18 days' incubation.

Tests for virus were also carried out on airborne dust and settled dust. These procedures are described together with the results in the next section (p.179).

The sera obtained from specimens of cord blood and maternal blood of 15 cases and 30 healthy controls were examined for antibodies to the adenovirus and psittacosis groups by the complement-fixation technique (Cruickshank, 1960).

Part II

STUDIES IN A GENERAL HOSPITAL

(iii) RESULTS

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BACTERIAL CONTAMINATION OF THE HOSPITAL ENVIRONMENT.

The Air.

The annual mean values and the ranges of the total bacterial counts are shown in Table II. These counts did not vary to any great extent in the different departments. However, the slit sampler and settle plate counts of Staph. aureus, both in absolute terms and as percentages of the total counts, showed consistent differences in the various departments (Tables III and IV). A comparison of the two sets of air count made on the basis of Petri ratios showed that whereas the average diameters of particles carrying 'total' bacteria were in the range of 9μ to 11μ , the equivalent values for Staph. aureus ranged from 11.5 to 17μ .

The heaviest staphylococcal air contamination was found in the paediatric and maternity departments. As shown in figures 10 and 11, the differences in Staph. aureus counts amongst the various departments were well marked during the autumn and winter months, but were less distinct in the spring and summer months, particularly in the case of the settle plate counts.

The bacterial counts obtained with the sieve sampler are not represented in the tables and figures. Although the instrument can sample a relatively large volume of air, its

TABLE II. TOTAL BACTERIAL COUNTS IN THE AIR OF HOSPITAL WARDS AND IN THE MAIN OPERATING THEATRES.*

DEPARTMENT	SLIT SAMPLER COUNTS (per cu. ft.)		SETTLE PLATE COUNTS (per 10sq.in. per hr.)		AVERAGE PARTICLE DIAMETERS ⁺ (μ)
	Range	Annual Mean	Range	Annual Mean	
Paediatric Medicine	16-175	52	48-500	103	10.0
Paediatric Surgery	12-80	36	45-130	83	10.5
Maternity Nurseries	40-100	42	18-190	78	9.5
Maternity Wards	10-120	38	40-175	99	10.5
Urology	8-75	30	30-200	87	10.5
Gynaecology	12-110	33	28-180	68	9.5
Gastro- enterology	7-78	39	20-225	94	10.5
General Medicine	15-80	39	38-200	109	11.0
General Surgery	6-76	34	31-140	76	10.0
Theatres	13-38	25	28-72	40	9.0

* Readings taken on week days between 9 a.m. and 5 p.m.

+ Calculated to the nearest 0.5μ from Petri ratios (Lidwell, 1948).

TABLE III. SLIT SAMPLER COUNTS OF STAPH. AUREUS IN HOSPITAL WARDS
 AND IN THE MAIN OPERATING THEATRES[‡]

DEPARTMENT	COUNTS (per 100 cu. ft.)		PERCENTAGE OF TOTAL COUNT
	MAXIMUM	ANNUAL MEAN	
Paediatric Medicine	800	63	1.2
Paediatric Surgery	150	39	1.1
Maternity Nurseries	160	41	1.0
Maternity Wards	100	36	0.9
Urology	80	19	0.6
Gynaecology	140	29	0.9
Gastro-enterology	70	18	0.5
General Medicine	60	18	0.5
General Surgery	80	16	0.5
Theatres	10	-	-

‡ Readings taken on week days between 9 a.m. and 5 p.m.

- Very few Staph. aureus isolated.

TABLE IV. SETTLE PLATE COUNTS OF STAPH. AUREUS IN HOSPITAL WARDS AND
IN THE MAIN OPERATING THEATRES.^{*}

DEPARTMENT	COUNTS (per 10sq.in.per hr.)		PERCENTAGE OF TOTAL COUNT	AVERAGE PARTICLE DIAMETERS ⁺ (μ)
	Maximum	Annual Mean		
Paediatric Medicine	6.0	1.8	1.7	12.0
Paediatric Surgery	3.0	1.5	1.8	14.0
Maternity Nurseries	2.0	1.2	1.5	12.0
Maternity Wards	3.5	1.4	1.4	14.0
Urology	4.5	1.2	1.4	17.0
Gynaecology	2.5	0.7	1.0	11.5
Gastro- enterology	2.5	0.7	0.7	14.0
General Medicine	4.0	0.9	0.8	15.5
General Surgery	2.0	0.7	0.9	14.5
Theatres	1.0	-	-	-

* Readings taken on weekdays between 9 a.m. and 5 p.m.

+ Calculated to the nearest 0.5μ from Petri ratios (Lidwell, 1948).

- Very few Staph. aureus isolated.

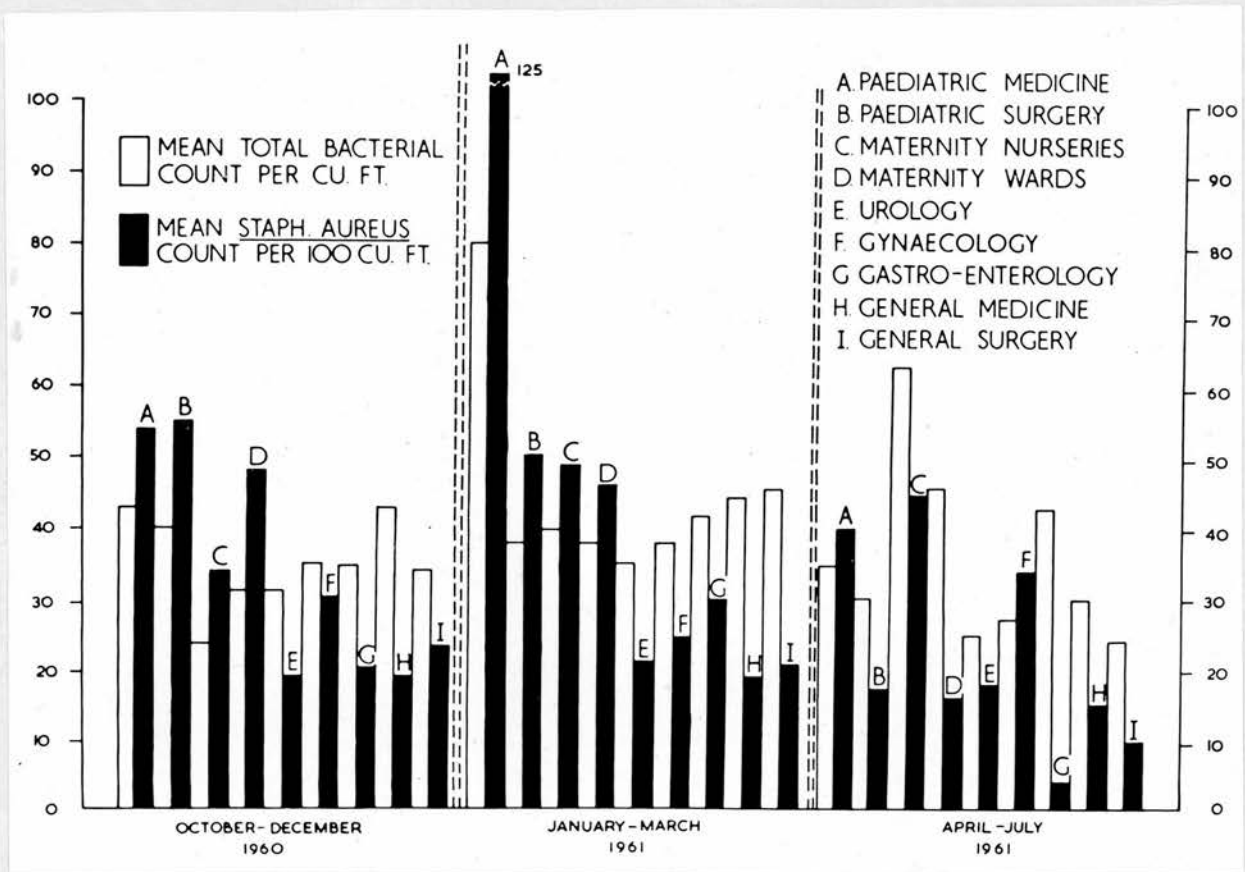


FIGURE 10. MEAN TOTAL BACTERIAL AND STAPH.AUREUS AIR COUNTS OBTAINED WITH THE SLIT SAMPLER IN THE VARIOUS DEPARTMENTS.

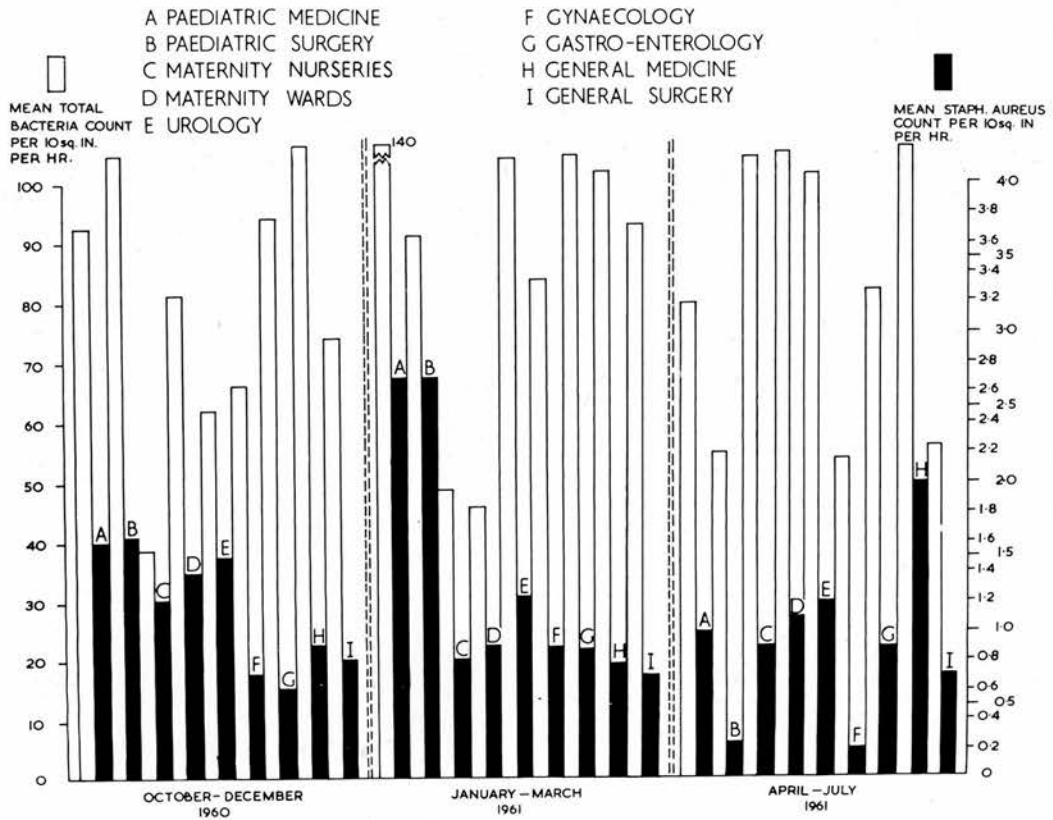


FIGURE 11. MEAN TOTAL BACTERIAL AND STAPH. AUREUS AIR COUNTS OBTAINED FROM SETTLE PLATES IN THE VARIOUS DEPARTMENTS.

efficiency is low. Thus, although the air flow is approximately 20 cu. ft. per minute as compared with 1 cu. ft. per minute in the slit sampler, the air counts obtained with the sieve sampler corresponded to those calculated for between 4 and 10 cu. ft. per minute on the basis of slit sampler counts. Accurate quantitative work is therefore not possible with the sieve sampler. The instrument has since been reserved for use as a readily portable means of sampling, semi-quantitatively, large volumes of air.

Figures 12 - 16 represent the mean diurnal variations in the total bacterial and Staph. aureus air counts within the different departments. In general, the counts were highest during the first part of the morning and fell thereafter, often rising again towards the end of the afternoon. These trends were not seen in the Maternity Nurseries or in the Paediatric Medical Department. In the nurseries the amount of activity remained relatively unchanged throughout the day, but was perhaps at its peak around the middle of the day. This seems to be reflected in the air counts (Figure 15). This pattern of increased activity during the late morning and early afternoon applied also to the Paediatric Medical Department and is very well correlated with the air counts (Figure 16). The parallelism between ward activities and bacterial air counts was found in most of the departments studied, although certain anomalies were encountered. Thus in the Urology Department during the afternoon the Staph. aureus settle plate counts followed a trend that was consistently different from the slit sampler counts

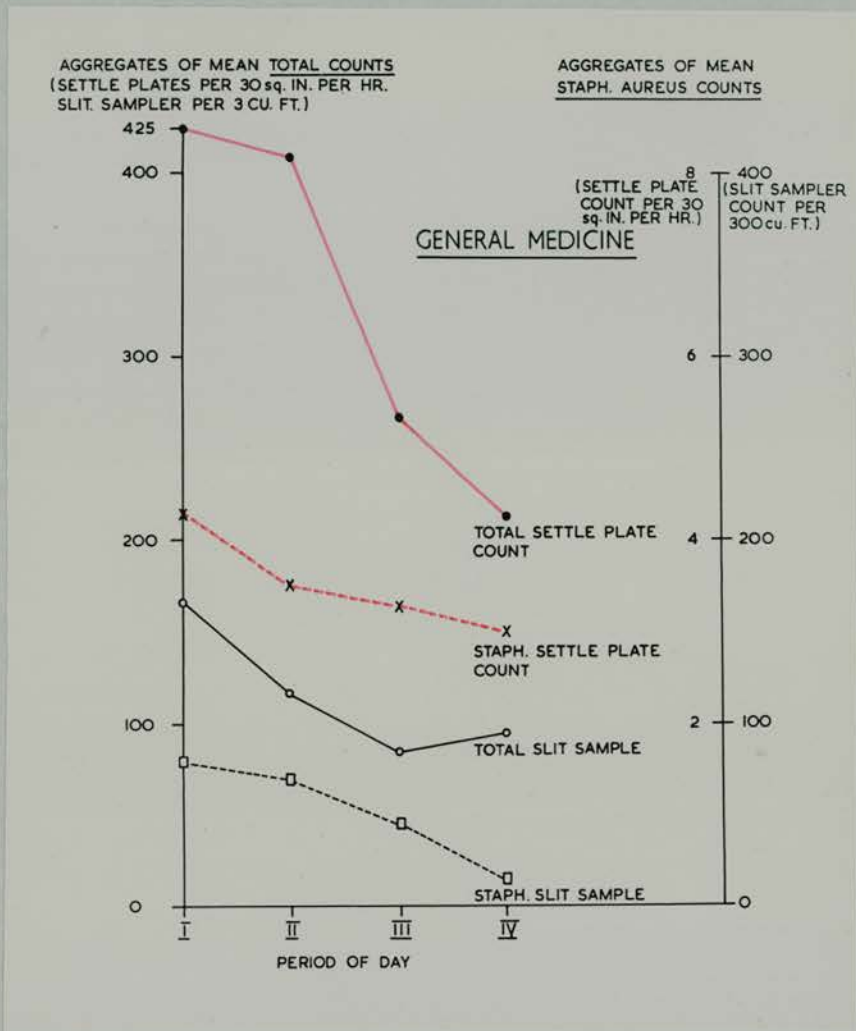


FIGURE 12. MEAN DIURNAL VARIATIONS IN TOTAL BACTERIAL AND STAPH. AUREUS AIR COUNTS IN THE GENERAL MEDICAL DEPARTMENT.

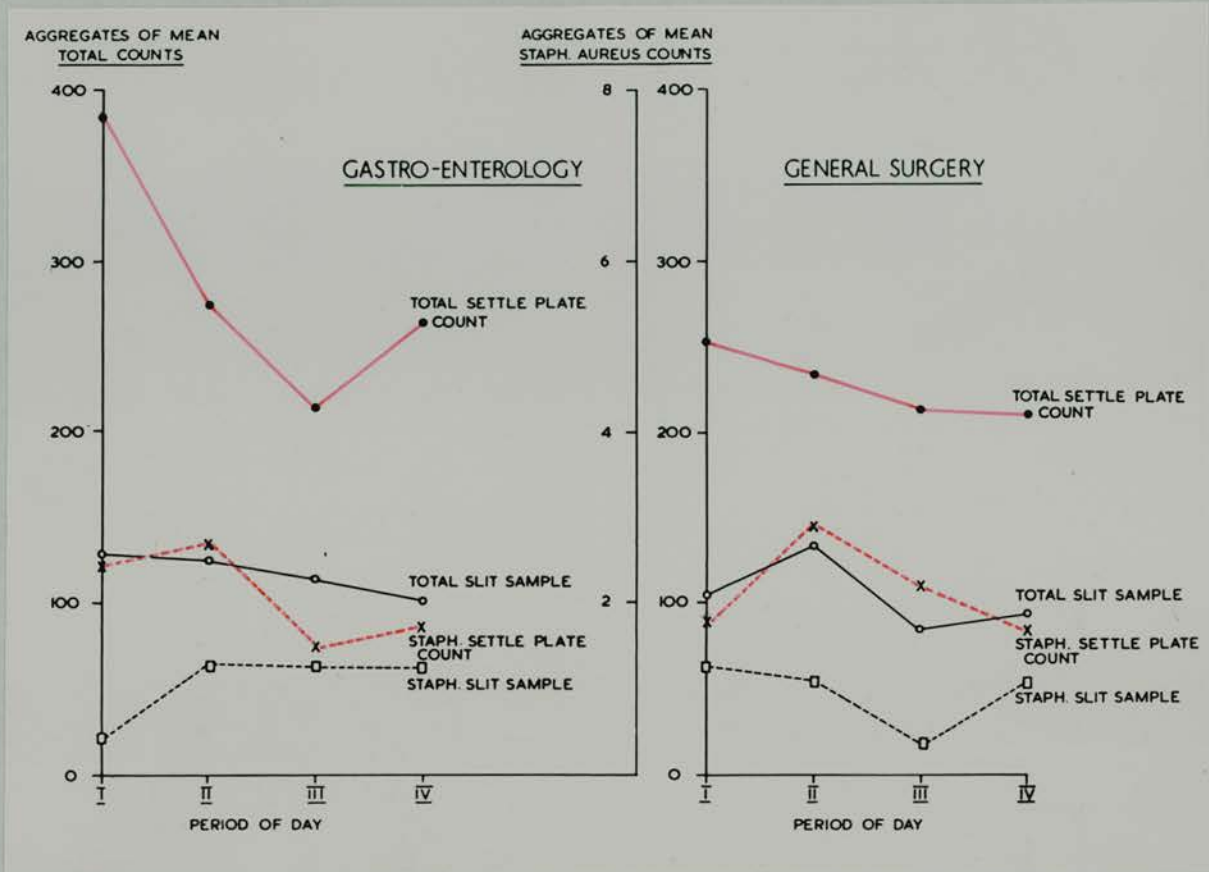


FIGURE 13. MEAN DIURNAL VARIATIONS IN THE TOTAL BACTERIAL AND STAPH. AUREUS AIR COUNTS IN THE DEPARTMENTS OF GASTRO-ENTEROLOGY AND GENERAL SURGERY.

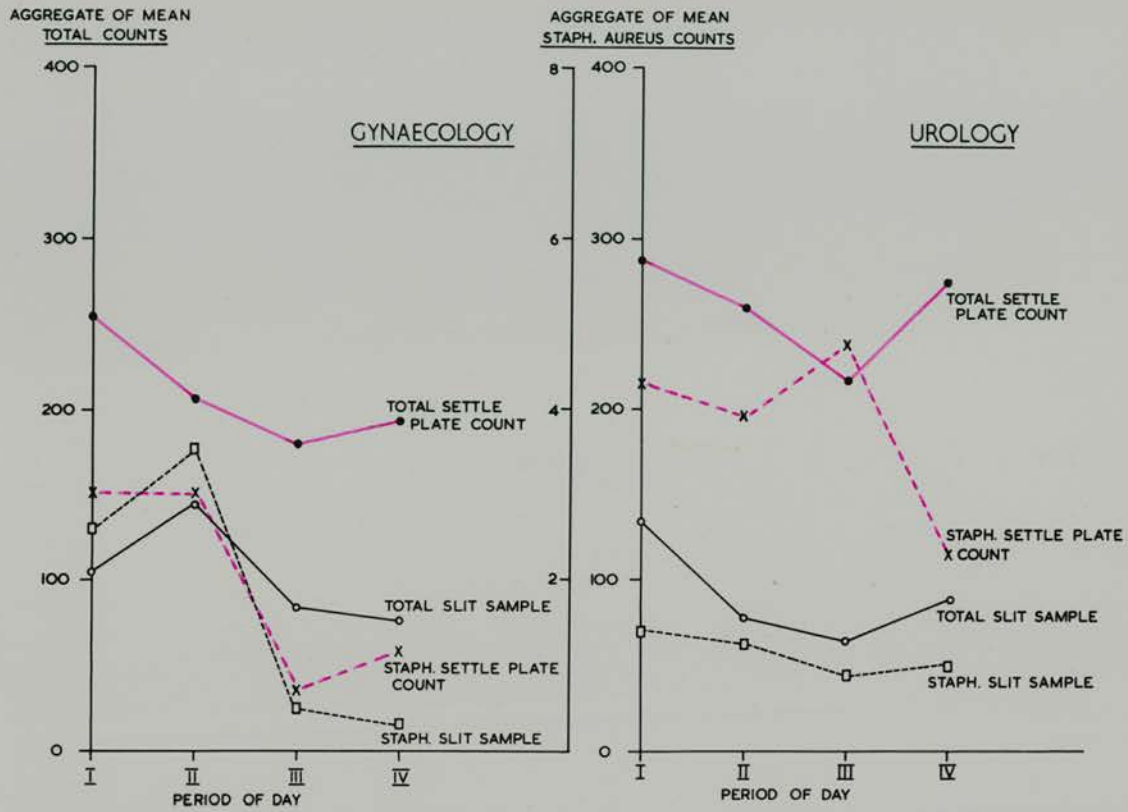


FIGURE 14. MEAN DIURNAL VARIATIONS IN THE TOTAL BACTERIAL AND STAPH. AUREUS AIR COUNTS IN THE DEPARTMENTS OF GYNAECOLOGY AND UROLOGY.

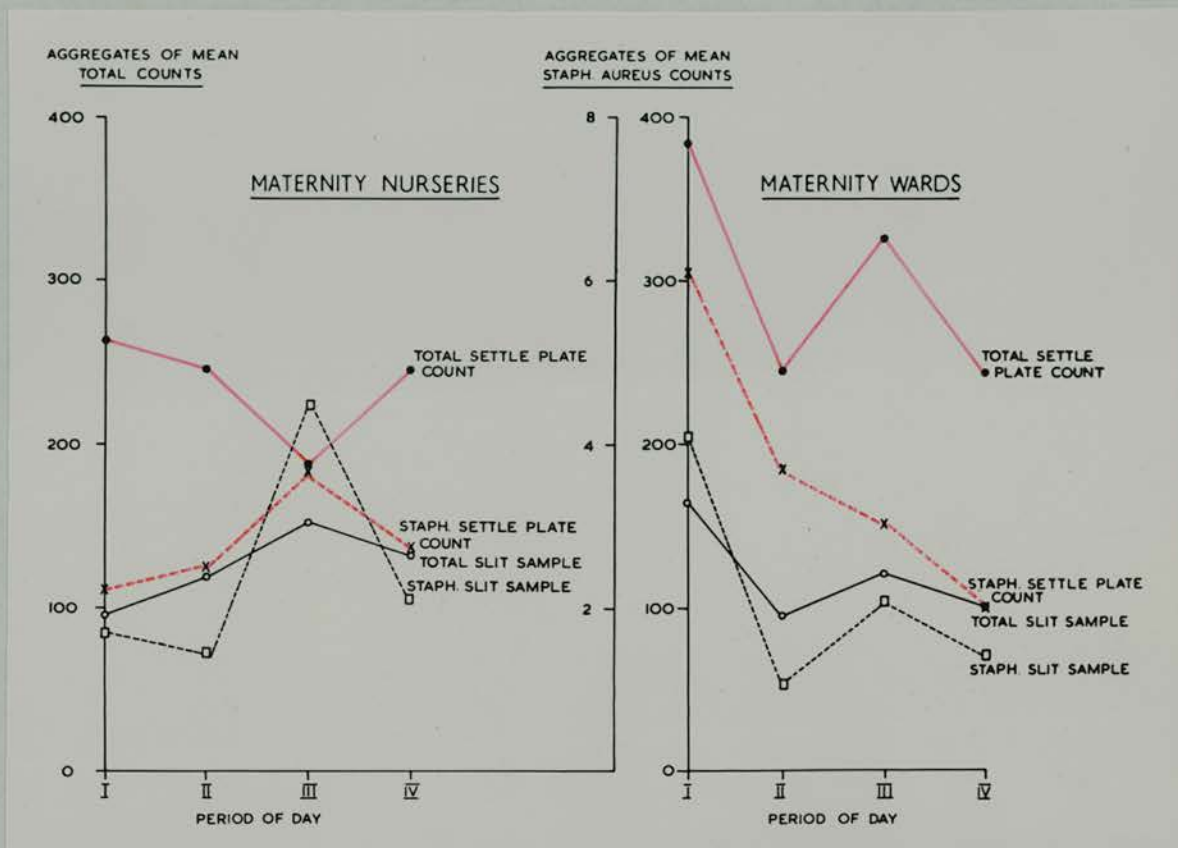


FIGURE 15. MEAN DIURNAL VARIATIONS IN THE TOTAL AND THE STAPH. AUREUS AIR COUNTS IN THE MATERNITY NURSERIES AND WARDS.

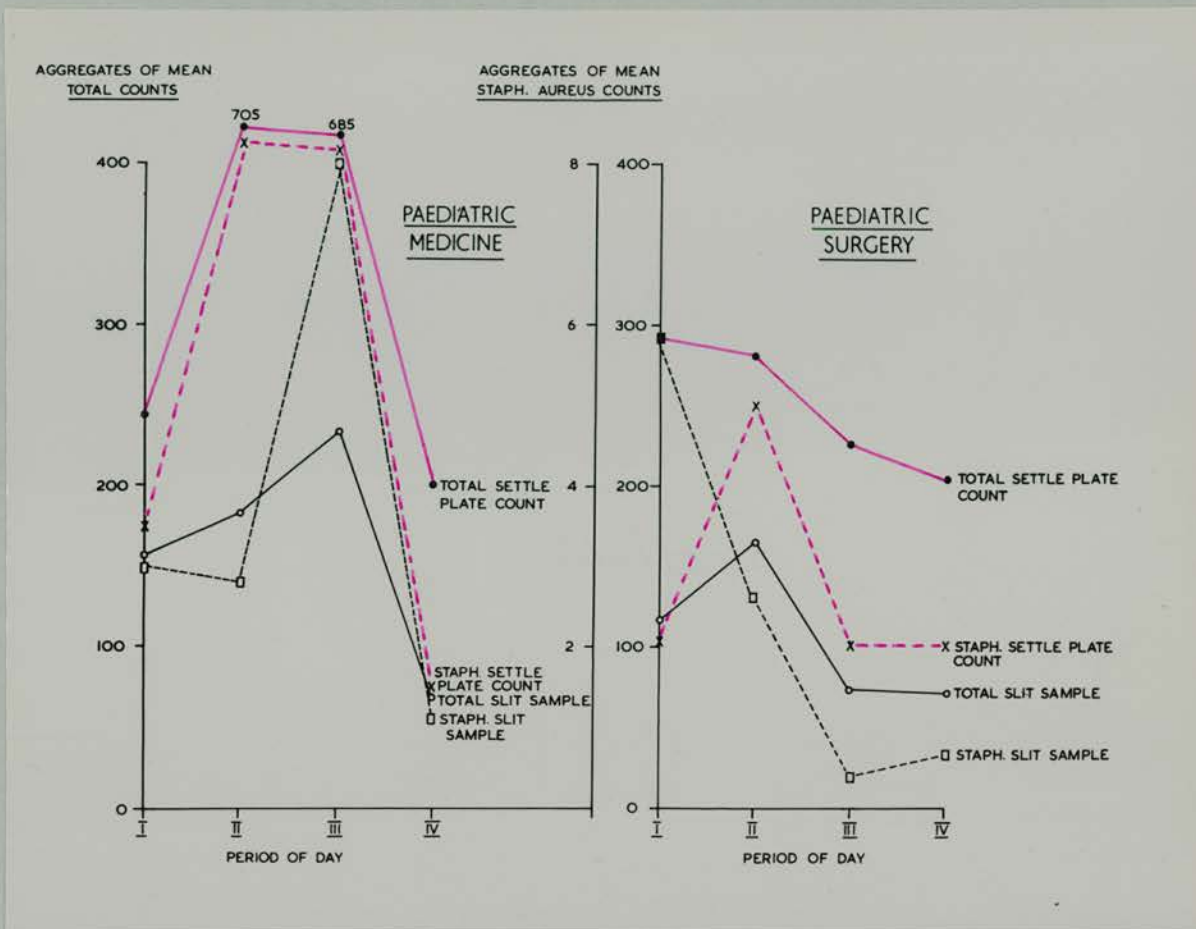


FIGURE 16. MEAN DIURNAL VARIATIONS IN THE TOTAL AND THE STAPH. AUREUS AIR COUNTS IN THE PAEDIATRIC MEDICAL AND SURGICAL DEPARTMENTS.

(Figure 14). This indicates the presence of unexplained fluctuations in the size of the particles bearing Staph. aureus. At the beginning of the afternoon these particles tended to be unusually large (c. 23μ average diameter).

Pathogenic bacteria other than Staph. aureus were intermittently isolated from the air. Proteus spp. (usually Pr. mirabilis) were the commonest of these isolates and were obtained with the air sampler and settle plates from wards in the maternity, gynaecology, general surgery and urology departments. The Urology Department was also a notable source of air-borne Ps. pyocyanea; as many as seven colonies were obtained on a single settle plate.

Solid Surfaces.

Most of the samples taken from table tops, window ledges and other surfaces in the hospital contained small numbers of Staph. aureus. Larger yields (e.g. >20 colonies per sq. in.) were, however, obtained in the paediatric and maternity departments where air counts were uniformly high. Elsewhere too the degree of contamination of surfaces with Staph. aureus was found to reflect general fluctuations in the air counts. In all departments tap handles were a notable source of Staph. aureus and often of coliform bacilli. The scales used for weighing infants in the maternity nurseries were usually heavily contaminated with the prevalent group III strain of Staph. aureus.

Between periods of occupancy, baths were found to be

a considerable reservoir of very diverse pathogenic bacteria. Apart from Staph. aureus which was usually abundant, isolations were made of Proteus spp., coliform bacilli and - especially in the Urology Department - Ps. pyocyanea.

Fabrics

The yields of bacteria from bedclothes and patients' dressing gowns were high even within a few hours of their issue to the patients. Total bacterial counts of more than 100 per sq. in. were common and Staph. aureus frequently constituted more than one-third of the population. Woollen blankets, which were changed less often than sheets, and pillow cases tended nevertheless to yield lower numbers of bacteria.

Bacteria and Fibres in Settled Dust.

The bacterial and fibrous composition varied widely on different occasions. Table V contains the results of one complete collection from all the departments. The bacterial counts are in general consistent with those obtained by other means, although the counts of Staph. aureus in the paediatric departments are relatively low in these samples.

Cellulose fibres (mainly cotton) predominated over protein fibres (mainly wool) in most departments. In the adult surgical wards, however, the two kinds of fibre were more equally distributed. Figures 17 and 18 show microscope fields of stained dust in which the fibres have remained intact. More

TABLE V. BACTERIAL AND FIBROUS CONTENT OF SETTLED DUST SAMPLES

DEPARTMENT	BACTERIA PER ML. OF WASHINGS		RATIO OF CELLULOSE FIBRES TO PROTEIN FIBRES
	TOTAL	STAPH. AUREUS	
Paediatric Medicine	1,500	400	3:2
Paediatric Surgery	6,000	500	3:1
Maternity Nurseries	15,000	8,000	98:2
Maternity Wards:			
Antenatal	2,500	2,000	1:1
Postnatal	50,000*	10,000	3:2
Urology	4,500+	400	1:1
Gynaecology	50,000	1,500	4:1
Gastro-enterology	2,500	50	2:3
General Medicine	3,000	600	3:1
General Surgery	2,000 ^x	30	1:1

* Including c. 800 mixed coliform bacilli

+ Including 100 Ps. pyocyanea

x Including c. 500 group D. Streptotocci

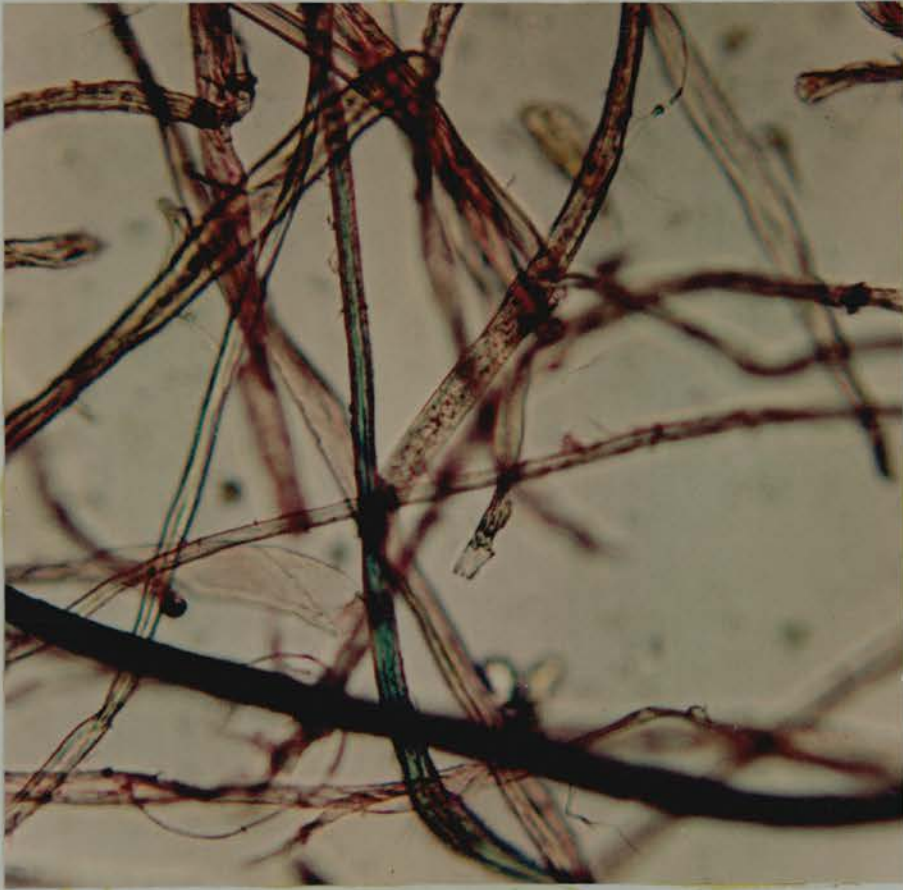


FIGURE 17. SETTLED DUST FROM THE MATERNITY NURSERIES STAINED BY PRESSLEY'S METHOD (x 250)

Most of the sample consisted of smaller fragments and was therefore less suitable for photography. The orange-pink fibres are cellulose (cotton); the green-blue fibres are keratin (wool), and are in the minority.

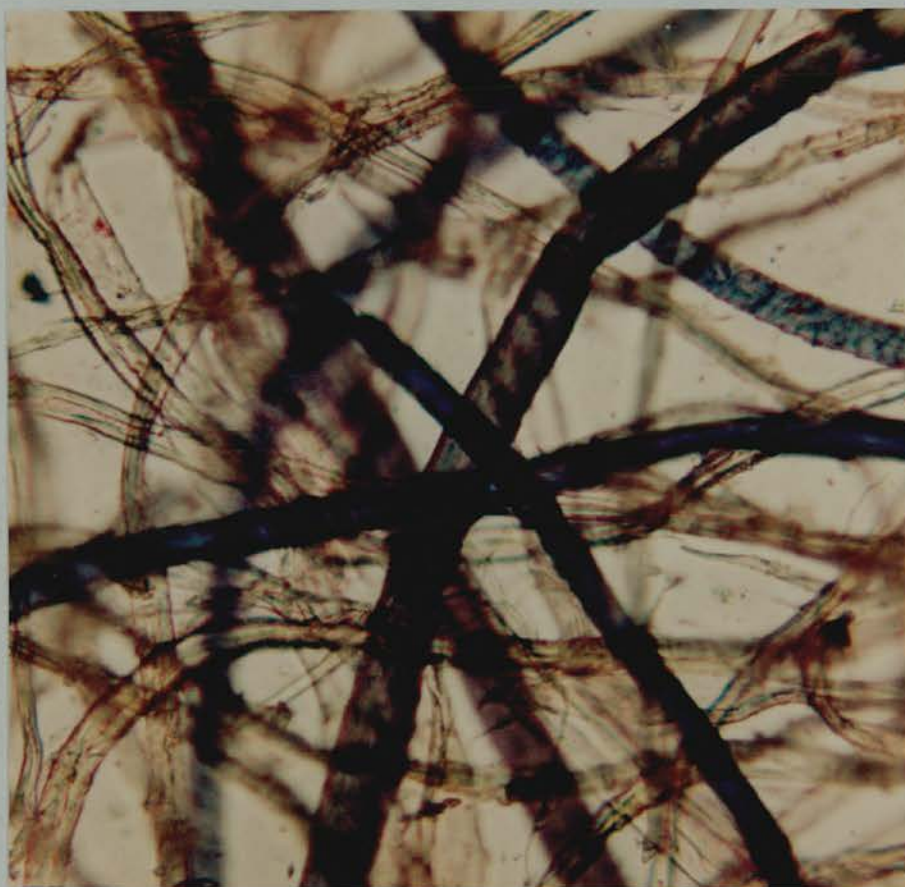


FIGURE 18. SETTLED DUST FROM THE GASTRO-ENTEROLOGY DEPARTMENT STAINED BY PRESSLEY'S METHOD (x250).
(see legend to Figure 17)

commonly the fibres were fragmented, and were identified with greater difficulty on the basis of staining reaction and morphology.

Nylon and other synthetic fibres, though present in many samples, did not constitute more than about 5 per cent of the total count on any occasion. In addition to fibrous structures, amorphous material of a protein nature was usually present in dust samples. This material had the appearance of desquamated skin fragments, and the particles were generally less than 20μ in diameter.

CLINICAL INFECTIONS OCCURRING IN THE HOSPITAL.

From the in-patient data summarised in Table VI it can be seen that the average duration of stay varied from about 8 days for infants in the Maternity Nursery to more than 26 days in the Gastro-enterology Department, where extensive investigations and operative procedures were common. During the period from November 1960 to October 1961, 7360 patients were admitted to the departments that were under investigation. The average ages of patients were very similar in the urology, gastro-enterology and general medical departments, and were lower in the general surgical and gynaecological departments. The average ages corresponded with those of patients in hospitals in England and Wales during 1961 (Ministry of Health and General Register Office, 1964).

Patients Admitted with Infection.

As shown in Table VII more than one-third of the admissions to the Department of Paediatric Medicine were on account of infection - predominantly in the respiratory tract. It should be emphasised that these were clinical diagnoses; most of the patients had received antibiotics before admission, and satisfactory bacteriological diagnosis was possible in less than half of the cases. The next highest incidence of clinical infection present on admission was in the Urology Department where 8 per cent of patients came into hospital for this reason. It was interesting to find that tuberculosis

TABLE VI. HOSPITAL IN-PATIENT STATISTICS DURING THE PERIOD OF STUDY

DEPARTMENT	MAXIMUM NO. OF BEDS	TOTAL NO. OF PATIENTS	NO. OF DEATHS	AVERAGE DURATION OF STAY (DAYS)	AVERAGE AGE (YEARS)
Paediatric Medicine	21	499	12	16.4	3
Paediatric Surgery	25	562	11	15.9	5
Maternity Nurseries	44	1448	33	7.8	(3.9 days)
Maternity Wards	52	1729	1	9.6	26
Urology	28	490	22	18.9	50
Gynaecology	22	734	7	9.9	37
Gastro- enterology	35	399	35	26.4	51
General Medicine	36	588	40	20.0	52
General Surgery	38	911	29	13.5	46
Radiotherapy*	107	1576	58	20.5	-
Neurosurgery*	60	992	41	20.1	-
Orthopaedic Surgery*	12	271	8	14.6	-
Private beds *	5	76	0	13.0	-
Other Medical beds *	61	989	84	19.8	-

* Departments excluded from the study.

TABLE VII. ADMISSIONS TO HOSPITAL ON ACCOUNT OF INFECTION

DEPARTMENT	ANNUAL TOTAL	INCIDENCE PER 100 ADMISSIONS	SITE OF INFECTION			
			SUPERFICIAL	URINARY TRACT	RESPIRATORY TRACT	OTHER
Paediatric Medicine	178	35.6	3	2	136	37x
Paediatric Surgery	43	7.6	26	3	2	12+
Maternity Nurseries	-	-	-	-	-	-
Maternity Wards	19	1.1	-	15	4	-
Urology	39	8.0	2	32*	-	5
Gynaecology	20	2.7	6	-	-	14'
Gastro-enterology	7"	1.8	2	-	-	5
General Medicine	33	5.6	-	2	15	16'''
General Surgery	40	4.4	30 ^{oo}	-	-	10xx
TOTALS	379	6.4	69	54	157	99

x includes meningitis (12), gastro-enteritis (11), rheumatic fever (8), glandular fever (3)

+ includes osteomyelitis (8), gastro-enteritis (3)

* includes urogenital tuberculosis (8)

' includes vaginal infection (12) - cases of chronic cervicitis excluded

" includes 2 patients re-admitted with wound abscesses, and 2 cases of infectious hepatitis

''' includes subacute bacterial endocarditis (4), rheumatic fever (3), glandular fever (3)

oo includes 9 patients re-admitted with wound abscesses.

xx includes 4 patients with breast abscesses who had recently been discharged from the Maternity Wards.

was responsible for 8 out of the 32 urinary tract infections which necessitated admission to this department.

Although the Department of General Surgery had a relatively low incidence of infection at the time of admission, the 9 patients who were re-admitted with wound sepsis form a notable group. Eight of the patients had undergone abdominal surgery (4 appendicectomies, 3 laparotomies, 1 closure of a perforated duodenal ulcer), and they returned to hospital with wound abscesses within one week of being discharged. The ninth patient had been surgically treated for varicose veins and she was re-admitted almost two weeks after leaving hospital, but had suffered from infections of her wounds for almost the whole of that period. In the order described above, the patients were aged 14, 25, 29, 66, 35, 43, 73, 28 and 50. From four of the infections 'types' of Staph. aureus were obtained which had previously been isolated in the wards. The remaining five abscesses yielded Gram-negative bacilli (Proteus spp. and coliform bacilli) as the predominant organisms.

Of interest also in the context of hospital-acquired infection were four women who were admitted to the General Surgical Department with breast abscesses more than a week after their discharge from the Maternity Department. In each case Staph. aureus of the 'endemic' (multiple-resistant, group III) type was isolated from the lesion.

Hospital-acquired Infections.

Table VIII presents the annual incidence of clinical infections which developed after admission to the various departments. In all, there were 1,231 such infections giving an incidence of 16.8 per hundred admissions.

With the exception of the maternity nurseries, the non-staphylococcal infections greatly outnumbered the staphylococcal infections arising in hospital. Figure 19 compares the percentages of hospital infections due to Staph. aureus during the six two-monthly periods in the different departments. The paediatric departments and the maternity nurseries had a consistently higher proportion of clinical infections due to Staph. aureus than did the other departments, and the paediatric departments had the highest incidence of such infections. In the maternity nurseries the actual incidence of Staph. aureus infections was slightly lower, however, and was very similar to that in the Urology Department (Table VIII). The General Medical Department had the next highest incidence.

The incidences and percentages of infections due to Staph. aureus are well correlated with the degree of staphylococcal contamination of the air, as shown by comparing Table VIII with tables III and IV, and Figure 19 with figures 10 and 11. The only notable exception to this parallelism was in the maternity wards which had a persistently high level of contamination with Staph. aureus, especially in the autumn and winter months, but had the lowest incidence and percentage of clinical infections due to Staph. aureus. Conversely, the percentage and incidence of

TABLE VIII. ANNUAL NUMBER AND INCIDENCE OF INFECTIONS DUE TO STAPH. AUREUS AND OTHER BACTERIA OCCURRING IN HOSPITAL

DEPARTMENT	NON-STAPHYLOCOCCAL INFECTIONS †		STAPHYLOCOCCAL INFECTIONS †		
	NO.	INCIDENCE ¹	NO.	INCIDENCE ¹	% OF ALL INFECTIONS
Paediatric Medicine	59	11.8	36	7.0	38
Paediatric Surgery	86	15.9	65	11.0	43
Maternity Nurseries	58	4.0	96	6.6	62
Maternity Wards	165	9.5	20	1.1	10
Urology	151	30.8	33	6.7	18
Gynaecology	96	13.1	20	2.7	17
Gastro-enterology	88	22.0	16	4.0	15
General Medicine	87	14.5	32	5.4	27
General Surgery	87	9.5	36	3.9	29
TOTALS	877	12.0	354	4.8	28

¹ Per 100 Patients.

† Further details in Tables IX - XII.

In Appendix tables I - III the infections are arranged in two-monthly periods.

PERCENTAGE OF
HOSPITAL INFECTIONS
DUE TO STAPH. AUREUS.

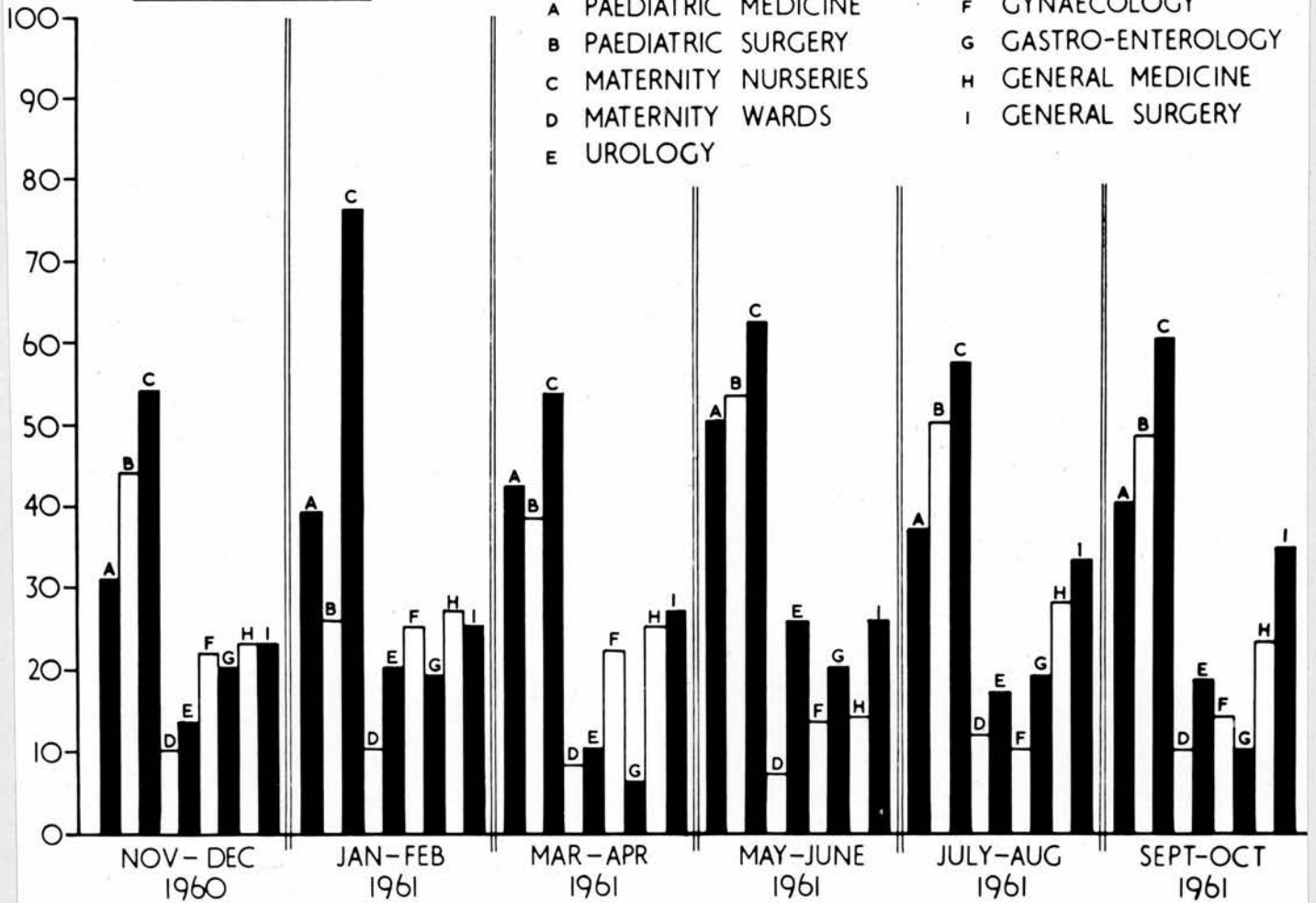


FIGURE 19. PERCENTAGES OF HOSPITAL-ACQUIRED INFECTIONS DUE TO STAPH.AUREUS
IN THE VARIOUS DEPARTMENTS .

(the alternation of black and white columns has no significance)

staphylococcal infections in the Department of General Surgery were comparatively high, particularly towards the end of the period of investigation (Figure 19 and Appendix tables II and III), and yet the levels of staphylococcal contamination of the environment were relatively low throughout the year.

Table IX classifies the principal pathogenic bacteria that were isolated from hospital-acquired infections, and also indicates the lesions from which the organisms were obtained. The footnotes to the Table explain some of the discrepancies which have arisen between the total number of isolates in each group of infection and the total number of cases in each group where these are greater. Nevertheless the over-all total number of isolates is considerably larger than the total number of infected cases, since in 110 cases mixed cultures were obtained in which two or more species of bacteria seemed to be of equivalent aetiological significance.

The distribution of the various kinds of infected lesions that occurred in the different departments during the year is given in tables X - XII. The annual incidences of infection (tables X and XI) are represented as histograms in figures 20 and 21. Only those clinical infections in which the diagnosis was supported bacteriologically are recorded. However, with the exception of respiratory tract infections, described below, there were very few occasions on which a clinical diagnosis of infection arising in hospital was not confirmed by the isolation of pathogenic bacteria from the lesions.

TABLE IX. DISTRIBUTION AND SOURCE OF THE PREDOMINANT BACTERIA, OTHER THAN STAPH. AUREUS, ISOLATED FROM LESIONS

ORGANISM	TOTAL NO. OF STRAINS ISOLATED	NO. OF STRAINS ISOLATED FROM			
		URINARY INFECTIONS	RESPIRATORY INFECTIONS	HOSPITAL WOUNDS	MISCELLANEOUS INFECTIONS
<u>Esch. coli</u> and 'coliforms'	481	354	24	37	66
<u>Proteus</u> spp.....	175	113	5	20	37
<u>Pg. pyocyanea.</u>	74	39	3	22	10
Non-haemolytic streptococci....	231	134	1	33	63
<u>Pneumococcus</u> &/or <u>Haemophilus influenzae.</u>	61	-	49	-	12
Totals	1022	640	82 [†]	112 [†]	188 ^x
Number of cases of infection in each category ..	877 (total)	472	83 [†]	104 [†]	218 ^x

[†] Discrepancy due to one case of Strep. pyogenes infection.

^x Discrepancy due to infection with Candida albicans (7 infants), Strep. pyogenes (9), Sh. sonnei (6) and gonococci (2 cases of ophthalmia neonatorum). A further 8 cases of 'sticky eye' yielded pure cultures of Strep. viridans.

TABLE X. DISTRIBUTION OF STAPHYLOCOCCAL HOSPITAL INFECTIONS

DEPARTMENT	NO. (AND INCIDENCE) [‡] OF STAPHYLOCOCCAL INFECTIONS OF			
	URINARY TRACT	RESPIRATORY TRACT ⁺	HOSPITAL WOUNDS	OTHER SITES [†]
Paediatric Medicine	1(0.2)	6(1.2)	1(5.5)	28(5.6)
Paediatric Surgery	2(0.3)	-	35(6.2) ^x	28(5.0)
Maternity Nurseries	1(0.1)	-	3(30.0)	92(6.5)
Maternity Wards	9(0.5)	-	-	11(0.6)
Urology	17(3.4)	1(0.2)	11(10.0)	4(0.8)
Gynaecology	3(0.4)	1(0.1)	7(4.5)	9(1.2)
Gastro-enterology	1(0.3)	3(0.8)	10(2.5)	2(0.5)
General Medicine	4(0.7)	13(2.2)	2(22.2)	13(2.2)
General Surgery	1(0.1)	1(0.1)	18(1.9)	16(1.7)
TOTALS	39(0.5)	25(0.3)	87(4.0)	203(2.7)

‡ Incidences per 100 patients given in parentheses.

† See Table XII ("Miscellaneous Infections")

+ Excluding infections of the nose, throat, ear or mouth (classified under "Other Sites")

x Including 3 cases of burns that became infected.

TABLE XI. DISTRIBUTION OF NON-STAPHYLOCOCCAL HOSPITAL INFECTIONS

DEPARTMENT	NO. (AND INCIDENCE) [≠] OF INFECTIONS OF			
	URINARY TRACT	RESPIRATORY TRACT ⁺	HOSPITAL WOUNDS	OTHER SITES [†]
Paediatric Medicine	17(3.4)	7(1.4)	3(16.6)	32(6.0)
Paediatric Surgery	31(5.5)	-	29(5.1) ^x	26(4.7)
Maternity Nursery	4(0.3)	-	1(10.0)	53(3.6)
Maternity Wards	98(5.6)	5(0.2)	-	62(3.3)
Urology	140(28.5)	3(0.6)	4(3.6)	4(0.8)
Gynaecology	70(9.6)	3(0.4)	5(3.2)	18(2.4)
Gastro-enterology	39(9.7)	18(4.5)	26(6.5)	5(1.2)
General Medicine	52(8.8)	28(4.7)	-	8(1.3)
General Surgery	22(2.4)	19(2.0)	36(3.9)	10(1.0)
TOTALS	472(6.4)	83(1.1)	104(4.8)	218(3.0)

≠ Incidences per 100 patients in parentheses.

† See Table XII. ("Miscellaneous Infections")

+ Excluding infections of nose, throat, ear or mouth.

x Including 2 cases of burns that became infected.

TABLE XII. DISTRIBUTION AND CLASSIFICATION OF 'MISCELLANEOUS' INFECTIONS

DEPARTMENT	NON-STAPHYLOCOCCAL INFECTIONS					STAPHYLOCOCCAL INFECTIONS				
	skin or eye	ear	Mouth or throat	others	Total no.	skin or eye	ear	throat	others	Total no.
Paediatric Medicine	11	5	6	10+	32	22	3	1	2	28
Paediatric Surgery	12	1	1	12*	26	15	2	-	11x	28
Maternity Nurseries	48	-	1	4	53	91	1	-	-	92
Maternity Wards	1	-	-	61'	62	2	-	-	9'	11
Urology	2	-	-	2	4	4	-	-	-	4
Gynaecology	1	-	-	17'	18	4	-	-	5'	9
Gastro- enterology	4	-	-	1	5	1	-	-	1	2
General Medicine	4	2	2	-	8	13	-	-	-	13
General Surgery	6	-	-	4	10	14	-	1	1	16
TOTALS	89	8	10	111	218	164	6	2	31	203

+ including 6 cases of dysentery (Shigella sonnei (isolated)).

* including 8 cases of infected ileostomy or ileal bladder.

x including 3 cases of post-operative meningitis and 4 cases of infected ileostomy.

' Cultures from high vaginal swabs - with the exception of 2 perineal abscesses (coliform bacilli) in the maternity wards.

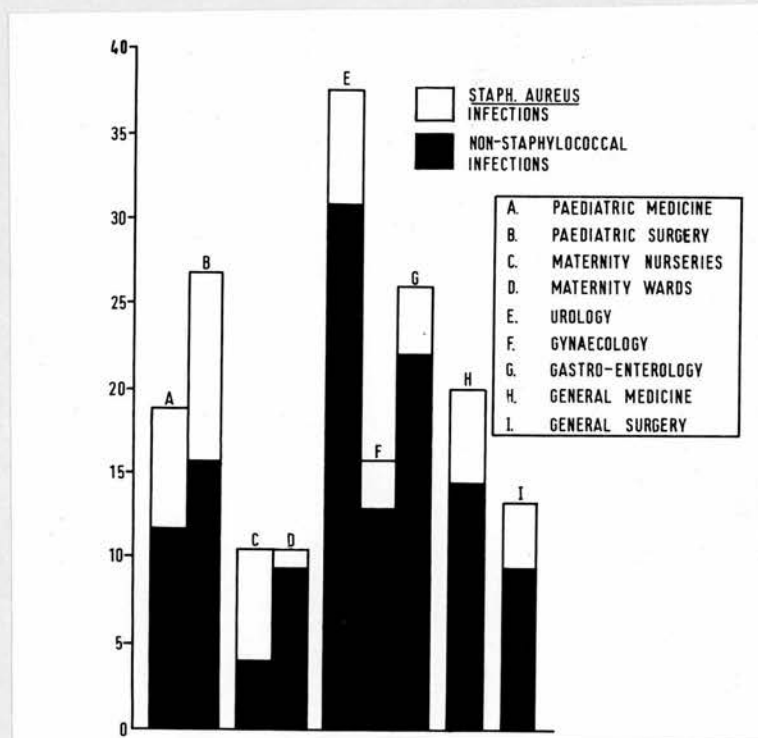


FIGURE 20. THE INCIDENCES OF HOSPITAL-ACQUIRED INFECTIONS (PER 100 PATIENTS) IN THE VARIOUS DEPARTMENTS.

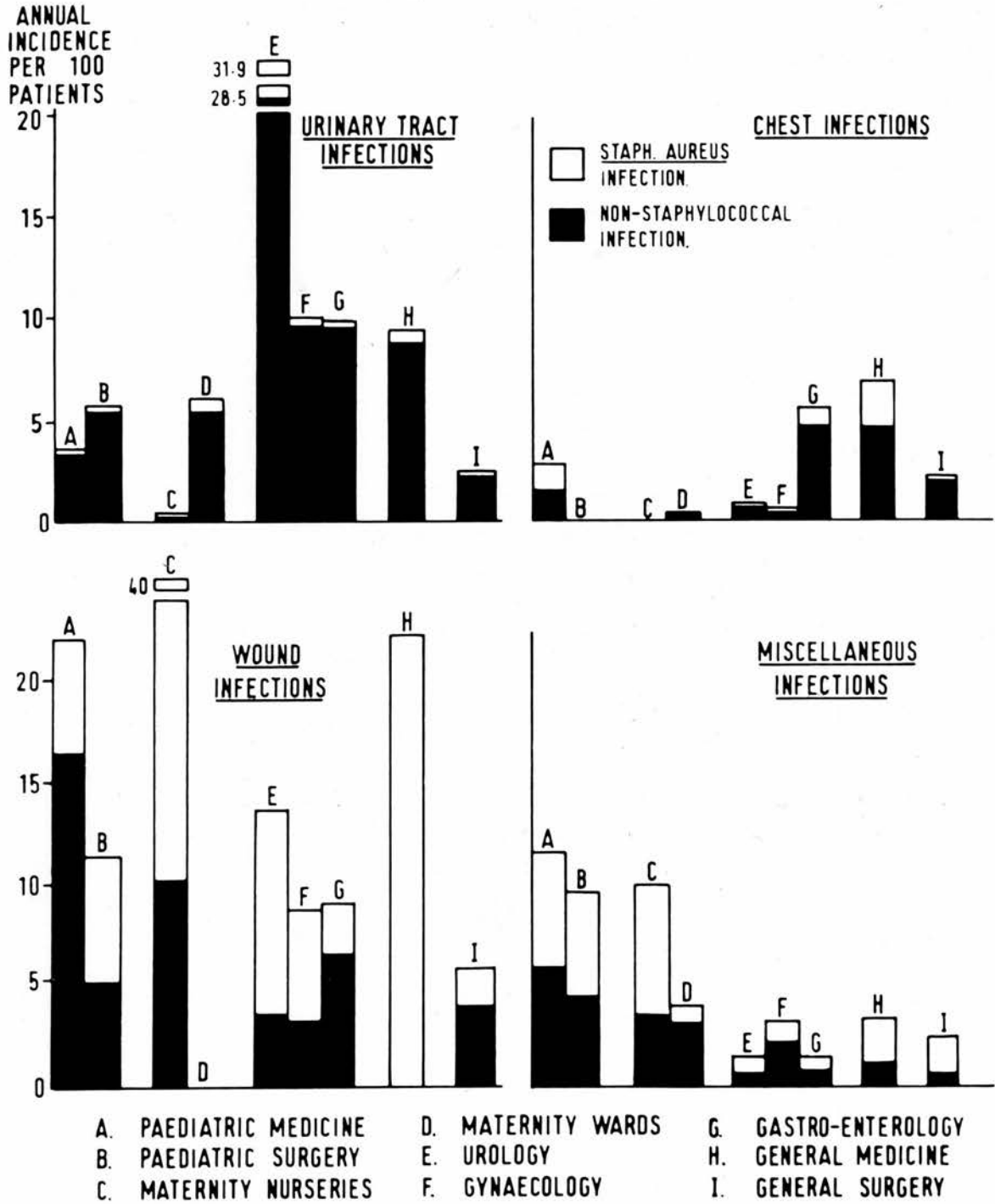


FIGURE 21. ANNUAL INCIDENCES OF THE DIFFERENT TYPES OF HOSPITAL-ACQUIRED INFECTION IN THE VARIOUS DEPARTMENTS (PER 100 PATIENTS AT RISK).

Urinary Tract Infections. The biggest single group (41 per cent) of infections involved the urinary tract; and although a relatively large proportion of these developed in the Urology Department, 355 out of the total of 511 cases (69 per cent) arose in other departments. In the Urology Department, 96 of the infections occurred in males and 61 in females. This distribution corresponded approximately to the proportion of male to female admissions. However, in both the gastro-enterology and general medical departments, where the incidence of urinary tract infection was also high, infection was commoner in female patients than in males. Thus infection developed in 29 females and 11 males in the Gastro-enterology Department, and in 46 females and 10 males in the General Medical Department.

It has already been shown (Table IX) that of the 640 bacterial strains which were believed to have played an aetiological role in the 472 cases of non-staphylococcal urinary tract infection, 506 were Gram-negative bacilli and 134 were non-haemolytic streptococci. Proteus spp.^x were responsible for 9 infections in the General Medical Department, 25 in the Urology Department, 11 in the Gynaecology Department and 14 in the maternity wards. The organism was an uncommon cause of infection in other departments. All the strains that were identified fully proved to be Pr. mirabilis. Staph. aureus constituted only 5 per cent of all urinary strains. The 39 infections in which Ps. pyocyanea predominated were all found in patients who were receiving anti-bacterial drugs, or following catheterization or urological surgery.

x As sole pathogen.

In the Urology Department the predominant bacteria isolated from non-staphylococcal urinary tract infections were: 100 strains of Esch. coli, 40 strains of Proteus spp., 16 strains of Ps. pyocyanea and 10 strains of paracolon bacilli; respectively, 23, 13, 11 and 1 of the strains were streptomycin-resistant. The incidence of sulphonamide-resistance was higher in each case. Strep. faecalis was involved in 39 of the cases. The urinary infection rate was particularly high in men following prostatectomy (42 out of 48 cases) and in the smaller group of women with indwelling catheters (15 out of 18 cases). Bladder drainage in both these groups was of the continuous 'open' variety.

Of the 73 patients in the Gynaecology Department who developed urinary infections, 48 were undergoing continuous 'open' bladder drainage - an incidence of 69 per cent in this particular group of patients, most of whom were being treated for uterine prolapse. The predominant bacteria in the non-staphylococcal infections were Esch. coli (53 strains, 7 of which were streptomycin-resistant and 18 sulphonamide-resistant), Proteus spp. (13 strains - 3 resistant to streptomycin, 8 to sulphonamides). Paracolon bacilli and Ps. pyocyanea were each isolated on only one occasion. Strep. faecalis was involved in 18 of the cases.

Although cross-infection is believed to have been responsible for many of the urinary infections that developed in the hospital, particularly in the Urology Department, proof was lacking except in those cases which were due to Staph. aureus and

Ps. pyocyanea (p.167) - accounting for only 11 per cent in all.

'Miscellaneous' Infections. The next most common group of infections are those classified as 'miscellaneous' which are considered further in Table XII. Infections of the skin or eyes accounted for 253 of the 421 miscellaneous cases (60 per cent.), and 139 of these infections arose in the maternity nurseries. Indeed, superficial lesions - more than two-thirds of which were due to Staph. aureus - constituted 91 per cent of clinical infections in the nurseries.

In contrast to the skin infections, almost all of which were due to Staph. aureus, 43 of the 91 cases of sticky eye which were of bacterial origin yielded organisms other than Staph. aureus. The isolates were coagulase-negative staphylococci (27 cases), non-haemolytic streptococci - including Strep. viridans (6 cases), coliform bacilli (6 cases), gonococci (2 cases), and single cases of infection with Haemophilus and pneumococci. The coagulase-negative staphylococci which have not been accepted as pathogens elsewhere in this work, were seen to be abundant in direct films of pus, and grew in profuse culture.

While cross-infection was implicated in almost all of the staphylococcal lesions in this category, the same cannot be said of the other common type of 'miscellaneous' infection - minor local uterine sepsis. There were 68 cases of this condition in the maternity wards following delivery, and 22 cases occurred in the Gynaecology Department post-operatively. The organism most commonly involved was Esch. coli often associated with

enterococci. 'Atypical' coliform bacilli predominated in 9 of the infections. Except in 4 of the 14 cases due to Staph. aureus, the infections were regarded as being probably of endogenous origin.

Apart from minor uterine sepsis, the 'miscellaneous' category in the maternity wards consisted of three cases of skin infection. Two of these were due to Staph. aureus, other than the endemic type, and the third was a coliform infection which developed in an eczematous area.

Wound Infections. Surgical wound sepsis accounted for 191 (15 per cent) of the infections arising in hospital, and 54 cases occurred in the General Surgical Department. This represents a wound sepsis rate in that department of 6 per cent; with Staph. aureus accounting for only one-third of the infections. Diverse phage types were isolated from the 18 staphylococcal wound infections which developed in the department. However, the Paediatric Surgical Department with 64 wound infections had an incidence that was almost twice as high as in the General Surgical Department (Figure 21). Furthermore, in 33 of the paediatric cases Staph. aureus of the endemic group III type predominated. The wound sepsis rate was also relatively high (9 per cent) in the Gastro-enterology Department, but, as in the case of the General Surgical Department, two-thirds of the lesions were of non-staphylococcal origin, and the 10 lesions that were due to Staph. aureus yielded several different phage types of which only 2 were prevalent 'hospital' strains.

Although relatively few patients were 'at risk' in departments other than General Surgery, Paediatric Surgery and Gastro-enterology, the true incidence of wound sepsis was high in the remaining departments. In the Urology Department 15 out of 110 wounds (including suprapubic drainage incisions) became infected; from five of these there was isolated a Staph. aureus of type 80/81, resistant to penicillin, streptomycin and tetracycline. This organism was prevalent in the unit for two months. In the Gynaecology Department 12 out of 156 operation wounds became infected (3 with the endemic, group III staphylococcus). On account of minor procedures there were 10 and 18 patients at risk in the maternity nurseries and Paediatric Medical Department, respectively. In the General Medical Department, 9 patients were nursed after either thoracotomy (4) or mitral valvulotomy (5), and the wounds of two became infected.

Caesarian section was performed on 82 patients in the Maternity Department, but although 9 of the patients developed local uterine sepsis with pyrexia and offensive lochia, wound infection was present in none of the cases. Indeed, the entire wound ruptured in two patients and yet even in these cases there was no clinical or bacteriological evidence of infection. Two patients in the puerperium developed perineal abscesses following spontaneous deliveries in which laceration of the perineum had occurred. These cases are, however, included in the group of miscellaneous infections (Table XII).

Chest Infections. Infections of the lower respiratory tract - referred to as 'chest infections' in Figure 21 - were responsible for 108 (9 per cent) of the bacteriologically-confirmed cases of hospital infection. In a further 48 sporadic cases, a firm clinical diagnosis of acute infection of the lower respiratory tract was not confirmed bacteriologically. The clinical verdict in these cases was expressed in terms such as 'possible viral aetiology'. Virological studies were carried out in only ten cases, but no viruses were isolated using eggs and tissue cultures (Hela cells and Monkey kidney cells), and serological tests were negative for the psittacosis, adenovirus and influenza groups. As shown in Table IX, almost half of the bacteriologically-confirmed infections at this site were apparently due to pneumococci or Haemophilus influenza (or a combination of both). It was, however, interesting to find that Staph. aureus predominated in 23 per cent of cases, and Gram-negative bacilli in 30 per cent of cases.

The highest incidence of chest infections in hospital was found in the General Medical Department (Figure 21), and these infections developed almost exclusively in patients suffering from serious disease of the cardio-vascular or respiratory systems. Three of the 41 cases in the department formed part of an outbreak of infection described below. Hospital strains of Staph. aureus were isolated in 4 of the remaining 10 staphylococcal chest infections. The next highest incidence of hospital infection of the respiratory tract was in the Gastro-enterology Department where post-operative bronchopneumonia

accounted for 15 of the 21 cases. Strains of Staph. aureus previously identified in the wards were isolated in only 3 of these patients. The only other unit in which lower respiratory tract infection was shown to be due to cross-infection was in the Paediatric Medical Department. Here, 6 out of a total of 13 bacteriologically-confirmed cases yielded the endemic group III strain of Staph. aureus.

Outbreaks of Hospital Infection.

During the period of this investigation cross-infection was, as already noted, responsible for a considerable incidence of staphylococcal sepsis in the paediatric departments and maternity nurseries, and was believed to be involved in many of the infections encountered in the Urology Department; however, epidemic as opposed to endemic infection was surprisingly uncommon, and there were indeed only two noteworthy outbreaks during the year.

The first of these occurred in the General Medical Department at the beginning of the study, and it followed the admission to the main male ward of a patient suffering from an acute exacerbation of chronic bronchitis. At the time of admission his sputum yielded a profuse growth of Staph. aureus, phage type 52/52A/80/81 and resistant to penicillin, streptomycin and tetracycline. During the next three weeks, the same organism was isolated from the lesions of seven male patients and two members of staff. The clinical infections

which developed amongst the patients consisted of four cases of furunculosis and three chest infections. Two of the chest infections took the form of moderately severe bronchitis with profuse purulent sputum. Erythromycin was effective in these cases. In the third case, however, staphylococcal broncho-pneumonia developed in a man suffering from bronchogenic carcinoma, and he died three days after the onset of the infection. A doctor working in the unit suffered from both furunculosis and a stye, and a nurse developed furunculosis too.

The organism was isolated from many air samples and surfaces in the male ward during the four months following the admission of the first infected patient; it was also occasionally found in small numbers in the air of the corridor and the main female ward where there were no clinical infections due to this organism. Six of the 13 male patients and four members of staff were nasal carriers of the organism at the end of the three-week period, whereas only two nasal carriers of this strain had been detected two weeks earlier, when the first case of hospital infection developed. These two carriers were the index case and the first patient to develop furunculosis. Although the organism was still present in the environment of the unit and in the noses of members of staff for at least four months after the outbreak, no further cases of clinical infection developed after the first month. Towards the end of February a strain of Staph. aureus was isolated from the environment which was of the same phage type as the original organism but was resistant to erythromycin as well as penicillin,

streptomycin and tetracycline. Fortunately there were no cases of clinical infection due to this organism.

The second outbreak was one of dysentery in the paediatric departments. The index case was not discovered, but within a period of two weeks eight children (six in the medical unit and two in the adjacent surgical unit) who had been admitted to hospital suffering from other conditions each developed dysentery after being in the ward for more than three days. Shigella sonnei was isolated from the faeces of five of the children in the medical ward and one child in the surgical ward. Unsuccessful attempts were made to isolate the organism from the ward environment using MacConkey's agar as a selective medium in air sampling and surface-swabbing procedures.

Deaths during the Investigation.

Table VI (p.127.) presents the number of deaths that occurred in the various departments during the period of this investigation. While infection played no part in the 34 deaths occurring in the maternity nurseries and wards, it was a factor in a number of deaths that took place in the other departments.

In the Paediatric Medical Department infection played an important role in 7 of the 12 deaths. Two of these were due to overwhelming meningococcal infection, and occurred within 24 hours of admission to hospital. Another child had been treated with chloramphenicol for a chest infection outside hospital and he developed aplastic anaemia which proved fatal.

Two further deaths were due to bronchopneumonia present on admission to hospital; the chest infection was, in one of the children, superimposed on congenital heart disease. Hospital cross-infection was a factor in the remaining two deaths. In one of these cases a child with hydrocephalus developed a fatal staphylococcal pneumonia in the ward. The causative organism was the endemic group III staphylococcus. The other death occurred in a 5 month-old infant who was already suffering from bilateral hydronephrosis but who developed a severe terminal gastro-enteritis in the ward. Esch. coli serotype 0.26 was isolated from his stools.

Infection was also a factor in 5 out of the 11 deaths in the Paediatric Surgical Department. A child who was being treated for a meningocele died from purulent meningitis. Her cerebro-spinal fluid yielded a pure culture of Ps. pyocyanea of the prevalent type (p.167). Another child died six days after an operation to relieve biliary obstruction. A severe post-operative wound infection due to the endemic group III Staph. aureus was thought to have been a contributory factor in this death. However, post-mortem examination was not carried out. In another case an infant was admitted to the ward with intestinal obstruction. Following catheterization he developed, pre-operatively, a coliform infection of the urinary tract, and post-operatively his ileostomy wound became heavily infected with the 'hospital' staphylococcus. An infant under investigation for urinary tract abnormalities developed a fatal coliform infection of the urinary tract one

month after admission to the department. In the fifth case death was due to a pelvic abscess with generalised peritonitis in an eleven year old boy who had a ruptured appendix. The diagnosis had been missed outside hospital and the child died two days after admission to the Department.

One of the seven deaths that occurred in the Gynaecology Department was due to peritonitis following an operation to resect a carcinoma which was invading the rectum from the uterus.

In the General Medical Department, infection was the leading factor in 5 out of the 40 deaths. One of these was, as already noted, due to staphylococcal pneumonia acquired by cross-infection. The other four cases were due to infections that were present on admission. One was a case of sub-acute bacterial endocarditis in a man aged 60. Another patient admitted with severe infectious hepatitis died from hepatic failure. Two other patients died as a result of broncho-pneumonia - in one case superimposed on mitral stenosis.

Post-operative wound infection was a major factor in 3 of the 29 deaths that occurred in the General Surgical Department, following extensive abdominal surgery in each case. Two of the infections were due to Gram-negative bacilli and might have been of endogenous origin. The third case was a staphylococcal infection from which was isolated a strain of Staph. aureus that had not previously been found in the Unit. Cross-infection was, however, responsible for a case of severe wound sepsis that developed following biliary tract

surgery in the Gastro-enterology Department. The patient who was already debilitated by obstructive jaundice developed a post-operative wound infection due to the ubiquitous group III staphylococcus. This did not respond to antibiotic treatment, and two days before his death the patient's wound became superinfected with Ps. pyocyanea. The terminal condition was clinically diagnosed as 'bacteraemic shock', though a blood culture (taken during chloramphenicol therapy) proved to be negative.

In the Urology Department, post-operative urinary tract infection appeared to play a significant role in 10 of the 22 deaths. Gram-negative bacilli were isolated from the urine in each case, but, once again, although clinical diagnoses of terminal 'bacteraemic shock' or 'septic shock' were made in 6 of the cases, blood cultures were negative.

SUBCLINICAL INFECTIONS

Carriers of Pathogenic Bacteria

While no attempt was made to gather regular and detailed information on healthy carriers, the results of the intermittent examination of the staff are presented in Table XIII. In only seven cases were the strains of Staph. aureus carried in the nose the same as prevalent ward strains. The endemic group III strain was carried by five members of staff, two of whom worked in the maternity unit (one being a student midwife who helped in the nursery). The other two carriers of "hospital" staphylococci worked in the general medical unit and yielded group I strains that were indistinguishable from the organism causing an outbreak of infection in the same unit (p.146.).

Contamination of hands with pathogenic bacteria had a uniformly higher incidence than nasal carriage (Table XIII). In contrast to nasal carriage, the strains of Staph. aureus isolated were usually those present in the environment and in patients' lesions. In addition to Staph. aureus, coliform bacilli and Proteus spp. were often cultivated from the hand impressions; approximately one-third of the positive results incorporated in Table XIII represent mixed cultures. Repeat examinations of nurses' hands almost always showed a complete change in the bacterial flora indicating that transient contamination rather than persistent skin carriage was responsible for the positive hand impressions.

TABLE XIII. INCIDENCE OF HEALTHY CARRIERS AMONGST
MEMBERS OF STAFF (CUMULATIVE RESULTS)

DEPARTMENT	NO. EXAMINED	NASAL CARRIERS [*]		POSITIVE HAND IMPRESSIONS	
		No. ⁺	%	No. ⁺	%
Paediatric Medicine	39	21	54	28	72
Paediatric Surgery	26	12	46	20	77
Maternity Nurseries	32	9	28	20	63
Maternity Wards	50	23	46	30	60
Urology	23	8	35	17	74
Gynaecology	23	9	39	11	48
Gastro-enterology	29	10	34	23	79
General Medicine	22	14	63	17	77
General Surgery	20	5	25	8	40
Main Theatres	8	2	(25)	5	(63)
TOTALS	272	113	42	179	66

* of Staph. aureus

+ Yielding significant cultures on two or more occasions
(separated by more than one week).

Occasional surveys of nasal carriage of Staph. aureus amongst patients showed fluctuating incidences of from 13 per cent to 66 per cent (the latter rate was observed in the maternity nurseries). More systematic nasal swabbing of newborn infants was carried out, and it was found that of 150 babies, 136 (91 per cent) had become carriers of Staph. aureus before discharge from hospital. However, colonization of the abdominal skin preceded nasal carriage, by one day or more in 82 of the babies.

Bacterial Contamination of 'Clean' Wounds

Healthy surgical wounds were swabbed on a number of occasions throughout the hospital, and the procedure was restricted to wounds that were not more than four days old. The results of these examinations and the numbers of subsequent clinical infections are presented in Table XIV. It may be noted that the majority of the cultures obtained consisted of relatively scanty growths.

Whereas 19 of the 44 strains of Staph. aureus isolated from wounds in the Paediatric Surgical Department were of the 'hospital' type (group III, erythromycin-resistant), only 3 wounds in the Gynaecology Department, and none in the other departments, yielded this type. The remaining strains of Staph. aureus were of numerous phage types, and 17 of the strains from the General Surgical Department were sensitive to penicillin. Penicillin-sensitivity was also found in 14 strains from the Gastro-enterology Department, in 12 strains from the Urology Department, and in 7 strains from the Gynaecology Department.

Apart from Staph. aureus, the commonest potential pathogens were coliform bacilli of which there were 52 isolates, 38 being Esch. coli. However, Ps. pyocyanea was isolated from five wounds in the Urology Department and from two in the Gastro-enterology Department. Proteus spp. occurred in 9 wounds. The remaining isolations were of enterococci, and this organism occurred in several mixed cultures.

As shown in Table XIV, relatively fewer wounds which were contaminated with Staph. aureus progressed to clinical infection than did wounds contaminated with Gram-negative bacilli and enterococci.

TABLE XIV. CONTAMINATION OF 'CLEAN' WOUNDS BY PATHOGENIC BACTERIA

DEPARTMENT	NO. OF WOUNDS TESTED*	NO. YIELDING CULTURES OF	
		<u>Staph. Aureus</u>	Other Potential Pathogens ¹
Paediatric Surgery	83	44 (6)	19 (4)
Urology	44	20 (3)	15 (0)
Gynaecology	32	17 (2)	7 (1)
Gastro-enterology	90	30 (2)	18 (5)
General Surgery	126	26 (1)	30 (3)
TOTALS	375	137 (14)	89 (13)

* Swabs were taken on 11 occasions during the year (p.98.).

¹ Aerobes only.

Figures in parentheses represent the no. of wounds in each category which later became clinically infected.

IN VITRO PROPERTIES OF PATHOGENIC BACTERIA ISOLATED IN HOSPITAL

Antibiotic Sensitivities.

Table XV presents the results of testing the main groups of pathogenic bacteria against sulphonamides and the principal antibiotics. More than half of all the strains possessed resistance to two or more of these drugs, and multiple resistance was particularly common amongst Proteus spp., Ps. pyocyanea and non-haemolytic streptococci.

The antibiotic sensitivities of strains of Staph. aureus isolated from lesions are given in greater detail in Table XVI and can be compared with the sensitivities of strains isolated from the environment (Table XVII). A comparison of the two sets of results is more readily made by reference to Figure 22 which consists of paired histograms representing the incidences of antibiotic resistance. It can be seen that there is, in general, a close correlation between the sensitivities of both groups of Staph. aureus, although in the paediatric departments and the maternity wards the environmental strains were more frequently resistant to penicillin (and streptomycin, except in the paediatric medical unit) than were the strains isolated from lesions. More than 80 per cent of all strains were penicillin-resistant, over 50 per cent were streptomycin-resistant and more than 30 per cent were tetracycline-resistant. Erythromycin-resistance was present in 28 per cent of all strains isolated from lesions

TABLE XV. DRUG SENSITIVITIES OF THE MAIN PATHOGENIC BACTERIA ISOLATED FROM CLINICAL INFECTIONS.

ORGANISM	INFECTION	NO. OF STRAINS	PERCENTAGE OF STRAINS SENSITIVE TO [⊗]					
			P.	SU.	ST.	T.	C.	E.
<u>Esch.coli</u> and 'coliforms'	Urinary	35 ⁺	-	46	84 ⁺	8 ⁺	85	-
	Other sites	127	-	72	58	11	97	-
<u>Proteus</u> spp.	Urinary	113	37 ⁺	45	79 ⁺	0 ⁺	70	-
	Other sites	62	5	37	53	2	84	-
<u>Ps.pyocvanea</u>	Urinary	39	0 ⁺	34	18 ⁺	0 ⁺	6	-
	Other sites	35	0	17	3	0	0	-
Non-haemolytic streptococci	Urinary	134	78 ⁺	1	34 ⁺	37 ⁺	61	-
	Other sites	97	70	4	9	50	75	-
<u>Staph.aureus</u> '	All sites	35 ⁺	23	-	39	50	99	73

⊗ P.= penicillin; SU.= sulphonamide; ST.= streptomycin; T.= tetracycline; C.= chloramphenicol; E.= erythromycin.

+ For urinary strains the criteria of sensitivity were growth inhibition by

Penicillin: <50 units per ml.

Streptomycin:<25 micrograms per ml.

Tetracycline:<12.5 micrograms per ml.

' Further details are given in Table XVI.

TABLE XVI. ANTIBIOTIC SENSITIVITIES OF STAPH. AUREUS ISOLATED FROM LESIONS.

DEPARTMENT	NO. AND PERCENTAGE* OF STRAINS SENSITIVE TO ^x					TOTAL NO. OF STRAINS
	P.	ST.	T.	E.	C.	
Paediatric Medicine	11(30)	17(47)	20(56)	30(83)	36(100)	36
Paediatric Surgery	16(25)	35(54)	37(57)	47(72)	64(98)	65
Maternity Nurseries	15(16)	29(31)	30(32)	37(39)	96(100)	96
Maternity Wards	10(50)	13(65)	16(80)	17(85)	20(100)	20
Urology	13(39)	15(45)	17(51)	33(100)	30(90)	33
Gynaecology	4(20)	9(45)	7(35)	12(60)	19(95)	20
Gastro-enterology	4(25)	8(50)	8(50)	16(100)	16(100)	16
General Medicine	6(19)	11(34)	16(50)	30(94)	32(100)	32
General Surgery	16(44)	23(63)	28(78)	34(94)	36(100)	36
TOTALS	95(27) ⁺	160(45)	177(50)	256(72)	349(98)	354

* Percentages in parentheses.

x See footnote to Table XV.

+ No strains were found to be resistant to methicillin.

TABLE XVII. ANTIBIOTIC SENSITIVITIES OF STAPH. AUREUS ISOLATED FROM THE HOSPITAL ENVIRONMENT.

DEPARTMENT	NO. AND PERCENTAGE* OF STRAINS SENSITIVE TO ^x					TOTAL NO. OF STRAINS
	P.	ST.	T.	E.	C.	
Paediatric Medicine	8(2)	171(52)	259(80)	302(93)	311(96)	323
Paediatric Surgery	11(4)	103(40)	174(68)	212(82)	251(97)	260
Maternity Nurseries	106(17)	220(35)	280(45)	336(54)	618(99)	625
Maternity Wards	27(12)	227(28)	265(38)	128(56)	227(100)	227
Urology	90(27)	149(44)	205(60)	323(94)	332(97)	343
Gynaecology	73(27)	135(50)	174(64)	235(87)	273(100)	273
Gastro-enterology	66(27)	127(52)	176(71)	244(98)	248(99)	250
General Medicine	73(23)	160(47)	182(53)	312(82)	367(97)	379
General Surgery	80(24)	187(57)	231(70)	312(94)	329(99)	332
TOTALS	534(18) ⁺	1479(49)	1946(65)	2404(80)	2956(98)	3012

* Percentages in parentheses.

x See footnote to Table XV.

+ No strains were found to be resistant to methicillin.

L=LESION STRAINS. E=ENVIRONMENTAL STRAINS. ■ = STRAINS RESISTANT TO CHLORAMPHENICOL.

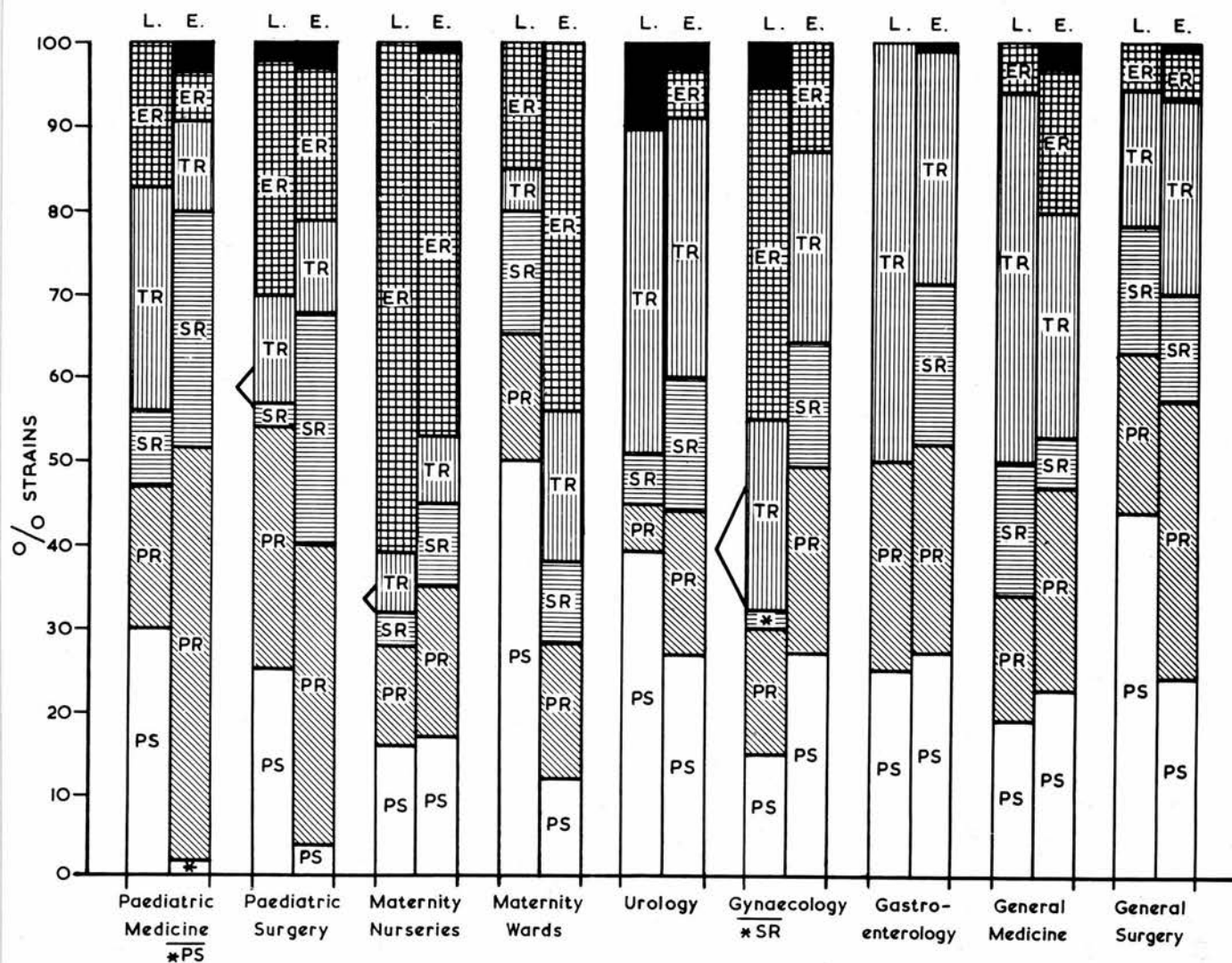


FIGURE 22. A COMPARISON BETWEEN THE ANTIBIOTIC SENSITIVITIES OF STAPH. AUREUS ISOLATED FROM LESIONS AND FROM THE ENVIRONMENT.

- 'PS' = sensitive to penicillin, streptomycin, tetracycline, erythromycin.
 'PR' = resistant to penicillin, sensitive to the remainder.
 'SR' = resistant to penicillin and streptomycin, sensitive to tetracycline and erythromycin.
 'TR' = resistant to all but erythromycin.
 'ER' = resistant to all four antibiotics.

(The converging lines inserted next to 'TR' in three of the histograms indicate the percentage of strains resistant to tetracycline but sensitive to streptomycin.)

and in 20 per cent of all environmental strains; but in the maternity nurseries the incidence was 61 per cent and 46 per cent, respectively. In the maternity wards, however, while the incidence of erythromycin-resistance was 44 per cent amongst environmental strains, it was only 15 per cent in the case of the relatively few strains isolated from lesions.

Bacteriophage Typing of Staph. Aureus.

In tables XVIII and XIX the strains of Staph. aureus isolated from lesions and from the environment, respectively, are grouped according to their bacteriophage susceptibilities. As in the case of antibiotic sensitivities, the relative frequencies of the different phage groups amongst the lesion and environmental strains from each department are presented in the form of histograms (Figure 23).

There was good correlation between the phage grouping of strains from lesions and from the environment, although, as expected, there tended to be a larger proportion of non-typable strains isolated from inanimate sources. With the exception of the General Medical Department where the predominant types were of group I (including the type 52/52A/80/81, as described on p.146.), group III strains were in the majority throughout the hospital. A substantial proportion of the group III strains gave lysis with phages 42E/47/54/75/77 and were resistant to erythromycin. They constituted a homogeneous type that was constantly present in almost all parts of the

TABLE XVIII. BACTERIOPHAGE GROUPS OF STAPH. AUREUS ISOLATED FROM LESIONS (NOVEMBER 1960 - OCTOBER 1961).

DEPARTMENT	NO. AND PERCENTAGE [≠] OF STRAINS IN BACTERIOPHAGE GROUPS					TOTAL NO. OF STRAINS
	I	II	III	III ER [†]	NT ^x	
Paediatric Medicine	11(31)	2(6)	20(55)	6(17)	3(8)	36
Paediatric Surgery	18(28)	5(9)	36(55)	18(28)	4(8)	65
Maternity Nurseries	17(18)	1(1)	71(74)	59(61)	7(7)	96
Maternity Wards	3(15)	3(15)	13(65)	3(15)	1(5)	20
Urology	11(33)	3(9)	18(55)	0(0)	1(3)	33
Gynaecology	4(20)	3(15)	11(55)	8(40)	2(10)	20
Gastro-enterology	4(25)	1(6)	11(69)	0(0)	0(0)	16
General Medicine	17(53)	2(6)	11(35)	2(6)	2(6)	32
General Surgery	14(39)	5(14)	14(39)	2(6)	3(8)	36
TOTALS	99(28)	25(7)	205(58)	98(28)	23(7)	354

≠ Percentages in parentheses.

† Erythromycin-resistant "endemic" strain.

x Non-typable with the standard set of bacteriophages.

TABLE XIX. BACTERIOPHAGE GROUPS OF STAPH. AUREUS ISOLATED FROM THE HOSPITAL ENVIRONMENT (OCTOBER 1960 - OCTOBER 1961).

DEPARTMENT	NO. AND PERCENTAGE* OF STRAINS IN BACTERIOPHAGE GROUPS					TOTAL NO. OF STRAINS TESTED
	I	II	III	III ER [†]	NT ^x	
Paediatric Medicine	77(24)	63(19)	102(32)	19(6)	81(25)	323
Paediatric Surgery	58(23)	32(12)	130(50)	48(18)	40(15)	360
Maternity Nurseries	102(16)	62(10)	437(71)	289(47)	24(3)	625
Maternity Wards	47(21)	12(5)	135(60)	99(44)	33(14)	227
Urology	100(29)	14(5)	148(43)	13(4)	81(23)	343
Gynaecology	29(11)	35(13)	154(56)	38(13)	55(20)	273
Gastro- enterology	58(23)	14(6)	98(39)	0	80(32)	250
General Medicine	185(49)	17(4)	150(39)	67(17)	27(7)	379
General Surgery	96(30)	17(5)	171(51)	20(6)	48(14)	332
TOTALS	752(25)	266(9)	1525(50)	593(20)	469(16)	3012

* Percentages in parentheses.

† Erythromycin-resistant "endemic" strain.

x Non-typable with the standard set of bacteriophages.

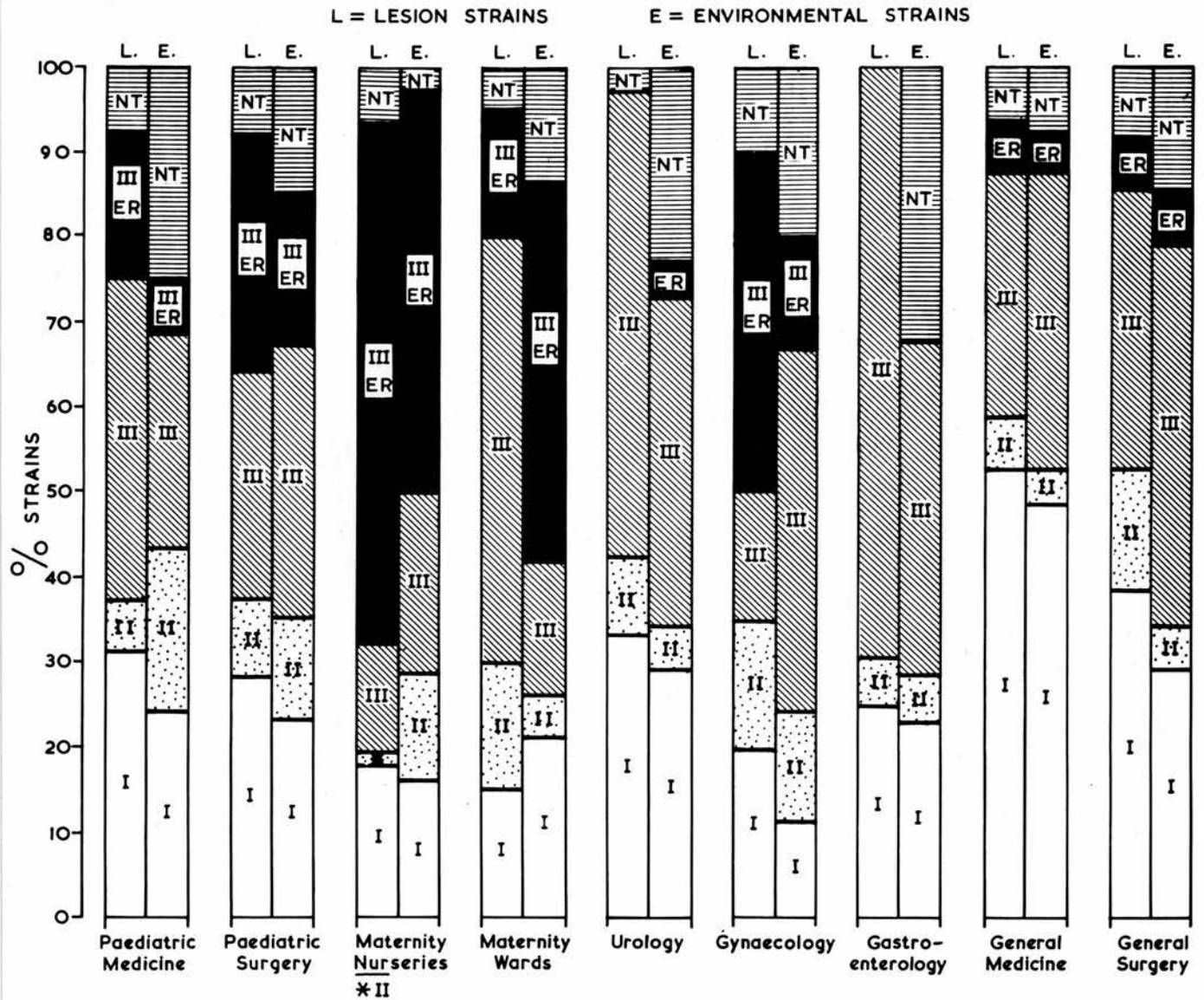


FIGURE 23. THE DISTRIBUTION OF BACTERIOPHAGE GROUPS AMONG STAPH. AUREUS ISOLATED FROM LESIONS AND FROM THE ENVIRONMENT.

NT = non-typable with the standard set of bacteriophages.

IIIER = group III strains that were resistant to erythromycin.

hospital. The Gastroenterology Department was the only unit in which this strain was not isolated from lesions or from the environment. This erythromycin-resistant group III organism was responsible for 61 per cent of the lesions occurring in the newborn and accounted for almost half of all the strains isolated from the environment of the maternity nurseries. It was prevalent too in the maternity wards and to a lesser extent in the paediatric and gynaecology departments, but remained relatively unimportant in the general medical, general surgical and urological departments.

The composite histograms in Figure 24 represent the relative frequencies with which strains of Staph. aureus of the different bacteriophage groups and antibiotic sensitivity patterns were isolated in the hospital taken as a whole. It can be seen that there is close correlation between the strains isolated from lesions and from the environment as regards the frequencies of their bacteriophage groups and sensitivity patterns. The predominance of group III strains, a large proportion of which consisted of the endemic, erythromycin-resistant type, has already been referred to in connection with individual departments. Similarly, mention has already been made of the high incidence of resistance to penicillin, streptomycin and tetracycline which was a notable feature of both the lesion and environmental strains throughout the hospital.

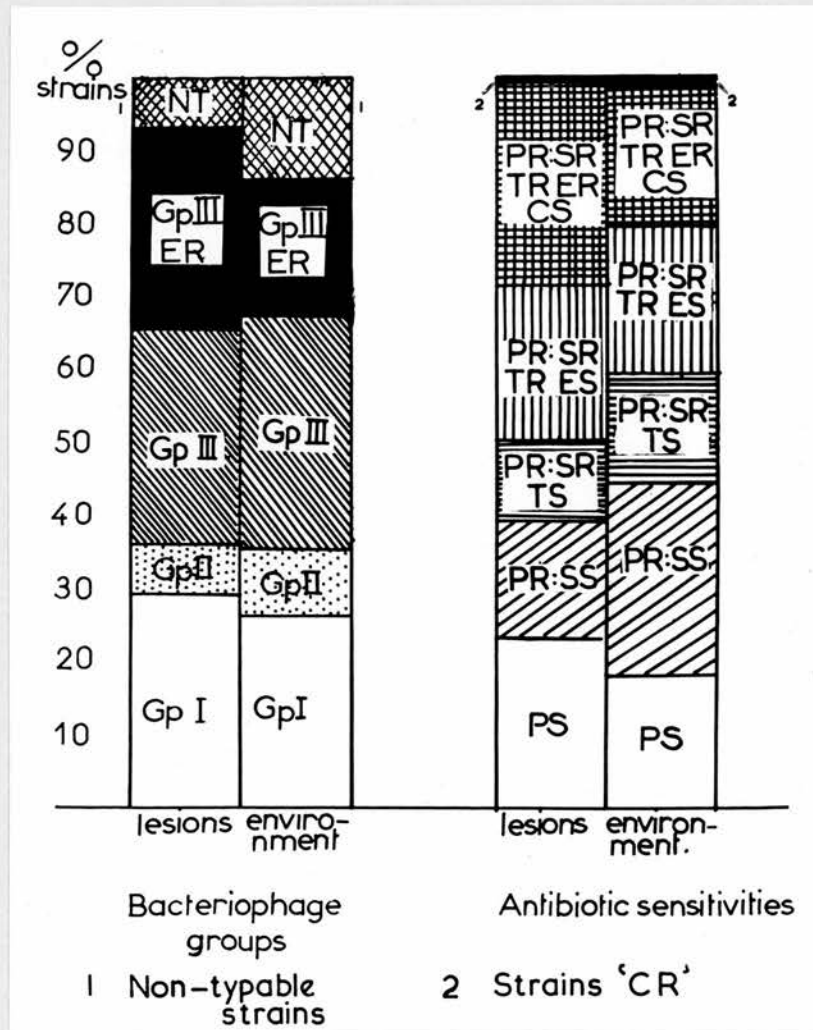


FIGURE 24. BACTERIOPHAGE GROUPS AND ANTIBIOTIC SENSITIVITY PATTERNS OF STRAINS OF STAPH.AUREUS ISOLATED IN HOSPITAL.

P = penicillin, S = streptomycin, T = tetracycline,
 E = erythromycin, C = chloramphenicol, PS = penicillin-sensitive,
 PR = penicillin-resistant.

Similar compound symbols apply to the other antibiotics.

Bacteriophage Typing of Pseudomonas Pyocyanea.

The strains of Ps. pyocyanea isolated during the year from lesions throughout the hospital were mainly of three homogeneous types (Table XX). The predominant type in the Urological Department (found in urine and wounds) was susceptible to bacteriophages Q and U employed at routine test dilutions. This strain was also isolated from two patients in the General Medical Department. In the Maternity Department strains isolated from urine, from infants' nasal swabs as well as from an ear swab and an infected meningocele were all of type T/V. Several lesions in the Paediatric Surgical, General Surgical and Gastro-enterological departments were infected with strains having a broader susceptibility to the test phages (being lysed by D/F/J/K/M/N/O/P/Q). These three surgical departments used the same operating theatre suite. Minor urological procedures, such as cystoscopy, were performed in a different theatre.

In the Maternity Wards and Nursery and in the Urological Department, Ps. pyocyanea was isolated occasionally from dust and from air samples, and was always identical with the prevalent strains found in lesions (T/V and Q/U respectively). However, no environmental reservoirs of the organism were detected in either department.

TABLE XX. DISTRIBUTION OF BACTERIOPHAGE TYPES OF PSEUDOMONAS PYOCYANEA IN THE HOSPITAL.

DEPARTMENT	LESION STRAINS TESTED		ENVIRONMENTAL STRAINS TESTED	
	No.	Prevalent type	No.	Prevalent type
Paediatric Medicine	-	-	-	-
Paediatric Surgery	21	D/F/J/K/M/N/O/P/Q	-	-
Maternity Nurseries	2*	(T/V)	9	T/V
Maternity Wards	2	(T/V)	3	T/V
Urology	18	Q/U	16	Q/U
Gynaecology	2	-	-	-
Gastro-enterology	17	D/F/J/K/M/N/O/P/Q	-	-
General Medicine	4	(Q/U)	-	-
General Surgery	10	D/F/J/K/M/N/O/P/Q	-	-

* Strains from nasal swabs of 2 infants also type T/V.

Coliform Bacilli and Proteus Species.

The infective lesions that developed after admission to hospital yielded 554 strains of coliform bacilli and 182 strains of Proteus spp. (Table XXI). The antibiotic sensitivities of some of these have been omitted from Table XV because the strains occurred in mixed infections in which other organisms appeared to predominate. In addition to the antibiotic sensitivity tests performed on all pathogens, detailed biochemical tests were carried out on representative strains of coliform bacilli and Proteus spp. Although these tests allowed the characterization of individual organisms, the results were of no epidemiological value, lacking both precision and reproducibility.

A high degree of resistance to anti-bacterial agents was commonly seen in strains from cases of hospital infection (Table XV). Conclusive evidence of cross-infection was not, however, available. To meet the need for more precise identification of strains of Proteus mirabilis (the species of all except two of the Proteus strains) Dienes' phenomenon and bacteriocine typing were employed in later studies (Part III). The two exceptional strains of Proteus were identified as Pr. vulgaris and were isolated on separate occasions from the air of the maternity wards.

TABLE XXI. ORIGINS OF 554 STRAINS OF COLIFORM BACILLI AND 182 STRAINS OF PROTEUS SPP. ISOLATED FROM HOSPITAL INFECTIONS

DEPARTMENT	COLIFORM BACILLI [‡]		PROTEUS SPECIES [†]	
	URINARY STRAINS	STRAINS FROM OTHER LESIONS	URINARY STRAINS	STRAINS FROM OTHER LESIONS
Paediatric Medicine	16(2.9)	8(1.4)	3(1.6)	5(2.7)
Paediatric Surgery	20(3.6)	25(4.5)	9(4.9)	10(5.5)
Maternity Nursery	3(0.5)	8(1.4)	2(1.1)	2(1.1)
Maternity Wards	79(14.3)	52(9.4)	17(9.4)	14(7.7)
Urology	111(20.0)	3(0.5)	43(23.7)	4(2.2)
Gynaecology	54(9.7)	18(3.3)	13(7.2)	4(2.2)
Gastro-enterology	37(6.7)	30(5.5)	10(5.5)	15(9.9)
General Medicine	34(6.1)	10(1.8)	11(6.0)	4(2.2)
General Surgery	18(3.3)	28(5.1)	7(3.8)	9(4.4)
TOTALS	372(67.1)	182(32.9)	115(63.2)	67(36.8)

[‡] Values in parentheses represent the isolates as a percentage of total coliform bacilli in lesions.

[†] Values in parentheses represent the isolates as a percentage of total Proteus spp. in lesions.

Further In Vitro Tests on Strains of Staph. aureus.

Mercuric Chloride Sensitivity. As shown in Table XXII all the group II strains examined were sensitive to mercuric chloride. Conversely, resistance to this chemical was a uniform finding amongst all group III strains that were resistant to tetracycline (or to erythromycin). Similarly all group I strains of the type 52/52A/80/81 that were resistant to penicillin, streptomycin and tetracycline were also resistant to mercuric chloride, although there were mercuric chloride sensitive strains of phage type 80/81 amongst organisms that were resistant to penicillin and streptomycin but sensitive to tetracycline. In general, as can be seen in Table XXII, an increasing incidence of mercuric chloride resistance amongst strains of groups I and III was paralleled by an increasing incidence of antibiotic resistance.

Approximately half of all strains obtained from lesions or from the environment were resistant to mercuric chloride. (Table XXIV).

Egg Yolk Turbidity. None of the coagulase-negative staphylococci tested produced opacity in egg-yolk broth, but as shown in Table XXIII the majority of strains of Staph. aureus that were tested were found to be egg yolk positive. There was, however, no correlation between the egg yolk reaction and antibiotic sensitivity pattern, and a similar proportion of strains from the environment and from lesions produced egg yolk turbidity (Table XXIV).

TABLE XXII. CORRELATION OF MERCURIC CHLORIDE SENSITIVITIES AND ANTIBIOTIC SENSITIVITIES OF STAPH. AUREUS STRAINS ISOLATED IN HOSPITAL

Phage group	Total no. of strains	Percentage mercuric chloride resistant with antibiogram*				
		PS SS TS ES CS	PR SS TS ES CS	PR SR TS ES CS	PR SR TR ES CS	PR SR TR ER CS
I	112	14	24	53	82	(100)
II	72	-	-	-	-	-
III	227	16	24	88	100	100

TABLE XXIII. CORRELATION OF EGG YOLK REACTIONS AND ANTIBIOTIC SENSITIVITIES OF STAPH. AUREUS STRAINS ISOLATED IN HOSPITAL

Phage group	Total no. of Strains	Percentage egg yolk positive with antibiogram*				
		PS SS TS ES CS	PR SS TS ES CS	PR SR TS ES ES	PR SR TR ES CS	PS SR TR ER CS
I	112	81	100	100	100	(100)
II	72	77	7	(50)	-	-
III	227	80	85	83	76	100

* See footnote to Figure 22.

TABLE XXIV. EGG-YOLK REACTIONS AND MERCURIC CHLORIDE RESISTANCE IN STAPH. AUREUS FROM LESIONS AND THE HOSPITAL ENVIRONMENT.

SOURCE OF STRAINS*	TOTAL NO.	EGG-YOLK POSITIVE		MERCURIC CHLORIDE RESISTANT	
		NO.	%	NO.	%
LESIONS	219	175	80	109	49
ENVIRONMENT	207	143	69	106	51

* These are represented in Tables XXII and XXIII except for 15 additional strains from the environment.

Neomycin Sensitivity. Disks containing 1 μ g. and 2 μ g. of neomycin were used as described by Greer and Menard (1957-8) to test the sensitivities of 24 strains of coagulase-positive staphylococci and 24 strains of coagulase-negative staphylococci which had been isolated from human and environmental sources in the hospital. The report that coagulase-negative staphylococci were consistently more sensitive to neomycin than Staph. aureus was not confirmed; the zones of inhibition in both groups overlapped completely (10-20 mm. diameter with 1 μ g. disks, and 15-26 mm. diameter with 2 μ g. disks).

Pigmentation. Following the report of Willis and Turner (1962),

200 strains of Staph. aureus isolated from hospital sources were subcultured onto 1 per cent glycerol monoacetate agar. With the exception of the endemic group III "hospital" staphylococcus, all examples of which produced "yellow" pigmentation, no correlation was found between phage type and pigmentation. Strains which were closely similar as regards phage susceptibility and antibiotic sensitivity produced widely-different pigments over the full range from cream to orange. Repeated testing of individual strains over a period of six months showed, however, that the kind of pigment produced on 1 per cent glycerol monoacetate remained constant in each case.

Survival Powers of Staph. aureus in vitro.

(a) In naturally-infected dust:

When examined by the method described on p.94 a specimen of dust from the maternity nursery gave a viable count of 8,000 Staph. aureus per ml. of washings. Twenty colonies were picked at random and subcultured for phage typing and sensitivity testing. Two types of Staph. aureus were present: 54/77/81 (penicillin-sensitive) and the 'endemic' Group III type, in the ratio of 4 to 1.

The dust was distributed into bijou bottles which were stored at room temperature under various conditions of light and humidity. The results of repeated viable counts are given in Table XXV together with the estimated proportion of the two types of organism. As shown, survival was prolonged

TABLE XXV. SURVIVAL OF TWO STRAINS OF STAPH. AUREUS IN DUST

STORAGE	LOG. OF STAPH. AUREUS COUNT PER ML. OF WASHINGS AFTER (DAYS) ¹									
	0	7	15	31	52	66	100	130	190	
Desiccator (dark)	3.9(2)	3.8(2)	3.7(4)	3.4(7)	2.6(9)	2.4(10)	2.2(10)	1.7(10)	< 1	
Normal } (dark)	3.9(2)	3.7(2)	3.6(4)	2.7(8)	2.6(7)	2.3(10)	1.3(10)	1.3(10)	-	
atmosphere } (daylight)	3.9(2)	3.7(1)	3.2(2)	2.6(6)	1.7(10)	1.5(9)	1.1(10)	1.0(10)	< 1	
High humidity (dark)*	3.9(2)	4.0(3)	3.3(2)	3.0(4)	1.0(10)	FUNGAL				
						← OVERGROWNTH →				

¹ Values in parentheses represent the no. of colonies of the endemic group III strain out of 10 colonies picked at random from plates with the lowest counts.

* Bijou bottles were loosely stoppered and kept above water in a sealed jar.

both in the desiccator and under normal atmospheric conditions. Although the penicillin-sensitive strain was not identified after 52 days' storage the endemic strain survived for more than six months. In contrast, a more rapid fall-off in viable counts was seen under very moist conditions; but an overgrowth of moulds occurred after 31 days. An antibiotic effect may therefore have contributed to the poorer bacterial survival, particularly in the case of the penicillin-sensitive strain.

(b) On artificially-contaminated surfaces:

Five different strains of Staph. aureus (Table XXVI) were cultivated overnight in nutrient broth, and, following centrifugation, each was resuspended in sterile distilled water. The aqueous suspensions were then spread over the surfaces of sterile ceramic tiles, and drying was accelerated by means of a stream of cool air from a domestic hair dryer. It was estimated that approximately 3×10^6 viable bacteria per sq. in. were deposited on each tile.

After drying, the surface of each tile was examined using the cellulose tape method described on p.93 . The tiles were then stored in metal boxes at room temperature and fresh areas were examined at weekly intervals. Two colonies of Staph. aureus were subcultured from each test plate, and their identity was confirmed by phage typing and sensitivity tests. The results of the tests are presented in Table XXVI. As shown, survival of the group II strain and of the type 80

TABLE XXVI. SURVIVAL OF FIVE STRAINS OF STAPH. AUREUS DRIED ON CERAMIC TILES

STRAIN	CULTURE* AFTER (WEEKS)															
	0	1	2	3	4	5	6	7	8	9	10	11	12	15	20	
52/52A/80/81'	+++	+++	+++	+++	++	++	+	+	+	+	-	+	+	-	-	
80(propagating)	+++	+++	+++	++	+	+	+	+	-	-	-	-	-	-	-	
3A(")	+++	+++	++	+	-	+	-	-	-	-	-	-	-	-	-	
75(")	+++	+++	++	++	+	++	+	+	+	-	+	-	-	-	-	
Group III endemic	+++	+++	+++	+++	++	++	++	++	++	+	++	+	+	+	-	

+++ = confluent growth (contact-transfer technique, p.92.)

++ = >20 colonies

+ = 1-20 colonies

- = no growth

' Epidemic strain isolated from the General Medical Department (p.146).

propagating strain could not be demonstrated after five weeks and seven weeks respectively. In contrast, the type 75 propagating strain survived for at least ten weeks, and the two 'hospital' strains could still be isolated after three months. The group I strain was not, however, recovered thereafter, but the group III endemic strain survived for at least 15 weeks.

RESULTS OF VIROLOGICAL TESTS

Culture. Using the methods described on p.104 no viral isolations were made in any of 15 cases of early 'sticky eye', or from the cervix uteri of the mothers of affected infants. Moreover, the microscopical examination of conjunctival and cervical scrapings provided no evidence of infection with agents of the trachoma-inclusion blenorrhoea group.

The conjunctival swabs from six of the affected infants yielded scanty growths of Staph. aureus (endemic group III strain); while the remaining nine cases yielded no significant bacterial cultures. However, swabs taken 24 hours after collecting the initial specimens gave moderate to heavy growths of Staph. aureus in all except three cases which remained free from pathogenic bacteria.

Serology. None of the serum specimens from mothers of either the affected or the healthy infants had an antibody titre against the psittacosis group greater than 1 in 4. Maternal antibody titres against the adenovirus group were also low - in no case exceeding 1 in 32.

Sampling of Air and Settled Dust. In an attempt to isolate viruses from the hospital air, the following procedure was developed. Calcium alginate wool (Medical Alginates Ltd.) was converted to the water soluble sodium salt as described by Richards (1955). A 300 mg. plug of the soluble wool was inserted into a glass tube (10 mm. internal diameter and 100 mm.

long) which had been constricted at the outlet to 5 mm. To prevent the wool from being sucked into the constriction, a fine, open spiral of glass was placed in the neck. The plugged tube was then sterilized in hot air at 125°C for two hours. The high efficiency of the wool as a bacterial filter was demonstrated in a maternity ward after coupling the plugged tube in series to a Casella slit sampler. Air flow through the tube was 10 litres per minute¹, compared with 28 litres per minute without the resistance of the wool; and the total bacterial count of the filtered air was 5 colonies of spore-bearing bacilli in 300 litres. Unfiltered air, however, yielded 150 bacterial colonies in the same volume.

Viral filtration was demonstrated after 1 ml. of an aqueous suspension of adenovirus type 3 (10^6 tissue culture doses per ml.) had been atomised in a closed inoculating cabinet. When 10 litres of the infected air had been drawn through a soluble wool plug, the wool was withdrawn with forceps and dissolved in 15 ml. of sterile alkaline buffer (sodium chloride, 8 gm; potassium chloride, 0.2 gm; disodium hydrogen phosphate, 2.54 gm; distilled water to 1 litre). The final solution had a pH of 7.5 and was of low viscosity and toxicity to tissue cultures. HeLa cell tube cultures were inoculated with 0.1 ml. volumes of the solution in tenfold dilutions. Specific cytopathic effects were obtained to a titre of 10^{-4} .

1 Tested by means of a "Rotameter" flowmeter coupled in series.

The air in several wards was sampled during periods when 'non-bacterial' upper respiratory tract infections were prevalent; but though the undiluted wool solutions were inoculated into chick embryos, monkey kidney primary cell cultures and human amnion cell cultures, in addition to HeLa cells, no viruses were demonstrated.

Samples of settled dust from the paediatric medical ward were examined virologically by the method used for faeces (Selwyn and Howitt, 1962) at a time when there was an outbreak of diarrhoea that could not be ascribed to pathogenic bacteria. As in the case of the air sampling, however, these tests gave negative results. Mould contamination of the cultures obtained from settled dust was a serious problem despite the presence of nystatin in the culture medium.

Part II

STUDIES IN A GENERAL HOSPITAL

(iv) DISCUSSION

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Infections Present on Admission to Hospital

During the period of investigation, 379 (6.4 per cent) of the admissions to the various departments were on account of infective disease. The incidence of such admissions showed very little variation in the individual departments, with the notable exception of the paediatric medical unit where infections accounted for 35.6 per cent of all admissions. Most of these children were suffering from severe respiratory tract infections; meningitis and gastro-enteritis were the next most frequent infective conditions in the unit, but together they amounted to only one-sixth of the number of cases of respiratory tract infection.

The proportion of patients who were admitted in 1961 to all hospitals in England and Wales on account of infection can be estimated from the Report on Hospital In-patient Enquiry (Ministry of Health and General Register Office, 1964). Almost 4 million patients were admitted to these hospitals, and it can be calculated from the data in the Report that about 7 per cent of admissions were due to infection. Paediatric admissions constituted 18 per cent of all hospital admissions, and approximately one-third of the children came into hospital because of infections; the majority of these were situated in the respiratory tract.

The findings in the present investigation are therefore in very close agreement with the recently-published hospital statistics for England and Wales. Comparable data from Scottish hospitals are not available for 1961, but the first

detailed analysis, which refers to the 1962, shows a very similar distribution of infective conditions amongst paediatric and adult admissions (Scottish Home and Health Department, 1965). These findings emphasise the continuing importance of infection as a leading cause of serious morbidity in childhood. The important role which infection also continues to play in childhood mortality was indicated in a recent survey carried out in the Edinburgh area (Selwyn and Bain, 1965). It was interesting to find that infections not only cause one-third of all paediatric admissions to hospital, but are also the primary cause of approximately one-third of all deaths in the age-group from three months to fourteen years.

Whereas patients with overt clinical infection at the time of admission can, if necessary, be nursed in isolation, and form a well-defined group which is quite distinct from that of hospital infections, those patients who are admitted to hospital during the incubation period of an infection are not only a potential danger to others but are also a source of error in any investigation into the incidence of hospital-acquired infections. In the case of specific infectious diseases, such as the exanthemata, a consideration of the maximum and minimum incubation periods will often indicate whether the infection was acquired in hospital or before admission. However, the more common infections encountered in hospital have ill-defined incubation periods, though these tend to be relatively short. In the present investigation, clinical infections rarely developed during the first two days of a patient's stay in hospital; and these early

infections were excluded from the study. The only exceptions to this rule were neonatal infections which sometimes occurred as early as the second day of life: these are discussed further on p.216.

Although over-estimates of the incidence of hospital infection may, therefore, be made because of infective conditions that are 'incubating' at the time of admission, it seems likely that such errors are more than compensated for by infections which are acquired in hospital but which are not clinically evident until after discharge(p.189).

The Ascertainment of Infections in Hospital

The validity of any investigation into hospital infection is entirely dependent upon the accuracy and quality of the methods of ascertainment which are used. The difficulties encountered in collecting detailed information on hospital infection were commented upon by Jeffrey and Sklaroff(1958). These investigators limited their enquiry to a clinical survey of wound sepsis in four surgical units of an Edinburgh hospital over a relatively short period of time; and, although they did not attempt a bacteriological investigation of the lesions or of the environment, they nevertheless were forced to discontinue their detailed statistical study after three months because it proved to be too laborious.

For the routine surveillance of hospital sepsis the Ministry of Health Report (1959b) recommends that a special register should be maintained in each ward. It is interesting to find that similar detailed registers were kept in the Edinburgh Royal Infirmary in 1739, and were completed meticulously (Appendix, p.383). But where ascertainment depends upon a large number of observers the results obtained may be very misleading. Thus in an extensive recent inquiry into staphylococcal hospital infection which was based on a review of laboratory records and case notes, the authors admitted that at least one-third of all infections had probably been overlooked (Frohman et al., 1964). Moreover, Cohen, Fekety and Cluff (1962) found in one teaching hospital that between 70 and 100 per cent of infections were recorded during the early part of the academic year, whereas only 14 to 50 per cent of infections were recorded during the succeeding period. This decline in the accuracy of reporting was ascribed to a gradual decrease in the enthusiasm of the house officers, and to changes in medical staffing. The recording of infections improved temporarily again following the arrival of new house officers. Cohen and his colleagues believed that better results are obtained when a senior member of the medical staff visits each patient from whom a pathogenic organism has been isolated; their own survey was, however, limited to cases of staphylococcal infection. Undoubtedly, even this method will result in an under-estimate of the incidence of infections since it depends upon the submission of suitable specimens to the laboratory by the ward staff.

The suggestion that the ascertainment of infections in hospital should be the duty of one individual employed for that purpose seems to have been first made by Colebrook (1955). He envisaged a senior member of the medical staff - the Infection Control Officer - who, on a full-time basis, would study and advise upon the epidemiology of hospital infection. This recommendation has seldom been put into effect, presumably because of the shortage of skilled personnel and the financial difficulties in establishing such senior appointments. As an interim arrangement Gardner et al. (1962) have emphasised the value of employing an Infection Control Sister whose main duties are to collect data on the incidence of infection, to encourage the staff to submit specimens from each case and to co-ordinate the laboratory and clinical findings.

In the present work the author undertook similar duties, but in addition carried out a systematic bacteriological survey of the environment and was responsible for the laboratory investigation of all cultures from this source. The value of this unified approach, in which a single investigator divides his time between the wards and the bacteriological laboratory, is now becoming widely appreciated, and several combined appointments of this type have been made recently in Britain. In 1960, however, the practicability of one individual studying hospital infection on this broad front had yet to be established. At the outset it was clear that the collection of detailed clinical data on a personal basis was not possible in a survey of departments which together contained more than 300 patients. The aim of the

investigation was therefore to obtain over a period of one year a general picture of hospital infection in its environmental setting. In this way it was hoped to view in perspective the problems of infection which face widely differing hospital departments. No attempt was made, however, to study in depth such important problems as the influence of operative techniques and after-care on the development of wound sepsis (p.72.), or the factors underlying post-operative urinary tract infection.

A group of hospital infections that could not be investigated in the present study consists of those conditions which are manifest only after the patient leaves hospital. They mainly comprise wound infections, of which more than 20 per cent may occur after patients have left hospital (Barnes et al., 1959), and maternal breast abscesses, most of which are diagnosed after patients have been discharged (Plueckhahn and Banks, 1964). Some examples of these late infections were encountered in re-admissions to the hospital (p.129.). A relatively large number of neonatal infections (up to 80 per cent) may also be missed if patients are not seen after discharge (Nahmias and Eickhoff, 1961; Levon and Sompolinsky, 1964). The further spread of infection in the general population has already been discussed (p.76.). The few special studies so far made of these problems have unfortunately been restricted to staphylococcal infections, as in the work of Smith et al. (1963).

The Relative Importance of Staphylococcal and other Infections in Hospital

During the past twenty years the term 'hospital infection' has tended to become almost synonymous with staphylococcal infection in hospital. However, in the present investigation 1,231 patients (16.8 per cent) developed bacteriologically confirmed infections during their stay in hospital, but Staph. aureus was responsible for less than one-third of these cases. The remaining 70 per cent of infections were due mainly to Gram-negative bacilli.

If the general hospital studied in this investigation is a representative one, then there has indeed been an undue emphasis placed on the staphylococcus in the modern literature on hospital infection. Several factors underlie this disproportionate amount of attention that Staph. aureus has received. Perhaps the most important factor is the tendency for the organism to be associated with obvious, well-defined outbreaks of infection; and these can be studied in detail by means of bacteriophage typing. Further points of interest that have attracted many investigators include the predominant role of a few well-known phage types in the majority of outbreaks throughout the world, as well as the facility with which 'hospital' strains develop multiple antibiotic resistance. Staph. aureus has also proved to be of special interest to students of air hygiene; and the organism is in fact the only pathogenic species that can be isolated from the hospital environment with any degree of regularity.

In contrast, hospital infections due to other common pathogens tend to be endemic rather than epidemic, and until recently suitable methods of typing the organisms were rarely available to the epidemiologist. With the development of detailed systems for serological, bacteriophage and bacteriocine typing of enterobacteria and Ps. pyocyanea (p.58.), it is to be hoped that these very important hospital pathogens will receive closer attention.

A significant increase has undoubtedly occurred in the incidence of hospital infections due to Gram-negative bacilli. The main factors which underlie this increase have been discussed and some of the earlier work was reviewed in the Introduction (pp.53-58.). The most serious aspects of the problem amongst both medical and surgical patients were first emphasised by Finland, Jones and Barnes (1959). They showed that at the Boston City Hospital during the period from 1935 to 1957, while the incidence of streptococcal bacteraemia fell, there was a considerable rise in the general incidence of bacteraemias, including those due to Staph. aureus. However, the most striking feature recorded in the report was the increase in the number of bacteraemias due to Gram-negative bacilli, especially Klebsiella spp., Proteus spp. and Ps. pyocyanea; and the infections were associated with a very high mortality. This rise occurred sharply after World War II, and the high level was maintained thereafter.

Fortunately, in the present investigation, infection by Gram-negative bacilli rarely threatened the life of the patient. There were, however, two deaths associated with Pseudomonas

cross-infection, and many patients were seriously ill as a result of urinary tract infections acquired in hospital; but in this group of infections - including ten cases that were fatal - bacteraemias could not be demonstrated.

Approximately two-thirds of the infections by Gram-negative bacilli were located in the urinary tract, and the remainder consisted of wound sepsis (10 per cent of Gram-negative infections) and miscellaneous conditions - chiefly minor uterine sepsis and a smaller number of respiratory tract infections. With the exception of infections due to Ps. pyocyanea, the relative importance of cross-infection and endogenous infection in these cases cannot be established with accuracy. This problem is considered below in connection with individual departments. In general, however, on the basis of the species isolated and their antibiotic sensitivities it was believed that cross-infection was involved in a large proportion of the urinary tract infections, but in relatively few of the general surgical wound infections or of the cases of local uterine sepsis encountered in the gynaecological and maternity units.

The considerable number of strains of Strep. faecalis which appeared to play a significant role in hospital infections - 231 cases in all - were usually associated with coliform bacilli and were generally assumed to be of endogenous origin. In recent years, however, there has been an apparent increase in hospital infections due to this organism (Wilson & Miles, 1964); but their epidemiology remains obscure in the absence of satisfactory methods for detailed typing.

The Problems of Hospital Infection in Individual Departments

When the different departments which were studied in this investigation are arranged according to the total incidence of hospital-acquired infection encountered in each (vide Figure 20, p.138.), the results are not, perhaps, as might have been expected. The lowest incidence of infection - 10.6 per cent - was in the maternity wards and nurseries. Next in ascending order was the General Surgical Department which had a total incidence of 13.4 per cent. Although in the present study these departments were the least subject to infection, maternity and general surgical units have, during the past 20 years, received the greatest amount of attention in relation to hospital cross-infection. On the other hand, considerably higher incidences of infection were encountered in the departments of general medicine, paediatrics and urology; yet there has been comparatively little published work since 1945 dealing with infections in such departments.

Some reasons have already been put forward to explain the popular emphasis on staphylococcal infections and the relative neglect of infections due to Gram-negative bacilli (p.190.). Similar reasons can be advanced to explain why sepsis in maternity and surgical departments has been the subject of much greater interest than infection in medical and other departments. The occurrence of obvious outbreaks, generally of staphylococcal infection, has drawn attention to the problem in obstetrical and surgical units, while elsewhere in the hospital a high level of endemic infections - which are often diverse in their nature and aetiology - can more easily be overlooked.

Infection in Medical Wards

Almost 20 per cent of patients developed infection in the adult wards. Infections of the chest and of the urinary tract were similar in incidence, and together they accounted for more than 80 per cent of hospital-acquired infections. Most of the remainder took the form of minor infections of the skin. However, in the paediatric medical wards, although the total incidence was similar, the relative frequency of these three groups of infection differed. Chest and urinary tract infections together were responsible for only one-third of the hospital sepsis, while superficial infections - due mainly to Staph.aureus - accounted for almost 50 per cent of cases.

Chest Infections. The patients who developed chest infections in the medical wards were almost always found to have pre-existing chronic diseases of the lungs, or lesions of the heart with oedema or other secondary changes in the lungs. The special role played by lung oedema in the pathogenesis of staphylococcal pneumonia was stressed by Gresham and Gleeson-White (1957); and the dangers which patients with chest diseases face in hospital were clearly shown in the report by Maccabe (1959) on outbreaks of staphylococcal chest infections which occurred in wards devoted to the care of such patients. More recently, Mitchell et al. (1961) on the basis of a series of post-mortem examinations, emphasised the importance of underlying lung disease as one of the main factors in cross-infection of the

chest. The outbreak of staphylococcal disease in the adult medical unit (described on p.146.) indicates the dangers which, in their turn, patients with chest infections present to others in the same ward. Such patients are also a potential menace in a surgical ward (Shooter et al., 1957).

Many of the chest infections which were encountered in this and other departments during the present study were possibly of endogenous origin, especially in those cases involving pneumococci and H. influenzae. Indeed, following a six-month investigation of respiratory disease in a general hospital, Holland et al. (1960) concluded that there was very little evidence of significant cross-infection affecting the respiratory tract. In the present study, however, a number of strains of Staph. aureus isolated from chest infections were identical with strains prevalent in the wards. Moreover, the isolation from sputa of coliform bacilli, Proteus spp. and Ps. pyocyanea - many of which were highly resistant to antibiotics - indicates the likelihood of cross-infection in some of the cases. Cross-infection with pneumococci, too, may be not uncommon in hospital although it will be overlooked unless typing facilities are available. This was shown by Turner (1963) who found that a type 7 pneumococcus was responsible for a protracted and serious outbreak of bronchitis and bronchopneumonia in two wards. The evidence for the air-borne route of transmission in these infections is reviewed later (p.226.).

The presence of Staph. aureus and other potential pathogens in the sputum does not, however, prove the aetiological role of these organisms in any particular case of chest infection. The

use of a quantitative cultural technique such as that recently described by Dixon and Miller (1965), may - by analogy with quantitative urine culture- help to distinguish significant organisms from contaminants. The preliminary results of these investigators indicate that after digestion with pancreatin (as in the present work) and subsequent dilution to 1 in 10,000, most upper respiratory tract commensals and transient contaminants will fail to grow on the culture plates. Dixon and Miller, however, make no mention of the valuable information which can be obtained more readily from the direct examination of stained films of homogenised sputum - a standard method in the Edinburgh area. This procedure should also help to distinguish between 'bronchial carriers' of Staph. aureus who are apparently common in hospital (Report, 1966) and cases in which there is staphylococcal disease. This distinction is unlikely to be achieved by a purely quantitative cultural technique such as that of Dixon and Miller.

A detailed evaluation of the relative importance of cross-infection and endogenous infection is therefore still not possible in all cases of 'endemic' chest infection which develop in hospitals. Nevertheless, because of the undoubted danger of serious hospital infection in patients with pre-existing disease of the lungs or heart, there is an urgent need for a logical system of isolation to be adopted in relation to these and other patients who are at special risk in our hospitals. Inquiry into isolation requirements, along similar lines to the survey recently conducted in surgical units (Report, 1965a), is long

overdue in medical wards.

Urinary Tract Infections. Whereas chest infections amongst medical in-patients have attracted the attention of several investigators, the occurrence of urinary tract infections in medical wards has received little comment in the literature. Such infections are predominantly non-staphylococcal and therefore the factors discussed on p.190 in connection with the general neglect of Gram-negative hospital infections may apply to this special aspect of the problem. In the present investigation, infection in the adult medical wards was on no occasion preceded by catheterization. If, therefore, cross-infection was involved, the process was an indirect one.

The authors of the Public Health Laboratory Service Report (1965b), which is reviewed below, comment in their discussion: 'The relatively high incidence of urinary infection in uncatheterized women is difficult to explain. Probably some of the infections thought to have been acquired in hospital were recrudescences of latent pyelonephritis.'

Two interesting examples of indirect routes of urinary tract cross-infection have been described in relation to Proteus and Ps. pyocyanea respectively. While investigating an outbreak of Proteus urinary tract infection, Edebo and Laurell (1958) concluded that the organism was probably transmitted on rectal thermometers. Similarly, McLeod (1958) suggested that colonization of the urethra may follow contamination of the perineal skin and genitals from infected bedpans and urinals,

and this route could be of importance in the transmission of Ps. pyocyanea infection of the urinary tract.

The finding in the present work that the hospital baths were frequently contaminated with diverse Gram-negative bacilli as well as with staphylococci suggests yet another important source of infection. Indeed, Michie (1959) has shown that bath water may enter the bladders of healthy girls. Moreover, the air and settled dust of the wards themselves often yielded potential pathogens. Colonization of the external genitalia by these organisms could thus occur. The sex-difference observed in the incidences of urinary tract infection (outside the Urology Department) is presumably due to the greater ease with which bacteria can migrate up the female urethra. A possible factor that may assist this process is intermittent or hesitant micturition, which in the female apparently allows urine that has passed into the urethra to re-enter the bladder, and in this way bacteria from the urethra can readily gain entry to the bladder (Hinman and Cox, 1965).

In debilitated patients, too, Hinman and Cox (1965) have described a reduction in the activity of 'intrinsic mural factors' which are said to eradicate bacteria from the bladder in the healthy individual. A special factor which may be important in the pathogenesis of infection in the bed-ridden patient is the presence of residual urine. The inefficient emptying mechanism in debilitated patients who are nursed in the supine position will encourage a residual level of urine in the bladder. This will, in turn, facilitate infection by bacteria that have

reached the bladder from exogenous or endogenous sources.

The prevention of urinary tract infection amongst medical patients can be carried out on a rational basis only after further investigation of the factors that are involved, together with the detailed bacteriological typing of the causative organisms, the patients' pre-existing flora and the environmental isolates.

The results of this part of the study may be compared with the findings of an investigation recently reported by the Public Health Laboratory Service (Report, 1965b). This survey of infections acquired in the adult medical wards of 13 hospitals was based on the clinical impressions of 30 physicians. The physicians were stated to have differed widely in the use they made of the laboratory, and, although 14 bacteriologists participated, many of the clinical diagnoses were unsupported by bacteriological data. The investigation did not include bacteriological sampling of the environment. The total incidence of reported infections, 5.7 per cent, was considerably lower than in the present study; 2 per cent of the patients acquired infections of the lower respiratory tract, 1.2 per cent developed urinary infection, and 1 per cent developed skin infections. Staph. aureus was involved in 38 per cent of the acquired infections which were studied bacteriologically, and more than

half of the cases were sporadic. A group III strain of a similar phage type to the endemic strain in this hospital caused 13 infections in one ward. Other staphylococci, including the 'epidemic' group I type, were responsible for only small incidents involving between two and six infections during the year. However, the investigation confirmed the important role of debilitating disease in hospital infection; moreover, during the survey, hospital infection, mainly of the chest, was believed to have contributed to 8 per cent of all deaths. Similar conclusions were reached in a parallel survey of necropsies carried out by the Public Health Laboratory Service (Report, 1966).

Infection in Urological Wards

In contrast to the obscurity which still permeates the subject of urinary tract infection in medical wards, there has, for almost a century, been a clear understanding of the main factors that are involved in the acquisition of similar infections by urological patients. The transmission of infection on contaminated catheters and bougies was first emphasised by Sir Henry Thompson (1879) who recommended that such instruments should be disinfected with carbolic acid before use. However, the Aberdeen surgeon, Ogilvie Will (1894), later pointed out that 'catheter fever' often arose in hospitals following the use of carefully sterilised instruments. Will, who noted that chronic disease of the urinary tract - especially if obstructive -

was an important predisposing condition, suggested that 'the germs of putrefaction gain access to the bladder(due to) the ingress of germ-laden air', which, he believed, passed by reflux through the catheter after the bladder has been completely emptied. Such a reflux may indeed take place up the lumen of the urethra itself in a similar manner to the ascent of infected urine up the ureters (Hutch, Miller and Hinman, 1965). Moreover, patients who are treated by continuous, 'open' drainage of the bladder may become infected by means of air bubbles rising up the tubing (Miller et al., 1958).

Although pathogenic bacteria, including Ps. pyocyanea and Proteus spp. were, in fact, isolated from the air of wards in the present study, true air-borne infection of the urinary tract was probably less important than spread by other environmental routes. The frequency with which the entire environment of urological wards may be contaminated with pathogenic bacteria is evident from this and other studies (e.g. McLeod, 1958 - described above; Gillespie et al., 1960).

One-third of the patients admitted to the Urology Department developed urinary tract infection during their stay in hospital. All the infections occurred after urological surgery or urethral instrumentation. However, following prostatectomy which involved routinely the use of continuous 'open' drainage, 42 out of 48 patients (88 per cent) developed infection. This high incidence is in keeping with the findings of Mitchell and Gillespie (1964) who reported an infection rate of 82 per cent under similar circumstances. When these investigators introduced

closed drainage with full aseptic precautions, together with pre-operative disinfection of the urethra and improved disinfection of cystoscopes, they obtained a reduction in the rate of infection to 13 per cent. Similarly, the high rate of infection among female patients who are treated with indwelling catheters and open drainage (confirmed in the present study) has been greatly reduced by the application of comparable counter-measures. These are discussed below in relation to gynaecological patients.

As noted earlier (pp.191 and 192) the frequent infections with Gram-negative bacilli in urological and other patients rarely endangered life in this hospital. Gillespie *et al.* (1960), however, in Bristol have observed a high incidence of bacteraemia in patients who developed local infection following urological procedures. Although most of the bacteraemias were transient and had no serious consequences, Gillespie and his colleagues reported that this group of patients accounted for 30 per cent of all hospital cases of septicaemia in their experience. The potential risk to urological patients is also stressed by Talbot (1962).

In the present investigation, Esch. coli was an aetiological agent in 100 of the 157 infections of the urinary tract acquired in the Urology Department; and streptomycin-resistance was present in approximately one-quarter of the strains isolated. Paracolon bacilli, Proteus spp., Ps. pyocyanea or Strep. faecalis played an important role in 105 cases, and, excluding Strep. faecalis (which was almost invariably resistant to streptomycin),

streptomycin-resistance was present in 50 per cent of these strains. Gillespie and his colleagues have assessed the role of cross-infection of the urinary tract chiefly on the basis of the antibiotic sensitivities and species distribution of the causative organisms. In particular, the occurrence of infection with streptomycin-resistant and sulphonamide-resistant Proteus spp., Klebsiella spp. or Ps. pyocyanea has been regarded as indicative of cross-infection, whereas an endogenous source has been ascribed to Escherichia spp. and sensitive strains of the other genera. (The source of Strep. faecalis has not been defined in these terms). In support of this view, Dutton and Ralston (1957) reported that Klebsiella aerogenes and the 'intermediate' group of coliform bacilli, though common in hospital infection, were found in only a small proportion of faecal specimens from healthy individuals. Moreover, Mitchell and Gillespie (1964) noted that after eliminating all possible sources of cross-infection in patients on bladder drainage, the relatively few infections which still occurred were due mainly to Escherichia spp. and were probably endogenous in origin.

Using colicine typing, Linton (1960) has, however, demonstrated that many urinary infections due to Esch. coli are also the result of cross-infection. More recently, serological typing has led to similar conclusions (Kennedy, Florde and Petersdorf, 1965). The application of serological typing to Klebsiella infections (Ørskov, 1954), serological and phage typing to Ps. pyocyanea (Gould and McLeod, 1960) and typing by Dienes' phenomenon to Proteus spp. (Story, 1954) has, likewise,

shown with considerable precision the important role of cross-infection of the urinary tract in surgical patients. From the extensive work of Gillespie and his collaborators it is clear that most of these infections are readily preventable.

Infection in Gynaecological Wards

Urinary tract infections developed in 10 per cent of patients following admission to the Gynaecology Department. The incidence was 70 per cent in women who had undergone pelvic floor repair, which routinely involved post-operative 'open' bladder drainage. Very few of the remaining patients who became infected had been catheterized.

As in the case of urological patients, Gillespie and his colleagues (Gillespie et al., 1964) have demonstrated that the incidence of urinary tract infection amongst gynaecological patients can be greatly reduced by relatively simple means. Apart from the importance of using closed 'aseptic' bladder drainage in all cases requiring indwelling catheterization, the Bristol team of investigators have emphasised the significance of the sliding action of indwelling catheters up and down the short female urethra. The more distal portion of a catheter, which is almost invariably contaminated with pathogenic bacteria, will thus intermittently rise up the urethra and may enter the bladder.

The finding, in the present work, of a higher incidence of organisms resistant to streptomycin and sulphonamides in the urological cases as compared with the gynaecological series suggests that self-infection was more common in the latter group. The transfer to the bladder of the patient's own vulval flora, as well as of organisms acquired in hospital, can readily occur in the presence of a mobile catheter. To prevent this mode of infection, Gillespie and his colleagues disinfect the urethra with chlorhexidine before catheterization, and they attach a sponge collar, which contains chlorhexidine, around the catheter at the point of contact with the external urethral orifice. As an additional precaution they recommend that an antiseptic solution should be instilled into the bladder before and after the period of continuous catheterization. By these means they obtained a reduction of the urinary tract infection rate from 97 per cent to 13 per cent in this group of patients. In the present study, the lower incidence of infection recorded amongst patients on 'open' drainage was probably due to the criteria of 'infection' adopted. The Bristol investigators examined urine samples daily and classified as infected all cases in which more than 100,000 organisms per ml. were present, whether or not there were accompanying clinical symptoms and signs, or pyuria.

The prevention of infection in patients who are not catheterized has already been discussed in connection with medical wards. However, apart from attention to such possible sources of infection as baths and bedpans, colonization of the perineum

and vulva can probably be minimised by the regular application of hexachlorophane, chlorhexidine or other bland antimicrobial agents to these sites. The avoidance of trauma to the bladder, urethra and cervix uteri during gynaecological examinations should also help to reduce the risk of subsequent urinary infection.

Careful attention to details of technique and perhaps the rational application of satisfactory antiseptics during gynaecological procedures may also lead to a reduction in the incidence of post-operative local uterine and cervical sepsis. In the present study the numbers of such infections were relatively small (22 cases - a rate of 2.9 per cent); but although there were no serious consequences, the condition was usually distressing to the patient and necessitated a more prolonged stay in hospital in most cases.

Wound sepsis constituted the third group of infections, in descending order of frequency; and although there were only 12 cases, the incidence was 7.7 per cent in relation to the number of patients who were operated upon through a superficial incision, usually of the abdomen. Three of the infected wounds yielded profuse growths of the endemic group III staphylococcus, and 4 of the 5 non-staphylococcal infections were due to coliform bacilli which were resistant to streptomycin, suggesting that cross-infection rather than endogenous infection was responsible.

Infection in General Surgical Wards

Non-staphylococcal infection accounted for 104 (54 per cent) of the 191 wound infections encountered in the various departments. This proportion is similar to that recorded without comment by McNeill, Porter and Green (1961) in their brief study of staphylococcal cross-infection in a surgical ward.

As can be seen from Figure 21 (p.139.), patients in the General Surgical Department had a lower incidence of wound sepsis than those in any of the other departments, with the exception of the maternity wards. The rate was indeed lower than that observed in most other recent surveys (e.g. McNeill, Porter and Green, 1961; Moore and Gardner, 1963; Report, 1964b, and other publications reviewed earlier). The apparently lower incidence of 2 per cent encountered by Ljungqvist (1964) referred to a selected group of 'clean' operations. It can be argued, nevertheless, that a sepsis rate of 5.8 per cent for all operations is still too high. However, on the basis of phage typing of staphylococci and antibiotic sensitivity tests upon other significant isolates, cross-infection seemed to be relatively unimportant among the general surgical patients, in contrast to the findings in other departments.

Endogenous Infection. The importance of endogenous infection of wounds has been emphasised by many workers but denied by others. Some of the conflicting evidence has already been discussed, in relation to staphylococcal nasal carriers (p.67).

Additional support for the endogenous route of infection has been provided by Ketcham, Lieberman and West (1963) who found that a large proportion of their observed wound infections were due to strains of Staph. aureus carried pre-operatively by patients. The problem is not, however, confined to staphylococci and nasal carriers but extends to all the potentially pathogenic bacteria which may form a part of the permanent or temporary flora of different parts of the body. Thus more direct evidence has been obtained by the reduction in wound sepsis which has followed improvements in pre-operative skin preparation (Harrison and Cruickshank, 1952; Shepherd and Kinmonth, 1962), and from bacteriological studies of patients' skin at the time of operation (e.g. Howe and Marston, 1962; Report, 1964b). Moreover, in almost all investigations in which operations have been classified according to the site and the likelihood of pre-existing bacterial contamination, the wound sepsis rate has been found to be lowest in 'clean' operations where endogenous bacteria are absent from the incision or are present in very small numbers; the rate rises, however, in parallel with the clinically estimated degree of endogenous contamination - arising notably from the abdominal viscera (e.g. Jeffrey and Sklaroff, 1958; Douglas, 1963; Report, 1964b).

In the present study, while endogenous infection is believed to have produced most of the wound sepsis in the General Surgical Department, this form of infection seemed to have been comparatively less important in the cases of wound infection that occurred elsewhere in the hospital. It may be useful - although

an oversimplification - to consider the relatively low rate of infection in the General Surgical Department as forming a baseline for surgical sepsis elsewhere in the hospital. Thus in the nearby Gastro-enterology Department and in the Gynaecology Department the incidence of wound sepsis was about 50 per cent higher, and it was evident that cross-infection was involved in a number of cases. The Paediatric Surgical Department had a still higher sepsis rate and there was abundant evidence of cross-infection and environmental contamination, mainly by Staph. aureus; likewise, cross-infection was demonstrated in the relatively few wounds that were treated in the maternity nurseries and General Medical Department.

When considering rational methods of prevention, it is essential to recognise the stratification of hospital infection into an underlying core of endogenous infection - which may be difficult to eliminate - and a superimposed component of cross-infection, which though varying widely in its relative importance should be more readily accessible to countermeasures.

It should be possible to reduce the incidence of wound infection due to the patient's own micro-flora by the use of effective antibacterial agents. These may be applied to remote carrier sites (Green, 1961) as well as to the skin in the region of the surgical incision (Lowbury, Lilly and Bull, 1964). The lack of success experienced by a number of investigators who have applied such methods may be more an indication of the difficulty in removing bacteria effectively from healthy skin and all carrier sites, than evidence of the unimportance of endogenous infection. In the special case of bowel surgery, a

satisfactory reduction in the numbers of intestinal commensals is not easily effected, and empirical attempts to 'prepare' the bowel by the prophylactic use of antibiotics may merely disturb the balance of the intestinal flora and actually increase the incidence of post-operative sepsis (Report, 1964b). Favourable results, however, have been obtained when antibiotics were administered under careful bacteriological control to patients undergoing bowel surgery (J.C. Gould, personal communication). Similarly, there is a recent report that the prophylactic administration of large doses of penicillin reduces wound sepsis in cardiovascular surgery, and in cases where clean tissues are brought into contact with infected material - as in the operative treatment of chronic empyema (Campbell, 1965). Such methods must, nevertheless, be considered as adjuncts to the use of careful surgical techniques which are designed to prevent soiling of the wound from the viscera.

Self-infection with organisms acquired in hospital preoperatively are examples of 'delayed' or indirect cross-infection, and though their immediate prevention at the time of operation is as for other forms of endogenous infection, their ultimate prevention depends upon combating cross-infection.

Cross-infection. Compared with the frequently disappointing results which have followed attempts to reduce the rate of endogenous infection, considerable success has been achieved in preventing wound sepsis due to hospital cross-infection. Although counter-measures may be introduced in the operating theatre or in the ward, most investigators have concentrated

their attention upon one to the exclusion of the other, and often the choice has appeared to be an arbitrary one. However, when the decision has been based upon previous investigations into the origin of wound infections in any particular hospital valuable results have been obtained.

Infection from the Operating Theatre. Much of the work on preventing infections in operating theatres has been concerned with improvements in air hygiene. The conflicting results that have been obtained will be discussed further in relation to the bacterial contamination of the environment which was encountered in the present study (p.232.). However, apart from the airborne route, cross-infection in the operating theatre is undoubtedly the source of wound sepsis in many instances; and staphylococcal infection has been traced to skin lesions or symptomless skin carriers amongst the theatre staff (e.g. Mitchell et al., 1959; Devenish and Miles, 1939). The methods of prevention range from careful scrutiny of surgeons' gloves (Penikett and Gorrill, 1958) to the instillation of anti-bacterial substances into the surgical wound during operation (Forbes, 1961); and the latter procedure deals with organisms reaching the wound from both exogenous and endogenous sources.

Infection acquired in the Ward. In the present investigation, however, most of the wound sepsis seemed to have arisen in the wards. The different departments used the same operating theatre suite which was served by the same staff, with the

exception of the surgeon and his first assistant. There was a low incidence of bacterial contamination of the two operating theatres, and although some wound sepsis was due to miscellaneous organisms which could be ascribed to endogenous sources, notably in the General Surgical Department, in many other instances it was due to organisms prevalent in the wards.

The importance of the ward rather than the operating theatre as the main source of surgical cross-infection has been emphasised in several recent publications. These include the report of Rountree et al. (1960), who observed an infection rate of 18 per cent for all operation wounds. The rate was halved by covering the wound with a plastic seal at the end of the operation; and 5 out of 12 infections which occurred despite this protection were of endogenous origin. In contrast Gillespie et al. (1961) attacked the problem of ward infection simultaneously on several fronts. Nasal carriage of Staph. aureus was greatly reduced by the application of anti-bacterial creams to the anterior nares of patients; wounds were treated prophylactically with anti-bacterial sprays or powders; and such vectors as bedding, baths, urine bottles and nurses' hands were disinfected. By these and other similar means the rate of cross-infection of open wounds fell to about one-third of its former level: those forms of sepsis that had been encountered other than wound infections (notably post-operative bronchopneumonia) also diminished considerably.

Still more recently, Shooter et al. (1963) have reported encouraging results in a surgical ward at St. Bartholomew's

Hospital, which was modified for the investigation of the effects of segregating patients before operation, so as to prevent them from acquiring hospital pathogens. It is interesting to recall that this concept was clearly formulated more than a century ago by Simpson (1859). If air-borne infection is indeed of importance in surgical wards (vide p.233.), it would seem reasonable to follow the recommendation of Colebrook (1950). On the basis of his experience in a burns unit (p.80.) he believed that all surgical wounds should be dressed in special rooms equipped with positive pressure ventilation and provided with a plentiful supply of filtered air. Despite this sound advice given 16 years ago, surgical wounds are still generally dressed in the open wards of British hospitals - often immediately after the disturbance of screens, curtains and bedding when air contamination is at its maximum.

Although the studies of Gillespie and his colleagues have demonstrated that a combination of counter-measures is necessary when the surgical sepsis rate is high, a more selective approach should prove effective in other circumstances. For the long-term prevention of all forms of cross-infection it would seem reasonable to concentrate upon the human sources of infection. A central theme of the third part of the present work is a detailed consideration of superficial sites of bacterial multiplication which appear to be important in the dissemination of hospital infection.

Infection in Maternity Departments

Maternal Sepsis. Infections of the urinary tract - in 6.1 per cent of patients - and local sepsis of the uterus - in 3.7 per cent of patients - were the only two significant groups of infection encountered among women in the maternity wards. The obstetricians estimate, however, that a further 5 per cent, or more, of their patients develop acute mastitis after they leave this hospital. The attendances of patients at the post-natal clinic six to eight weeks after discharge are unsatisfactory and the true incidence of breast abscess cannot be readily determined without special facilities for 'follow-up'. In a survey carried out in a different Edinburgh hospital during 1957, Knight and Nolan (1959) reported an incidence of 3.1 per cent. This appears to be lower than the estimated rate for this hospital, although it may approximate to the incidence of frank abscess formation among the cases of mastitis.

Plueckhahn and Banks (1964) have shown that the incidence of maternal breast abscess is greatly reduced by the regular application of a 3 per cent hexachlorophane emulsion to the infants' skin. This provides further evidence for the view that the infant is the main source of infection in maternal breast abscess. These and other measures to reduce neonatal hospital infection are considered below.

Women in labour were not catheterized routinely in this hospital, and the incidence of post-partum urinary tract infection observed was closely comparable with that reported by Brumfitt,

Davies and Rosser (1961). In their survey, 4.7 per cent of non-catheterized women became infected, whereas 9.1 per cent of catheterized women, who were free from obstetrical abnormalities, developed infection. Higher incidences for both groups - 15 per cent and 38 per cent respectively - were recorded more recently by Oseasohn et al. (1962), who employed as the single criterion of infection significant bacteriuria. These investigators did not usually isolate bacteria suggestive of cross-infection from either group of patients, and it appeared that organisms of endogenous origin were mainly responsible for the infections; this was also the impression obtained in the present work, in contrast, for example, to the position in the Urology Department (p.202). For the prevention of post-partum urinary infection there is general agreement that catheterization, prolonged labour and obstetric trauma must be avoided.

The long-term prognosis in infected women is still uncertain. It has been postulated that although the initial infection usually responds well to treatment, chronic pyelonephritis may be the ultimate sequel to infection in many of these women (Kass, 1962). However, follow-up in a group of women who had post-operative infections did not reveal any excess in the number of cases of continuing infection and renal damage as compared with a control group (Slade et al., 1965). And it has long been known that women in the puerperium who develop urinary infection have a far better immediate prognosis than patients with underlying genito-urinary disease (Will, 1894); the consequences of infection in these women, therefore, may not be

as serious as has been thought. Moreover, despite the higher incidence of urinary tract infection in females compared with males, chronic pyelonephritis apparently has a similar incidence in both sexes (Kimmelstiel et al., 1961).

As in the case of urinary infections, local uterine sepsis in the maternity wards seemed to ^{be} mostly endogenous in origin and no cases of a serious nature were encountered. The general factors considered in the discussion of these infections in gynaecological patients (p.206.) apply equally to maternity patients.

Neonatal Sepsis. The total incidence of endemic infection was rather more than 10 per cent. This sepsis rate, though lower than many reported in recent years (p.70.), is still unsatisfactorily high.

Superficial infections, of which two-thirds were due to Staph. aureus, accounted for 91 per cent of the sepsis in the nurseries. But although almost all the skin infections were due to Staph. aureus, as were 48 cases of 'sticky eye,' other Gram-positive and Gram-negative bacteria were apparently responsible for 43 cases. Nevertheless, a bacterial aetiology could not be invoked in the early stages of all cases of acute conjunctivitis; and recently, Eichenwald (1965) has commented on the frequency of 'sterile' cases in his nurseries. The isolation of the trachoma-inclusion conjunctivitis ('TRIC') agent from the eyes of affected infants and from the cervix uteri of their mothers was reported by Jones, Collier and Smith (1959). In view of this finding - which has since been confirmed by Mordhorst (1964)

and others - a virological investigation was performed over a two-month period in an attempt to clarify the aetiology of 'non-bacterial' cases of sticky eye in this hospital. During the period, 15 such cases were studied, but in none of them was there evidence of TRIC agent, adenovirus or any other viruses that could grow in the chick embryo or in the tissue cultures used. However, the finding of a low complement-fixing antibody titre against the TRIC group is not in itself conclusive evidence against infection by these agents (Jones, Collier and Smith, 1959). A clinical impression is that a number of these cases of 'sterile sticky eye' may be due to antiseptics applied to the mother's birth canal during delivery. The irritation produced by agents such as 'dettol' may also subsequently predispose the infant to bacterial infection of the conjunctiva.

Infants who become colonized with hospital pathogens, notably Staph. aureus, are not only a source of infection for other infants and their mothers but may transmit infection into the general community outside hospital (pp. 76 and 189.). This effect may persist for a considerable time. A follow-up study carried out over several years showed that recurrent staphylococcal infections were common for over a year amongst the families of infected infants, but the frequency of sepsis declined thereafter, and was minimal after five years (Hurst et al., 1964). The danger of maternity nursery infections to the community at large is thus well established, but the possible risks of spread throughout a general hospital have apparently received very little attention. In the present investigation there was evidence to

suggest that the nurseries formed a reservoir of staphylococcal infection. This point is discussed further in relation to environmental contamination (p.226).

In the past two decades several approaches have been explored in an attempt to prevent or delay the colonization of newborn infants by pathogenic micro-organisms. Cruickshank (1963) has reviewed much of the earlier work relating to nasal and skin disinfection, isolation of infants by 'rooming-in' or cohort segregation, and the introduction of measures designed to reduce environmental contamination. More recently, Plueckhahn and Banks (1964) and Simon (1965) have reported that disinfection of the infants' skin with hexachlorophane preparations markedly reduced the rate of neonatal cross-infection, and of maternal breast abscess in the the first of these investigations. Similar results have been achieved by concentrating upon disinfection of the attendants' hands.

As an entirely different approach, the interesting concept of 'bacterial interference' in relation to staphylococcal infections of the newborn has been studied by Shinefield et al. (1965). This principle is not, in fact, new. More than 50 years ago, cultures of Staph. aureus were inoculated on to the pharynx of diphtheria carriers in order to displace the diphtheria bacillus; and according to Ledingham and Arkwright (1912) successful results were obtained. In their recent work, Shinefield and his colleagues have succeeded in preventing nasal and umbilical colonization of infants with 'hospital' staphylococci by implanting a relatively avirulent strain of Staph. aureus ('strain

502A') in the anterior nares and on the umbilical skin within a few hours of birth. By these means they were able to terminate several epidemics of staphylococcal infection in maternity nurseries.

Understandably, micro-organisms other than Staph. aureus have during recent years received very little attention in maternity hospitals - with the possible exception of enteropathogenic Esch. coli (p.56.). Yet non-staphylococcal sepsis may be of considerable importance. Thus, following a retrospective survey at the Boston City Hospital, Eickhoff et al. (1964) reported that beta-haemolytic streptococci of Lancefield group B were apparently responsible for 25 per cent of all neonatal sepsis in 1962 and 1963. The organism was thought to have originated in the maternal genital tract, and infection was particularly common following premature rupture of the membranes. While obstetric complications such as this probably justify the prophylactic use of systemic antibiotics, some of the general measures discussed above may help to reduce the incidence of infections due to other bacteria. However, Simon (1965) was concerned that while skin disinfection prevented colonization by Staph. aureus in the newborn, it was ineffective against coagulase-negative staphylococci and Gram-negative bacilli. The replacement of the normal, predominantly Gram-positive skin flora by Gram-negative organisms following skin disinfection has been reported by Shehadeh and Kligman (1963). Although it is hoped that there will be no absolute increase in the frequency of infections due to other bacteria or fungi as a result of counter-

measures against Staph. aureus, a relative increase in such infections seems inevitable.

Bacterial Contamination of the Hospital Environment

In the various departments a broad correlation was found to exist between the environmental 'load' of Staph. aureus and the frequency of clinical infection due to this organism. Moreover, the distribution of the different phage types and antibiotic sensitivity patterns was similar in strains isolated from infections and from the environment. This parallelism does not necessarily indicate that infection was acquired via the air or other parts of the inanimate environment. Contamination of the environment with pathogenic bacteria is basically a secondary phenomenon reflecting the presence of infected individuals or symptomless carriers. Undoubtedly, however, a vicious circle can be established in hospital whereby susceptible patients acquire infection from their bacteria-laden surroundings and subsequently maintain or increase the environmental load. In this connection the two exceptions to the general correlation are illuminating when contrasted with other departments.

Discrepancies Between Ward Contamination and Infection Rates. The General Surgical Department had a moderate incidence of staphylococcal sepsis (3.9 per cent) which consisted mainly of wound and other superficial infections due to miscellaneous phage

types. However, relatively little staphylococcal contamination was observed in the department, and the incidence of subclinical infection of 'clean' wounds with Staph. aureus and other bacteria was the lowest in the hospital. The strains causing infection in the department were apparently of low communicability and virulence; and during the year there was no evidence of unusually active dispersers such as those occasionally encountered in surgical wards by Noble (1962). Moreover, though dressings were changed in the open ward, the use of careful techniques minimised the risks of disseminating bacteria.

In marked contrast, the maternity wards had the lowest recorded incidence of staphylococcal infection in the hospital - although an indeterminate number of cases of breast abscess developing after discharge could not be taken into account. Yet the levels of environmental contamination by Staph. aureus, and by Gram-negative bacilli in settled dust samples were among the highest encountered in the investigation. However, the great majority of the environmental staphylococci were resistant to penicillin, and most of these were also erythromycin-resistant, whereas half of the comparatively few strains isolated from lesions were penicillin-sensitive.

The abundant Gram-negative bacilli in the wards were presumably derived from perineal pads and bedding soiled with lochial discharges. The staphylococcal contamination is readily explained by the close proximity of the nurseries and the intermittent presence in the ward of infants, almost all of whom carried the endemic staphylococcus within a few days of birth.

It was interesting to note that even though the average incidence of airborne Staph. aureus in the nurseries was approximately ten times higher than that recorded in the same nurseries during 1947 by Wallace and Duguid (1952), the rate of staphylococcal infection among infants has not increased, despite almost invariable colonization of the newborn by the endemic staphylococcus.

The anomaly of a relatively low sepsis rate in the Maternity Department despite a high prevalence of staphylococci may be considered further in relation to host factors, dosage of infection and virulence of the infecting organism.

Host Factors. Although they are encompassed by ill-defined terms such as 'increased susceptibility' of 'debilitated' individuals, host factors are of fundamental importance in determining the outcome of infection. Their basic role in the changing pattern of hospital infection has already been discussed (pp. 44 and 53); and their influence was seen underlying the relatively high incidence of endemic infection, notably of the chest, amongst general medical and gastro-enterological patients. Similarly, the good general health of the young mothers in the maternity wards must be a partial explanation for their comparatively low sepsis rate. It is improbable, however, that resistance to staphylococcal infection has increased among infants since 1947. There has been no significant change in maternal health or nutrition, or in average birth weights; and though social improvements have occurred, especially in relation to housing,

it seems unlikely that host or external environmental factors are responsible for the relatively low sepsis rates encountered in the heavily contaminated nurseries.

Infecting Dose. The total number of bacteria reaching a patient from the environment is determined partly by his length of stay in hospital. The average duration of stay in the Maternity Department was the shortest in the hospital, and may be regarded as a mitigating factor in the presence of such heavy contamination.

During the period of the investigation, infants in the nurseries inhaled each day approximately ten particles carrying Staph. aureus. As each particle probably contains four or more viable organisms (Lidwell, Noble and Dolphin, 1959) the numbers of bacteria which entered the infants' noses daily were of the same order as the infecting doses that were required to establish nasal carriage in the experiments of Shinefield et al. (1965). Although the noses of infants obtain from the air relatively more staphylococci than does the skin, Hurst (1965) and others have shown that the skin is often colonized before the anterior nares. This may be because the skin of the newborn can be colonized as a result of a smaller infecting dose than the anterior nares, although the work of Shinefield and his colleagues does not support this hypothesis. On the other hand, it may indicate the greater importance of direct contact and other pathways of infection than of the air-borne route in the nurseries (vide p.234).

The adult patients in the maternity wards presumably inhaled twelve to fifteen times more Staph. aureus than did the infants, yet in the limited number of observations made, nasal carriage of the prevalent strain was found in none of the mothers. More extensive work on nasal carriage carried out previously in this department confirmed that mothers rarely become true carriers of the group III endemic staphylococcus, although transient contamination of the anterior nares is common (Maccabe, Gould and Forfar, 1961; A.F. Maccabe, personal communication). These observations also are in accordance with the experimental results of Shinefield and his colleagues, who found that the instillation of very large doses of Staph. aureus into the nostrils of adults rarely led to the true carrier state, unless pre-existing nasal bacteria were first suppressed by the local and systemic administration of cloxacillin. In the present study, however, there were evident differences in the facility with which different types of staphylococci were able to colonize adults (vide infra).

Less precise information is available concerning the minimum infecting dose of Staph. aureus required to produce clinical sepsis, although the experiments of Elek and Conen (1957) and Foster and Hutt (1960) in man, and of James and MacLeod (1961) and Taylor et al. (1962) in laboratory animals indicate that relatively small doses are effective in the presence of foreign bodies such as thread, or when the skin or deeper tissues are damaged. The vehicles of transmission of air-borne bacteria, discussed on p.349, may assist in the

establishment of infection in a similar way, as may surgical trauma.

Virulence. Despite numerous investigations there is still very little known about the factors underlying differences in virulence among strains of Staph. aureus; but that such differences exist is clear from epidemiological studies. In the present work, the Maternity Department fortunately did not experience infection with the notorious 80/81 hospital staphylococcus (p.49.). An organism of this type, however, produced several wound infections in the Urology Department, and, more dramatically, following its introduction into the General Medical Department, clinical infection and the carrier state developed in both staff and patients. But the communicability and virulence of the organism apparently declined after a month, and the outbreak was self-limiting.

On the other hand, the prevalent staphylococcus in the Maternity Department and elsewhere in the hospital did not readily colonize adults or produce severe infection. Thus in the presence of formidable contamination of the environment, infection was not acquired by the staff, and not only was the incidence of infection in adult patients low but the more highly susceptible group of infants, who seemed to be almost invariably colonized by this organism, developed only minor sepsis, and the rate was relatively low. The possibility that staphylococci lose their virulence when outside the body for more than a short period of time must also be considered in this

connection, and this point is discussed later.

The Endemic Group III Staphylococcus. The erythromycin-resistant staphylococcus of phage group III, though found in most parts of the hospital, was particularly abundant in the Maternity Department and in the adjoining paediatric units. The evolution of this organism is well-documented.

In 1951, the incidence of staphylococcal infection of the skin and eyes was 6.5 per cent in this nursery - exactly the same as that found ten years later in the present study. The infections in 1951 tended, however, to be more severe; and although 76.6 per cent of the staphylococci involved were already penicillin-resistant (compared with 84 per cent in 1960 - 1961) only 4.5 per cent were tetracycline-resistant (Forfar et al., 1953). Ten years later, 68 per cent of the staphylococci from neonatal infections were resistant to tetracycline, and 61 per cent were resistant to erythromycin also. Erythromycin was not available in 1951, and phage typing was not performed in Edinburgh at that time. In 1954 a further investigation which included phage typing was carried out on neonatal infections in this hospital (Forfar et al., 1955). The total sepsis rate in infants was found to be 14 per cent, and 70 per cent of cases were due to Staph. aureus. At this time, erythromycin was being used extensively in the unit and the antibiotic proved to be very effective when administered orally. No strains were found to be resistant to erythromycin, and the phage types were divided equally between group I (52/52A, mostly resistant to

penicillin but sensitive to streptomycin and tetracycline) and group III (6/7/47/76/77 and related types, mostly penicillin-resistant but sensitive to streptomycin and tetracycline).

The first appearance of erythromycin-resistance in Edinburgh was reported by Maccabe and Gould (1956). They isolated identical group III strains (type 44/47/53/54/77) from two infected patients in the Paediatric Surgical Department. Although erythromycin was not then in use in this hospital department, the patient who was believed to have introduced the infecting strain had been admitted from another hospital where the drug was being used freely.

From 1958 to 1960 a careful examination was made of all strains of Staph. aureus isolated in this hospital to determine the prevalence of the erythromycin-resistant group III organism, which now typed as 75/76/77 (Maccabe, Gould and Forfar, 1961). Between June 1958 and November 1959, the incidence of erythromycin-resistance amongst Staph. aureus was 1.7 per cent, but from November 1959 to September 1960 (one month before the present work began) the incidence had risen to 11.3 per cent.

Maccabe and his colleagues also reported the results of several air samples that were examined during October 1960 in a number of wards. The highest counts of Staph. aureus were obtained in the paediatric surgical ward where 10 per cent of strains were erythromycin-resistant. The counts in the maternity nursery were slightly lower, and 8 per cent of strains were erythromycin-resistant. Sampling was also performed in a gynaecological ward where counts of Staph. aureus were similar

to those in the nursery, but only 1 per cent of strains possessed erythromycin-resistance. In a general surgical ward the air count of Staph. aureus was very low.

The present work revealed a further rise in the incidence of erythromycin-resistance amongst strains from lesions and from the environment, the values for all the departments studied being 28 per cent and 20 per cent respectively. The gradients of the mean air counts of Staph. aureus and of the incidence of erythromycin-resistance in strains from the environment were similar. They were consistently at their maximum in the paediatric and maternity departments, and then descended through the gynaecological and general medical departments reaching their minimum in the three departments that occupy the pavilion block.

The erythromycin-resistant endemic staphylococcus thus appears, on the basis of environmental sampling and of clinical infections, to have had its reservoir on the first floor of the central block; and it seems to have spread from there to the ground floor - which houses the General Medical Department, and to the second floor - which houses the Gynaecology Department. The findings in the more distant but interconnected pavilion building also supports the theory of a geographical basis for the distribution of the endemic staphylococcus. This simple concept is, however, complicated by the possible presence in any department of clinically or subclinically infected individuals who are prolific dispersers of their organisms. Apart from causing a temporary intensification of contamination by the endemic strain, such patients (or staff) may produce heavy

dissemination of other strains which will obscure the underlying endemic pattern, as was seen in the General Medical Department.

Although apparently of relatively low virulence, the endemic group III staphylococcus possesses certain demonstrable features which favour its persistence in the hospital. Multiple antibiotic resistance is clearly one of these. It is possible that this organism is a descendant of the penicillin-resistant but otherwise sensitive group III organism that was isolated in the hospital by Forfar and his colleagues in 1954, and it may perhaps be derived from earlier strains documented since 1947. The reports from this hospital which were reviewed above have drawn attention to the development of resistance to penicillin and to each of the newer antibiotics in turn; and following the observations of Jackson, Lepper and Dowling (1954), the remarkable facility with which antibiotic resistance develops in related group III staphylococci has been widely recognised. This trend has been maintained recently in relation to methicillin and similar antibiotics (e.g. Colley, McNicol and Bracken, 1965).

Even though antibiotic therapy in the maternity nurseries during this study was almost entirely restricted to the administration of chloramphenicol eye drops, the endemic staphylococcus maintained and probably enhanced its pre-eminent position. It is interesting, therefore, that in the small-scale tests which were carried out on survival in vitro this organism fared better than did other staphylococci - including the well-known group I, 'epidemic' organism. Similar results

have been obtained more recently by Rountree (1963). Other investigators (e.g. Rogers, 1959; Schmidt and Spitzbart, 1962) have described the prevalence in hospital infections and the environment of staphylococci which were of low virulence; but antibiotic resistance alone has usually been considered as the underlying factor.

In Vitro 'Markers' of Virulence. Apart from the tests on the long-term survival of Staph. aureus which revealed significant differences amongst epidemiologically distinctive strains, the in vitro tests that were carried out added very little to the information obtained from phage typing and antibiotic sensitivity testing. The endemic strain proved to be resistant to mercuric chloride and to produce 'yellow' pigment on 1 per cent glycerol monoacetate agar. Thus the techniques developed by Moore (1960) and Willis and Turner (1962) respectively, could be useful as epidemiological 'screening' tests, if laboratory facilities are restricted.

Although the factors controlling mercuric chloride resistance and penicillinase production may be genetically linked (Richmond and John, 1964), the present results show considerable dissociation of these two properties. Of special interest was the observation that all penicillin-resistant strains of type 52/52A/80/81 were resistant to mercuric chloride, whereas several penicillin-resistant strains of type 80/81 which were sensitive to tetracycline were also sensitive to mercuric chloride. This may indicate the production, in these

strains, of at least two different forms of penicillinase, controlled by two or more distinct genes (Richmond, 1965). The findings support the view that there is considerable biological heterogeneity amongst strains with closely similar bacteriophage susceptibilities. However, in the case of group II strains the results of survival tests and mercuric chloride resistance taken together correlate with bacteriophage typing patterns. Staphylococci susceptible to phages 3A, 3B, 3C, 55 or 71 form a very distinctive group. Members of this group have a limited pathogenic and epidemic potential, and, among other characteristics, a restricted capacity for acquiring resistance to antimicrobial drugs. They also seem relatively unsuited for survival outside the body.

The apparently conflicting results obtained in studies upon egg yolk turbidity with different strains of staphylococci have already been discussed (p. 51.). To these findings may be added the report of Carter (1960) who used precipitation in egg yolk media as an alternative indicator of pathogenicity to the coagulase test. On the other hand, Smith, Willis and O'Connor (1965) found that most of the staphylococci causing hospital infections in Melbourne were unable to produce opacity of egg yolk. In the present study the egg yolk reaction did not correlate with antibiotic sensitivities, phage typing, or with the apparent virulence as indicated by the origin of the test strains.

Attempts to correlate staphylococcal virulence with other biochemical reactions and with the production of exotoxins have

had disappointing results, although the recent report of Ivler (1965) is of great interest. In preliminary experiments, he has found that 'virulent' staphylococci, including some coagulase-negative strains obtained from patients with endocarditis, differed from 'avirulent' strains in their amino acid transporting and respiratory activities. However, in vivo tests involving the inoculation of human volunteers have failed to distinguish between strains which are generally believed to differ in their virulence (Maibach, 1965); it is perhaps not surprising, therefore, that in vitro tests of virulence have proved relatively unrewarding.

The Practical Importance of Environmental Contamination. Hospital infection has often been ascribed uncritically to the acquisition of bacteria from the environment. Some of the more convincing demonstrations of this route of infection in operating theatres and wards have already been discussed (p.80). Several investigators, however, have not observed a fall in the sepsis rate after reducing the environmental contamination to a low level. This was the experience of Kinmonth et al. (1958) following improvements in the ventilation of an operating theatre together with the use of sterile suits and gowns by the entire surgical team. By these means, the average total bacterial air count was reduced from more than 20 per cu. ft. (a similar level to that found in the theatres of this hospital) to approximately 10 per cu. ft. - the level recommended by Bourdillon and Colebrook (1946) and Blowers (1963). Likewise,

extensive, double-blind trials of ultra-violet irradiation in the operating theatres of five American hospitals showed that although the counts of sedimenting bacteria in irradiated theatres fell to one-half or even one-third of the counts in control theatres, there was no significant difference in the total wound sepsis rates among patients operated upon in either group of theatres (Report, 1964b). In the irradiated theatres there was, however, a small reduction in wound sepsis rates among patients with closed undrained 'clean' wounds.

Neither of the publications cited above provides data concerning the air counts of Staph. aureus or other pathogenic bacteria, but it is clear that such organisms were isolated relatively infrequently, even in the absence of counter-measures. Contamination of the exposed tissues by air-borne pathogens during operation was probably an uncommon source of infection in these studies; improvements in air hygiene would not, therefore, be expected to lead to a lower sepsis rate in such circumstances.

A trial of air disinfection with ultra-violet light was conducted in two maternity nurseries by Manfield, Shooter and Lidwell (1960). They found that the sepsis rate seemed to be uninfluenced by the observed reductions in the levels of air contamination. They conceded, however, that the simultaneous use of skin disinfection possibly obscured the beneficial effects of improved air hygiene.

In a surgical ward, oiling of the floor and fabrics produced a reduction in bacterial air counts, but the infection

rate was the same as in a control ward (Clarke et al., 1954). The investigators pointed out, however, that the two wards were not entirely comparable.

Very recently, Mortimer et al. (1966) investigated a maternity nursery which was divided into two sections; in one, the infants were nursed 'in such a way that organisms from infant carriers could be transmitted to them only via the airborne route.' Between 6 and 10 per cent of the exposed infants acquired the prevalent Staph. aureus. 'In contrast, 126 infants who were handled by nurses who also handled the neighbouring carrier babies with little or no handwashing exhibited a 43 per cent rate of acquisition of carrier strains.' The investigators concluded that 'airborne organisms probably account for only a small proportion of staphylococcal transmission in the nursery.'

The importance of environmental sources of infection has also been questioned for different reasons. These relate to the possibility that pathogenic bacteria in the dried state may lose their infectivity while remaining viable. Evidence of this in the case of Strep. pyogenes was provided by Rammelkamp et al. (1958). They showed that group A streptococci when dried on blankets and in dust apparently lost their ability to infect human volunteers. Comparable experiments producing similar results have been carried out more recently with Staph. aureus in mice (Hinton, Maltman and Orr, 1960). In these tests, however, an old stock strain ('Wood 46') was used; Rountree (1963) has subsequently shown that this strain does not survive

desiccation as readily as do 'epidemic' strains of groups I and III (vide p.229). Less direct evidence of a loss of pathogenicity is provided by Arseni and Vasiloglou (1964) who reported that airborne Staph. aureus produced lower titres of coagulase than identical types isolated from human infections. Nevertheless, other investigators (e.g. Colbeck, 1960; Rountree, 1963) have found that Staph. aureus remains infective for prolonged periods in the dried state; and, recently, Rammelkamp and his colleagues have repeated their original experiments using fabrics contaminated with Staph. aureus in a maternity nursery. Their results show that staphylococci dried onto shirts and other textile goods can still colonize newborn infants after storage at room temperature for six days (Gonzaga et al., 1964).

On the basis of his own observations, however, Shooter (1965) has declared 'that once a staphylococcus has been shed by a patient it has lost much of its ability to cause new infections after 24 hours.' A rapid decrease in the pathogenic potential of viable staphylococci could, therefore, be another important factor underlying the relatively low infection rate in the Maternity Department of this hospital in the face of mounting environmental contamination. It could also explain the absence of further infections with the epidemic group I staphylococcus despite its prolonged presence in the General Medical Department.

Although the infectivity of pathogens which have been present in the environment for long periods of time is still

controversial, recent contamination is to be regarded as a source of danger to patients. The bacterial load to which patients are exposed in hospital must be reduced as far as possible, but the measures to be used need to be realistic ones that will neither be neglected by members of staff nor impose an excessive burden on them. Enthusiasms which are not soundly based on scientific observation must be discouraged. Thus, there has been a recent trend to abandon woollen blankets, in spite of the demonstration that these can be readily disinfected by heat at sub-atmospheric pressures (Alder and Gillespie, 1961), and despite the fact that the fibres in infected hospital dust consist mainly of cellulose, as was shown by Pressley (1958) and confirmed in the present study. Furthermore, the fibrous component of dust is probably of limited importance as a vehicle of infection (p.350).

Whereas general measures such as dust suppression and improved ventilation may be useful adjuncts, environmental contamination is best prevented at its source - the sites of bacterial multiplication in the human host. A plea has already been made for a rational isolation policy to allow the removal of individuals who seem most likely to contaminate the environment, as well as those most susceptible to infection. The menace of dispersal by a patient with a staphylococcal chest infection was demonstrated in the general medical ward, while the ease with which an intestinal infection may spread was shown in the outbreak of dysentery among paediatric patients. Skin infections have been regarded for many years as another dangerous source of bacterial contamination in hospital; and

the early interest in skin scales as one of the main vehicles of air-borne infection has been re-awakened by the work of Davies and Noble (1962; 1963). It seems likely that dissemination of Staph. aureus occurs principally from the umbilical stump and other skin sites in newborn infants (Hurst, 1965), while prolific sources of this and other hospital pathogens in older patients include burns (Lowbury, 1960a) and both healthy carrier sites on the skin and infected skin lesions (Hare, 1963). The design of the present investigation in the general hospital did not permit a detailed study of bacterial dispersal from skin; this subject, however, forms the central theme of the final section of this thesis.

Part II

STUDIES IN A GENERAL HOSPITAL

(v) SUMMARY

II (V)

SUMMARY

Over a 12-month period, all clinical infections which developed in the main departments of a large general hospital were investigated bacteriologically. Parallel studies of bacterial contamination of the environment were carried out in these departments, and a detailed comparison was made between pathogenic bacteria isolated from lesions and from the environment.

Infections were present on admission in 6.4 per cent of the 7,360 patients included in the investigation. Among paediatric medical patients, however, 35.6 per cent of admissions were on account of infection.

During their stay in hospital, 1,231 patients (16.8 per cent) developed bacteriologically confirmed infections. Staph. aureus was responsible for only 28 per cent of these, and Gram-negative bacilli accounted for most of the remainder.

The maternity wards and nurseries had the lowest incidence of acquired infection (10.7 per cent), although the nurseries had the highest proportion of staphylococcal sepsis in the hospital. The General Surgical Department had the next lowest total sepsis rate. In contrast, hospital infection was relatively common in the medical, urological, gastro-enterological and paediatric units (with rates ranging from 18.8 to 37.5 per cent).

In the paediatric wards, as in the maternity nurseries,

superficial infections predominated, whilst urinary and chest infections were especially prominent in the adult wards, and affected mainly those patients who were already debilitated. Many of the urinary infections in uncatheterized women appeared to be of exogenous origin on the basis of species identity and drug sensitivities. In the urological ward, the very high incidence of urinary infection was associated with surgical intervention; and almost all patients in these and in the gynaecological wards who were on continuous bladder drainage became infected. The strains of Ps. pyocyanea isolated from these and other infections were shown by bacteriophage typing to have been acquired in the hospital.

The incidence of wound sepsis in the General Surgical Department (5.8 per cent) was, with the exception of the maternity wards, the lowest in the hospital, and the infections appeared to be mainly endogenous. In contrast, the wound sepsis rate among paediatric patients was twice as high. Even higher rates were found among the relatively few surgical patients nursed in other departments; cross-infection in the wards seemed to play an important part in these cases.

More than half of the staphylococcal infections in the hospital occurred in the nurseries and adjoining paediatric units. These departments constituted the principal reservoir of an erythromycin-resistant group III staphylococcus which has for several years produced endemic infection throughout the hospital. This organism, though evidently of low virulence, was shown in vitro to possess features which favour its

persistence in the hospital.

There was a general correlation between the environmental 'load' of Staph. aureus and the frequency of staphylococcal infections in the various departments; the maternity wards were a notable exception.

In addition to Staph. aureus, large numbers of Gram-negative bacilli were isolated from the hospital environment. Notable sources were baths and settled dust; most of the latter consisted of cellulose (cotton) fragments and epidermal scales.

A virological investigation of 'non-bacterial' sticky eyes in infants produced negative results. Other special studies included a comparison of several in vitro properties of Staph. aureus from human and inanimate sources.

An outbreak of sepsis in the General Medical Department due to a resistant staphylococcus of type 52/52A/80/81 demonstrated the dangers of dispersal from a patient with a chest infection, whilst indirect evidence of dispersal from the intestinal tract and skin was obtained in the paediatric unit and nurseries, respectively.

Part III

STUDIES IN A DERMATOLOGY DEPARTMENT

(i) FOREWORD

(ii) MATERIALS AND METHODS

III (i)

FOREWORD

Towards the end of the period of investigation in the general hospital, Hare and Cooke (1961) drew attention to the possible importance of infected dermatological lesions as a source of bacterial contamination in hospital. These investigators reported that five patients with secondary staphylococcal infection of their skin lesions very heavily contaminated their immediate surroundings with Staph. aureus. Similarly, Thomas and Griffiths (1961) during their brief survey of bacterial air counts in Guy's Hospital observed particularly high counts of Staph. aureus in two small wards which housed patients with skin diseases.

Following these preliminary reports, the present investigation was started in the Dermatology Department of a large teaching hospital. The work was designed to test the hypothesis that dermatological wards could serve as ideal models for the planned, long-term study of hospital cross-infection. Although they had not previously been investigated in detail by a bacteriologist, these wards contain patients who often remain in hospital for long periods of time with extensive, susceptible skin lesions, some of which may become sources of heavy bacterial contamination. Conditions, therefore, seemed to be very favourable for a study of the dynamic relationship which exists between the superficial microflora of patients and the bacteria in their environment.

III (ii)

MATERIALS AND METHODS

Ward Accommodation

The Dermatology Department is attached to a large teaching hospital and is housed in a separate and relatively modern building which was erected in 1936. The ground floor consists of the out-patient department. The three wards for in-patients are on the third floor and fourth (top) floor of the building. The third floor contains a large ward of 16 beds for female patients and a smaller ward of 8 beds for male patients. On the top floor there is a large ward of 16 beds for male patients. Both large wards are of the same shape and size, being 68 ft. long, 28 ft. wide and 12 ft. high (22,848 cu.ft.). The smaller ward is 32 ft. long, 28 ft. wide and 12 ft. high (10,752 cu. ft.). Bed centres are between 7 ft. and 10 ft. apart. The communal bathroom attached to each large ward contains two baths and is 12 ft. long, 7 ft. wide and 12 ft. high in each case. The dayroom adjacent to each large ward is 18 ft. long, 12 ft. wide and 12 ft. high. Ventilation throughout is dependent on the opening of doors and windows.

The Investigation of Out-patients

During the first three months of 1962, the bacterial flora of skin lesions was studied in out-patients on their first appearance at the clinic. A swab moistened with sterile 3.8 per cent sodium citrate solution was rubbed over a

representative area of the skin condition in each patient (sampling approximately 4 sq. in.). The dermatologist at this time entered on a card the clinical diagnosis, including the presence or absence of clinical infection (the three categories agreed upon were 'infected lesions', 'non-infected lesions' and 'doubtful infection'). The swabs were examined by the author in the laboratory without any knowledge of the clinical diagnoses.

The Collection of Specimens from In-patients and Staff

From mid-February 1962 until May 1964, swabs of skin lesions were collected from all in-patients entering the department. The swabs were taken at the time of admission, in the manner described for out-patients. At the same time nasal swabs were collected (as described on p.98.). Thereafter paired swabs were taken at weekly intervals from patients until their discharge from hospital. During the first few months of the study 'skin maps' were also prepared by means of self-adhesive cellulose tape (p.92.).

During the first year of the investigation nasal swabs and hand impressions (p.98.) were taken from members of staff at intervals of approximately two weeks. No prior warning was given, in order to obtain a true picture of hand contamination.

With very few exceptions, the swabbing of in-patients and members of staff was personally conducted by the author to ensure standardised techniques.

The Ascertainment of Clinical Infection

At the time when swabs were taken, in-patients were examined in the presence of a member of the medical staff - usually the Senior Registrar, Dr. D. Chalmers. His decision was accepted both on the diagnosis of each patient's skin condition and on the presence or absence of clinical infection. This clinical information was entered on the index cards that were kept in the laboratory for each patient.

In a number of non-infective skin conditions that are characterized by exudate or inflammation an erroneous diagnosis of 'clinical infection' might readily be made without the guidance of an experienced dermatologist.

The Bacteriological Examination of the Environment

Detailed sampling was performed throughout the Department from February 1962 to May 1962, inclusive; from September 1962 to March 1963, inclusive; and from October 1962 to May 1964, inclusive. The three wards and their associated bathrooms and patients' dayrooms (described on p.244.) were examined on two days each week. Different sampling days were, however, chosen each week to obtain representative data.

Air sampling was carried out during four two-hourly periods at the centre of each room as described in Part II, but the sieve sampler was not used in these later investigations. The methods of examining solid surfaces and fabrics

were also the same as in the earlier study. During 1964, however, several additional procedures were introduced.

A size-grading impaction sampler (Figure 25) was constructed in the University Department of Bacteriology according to the specifications of Lidwell (1959). This apparatus was used mainly in the tests on individual patients described below, but occasional air sampling was carried out with it in the wards, to obtain information on the size distribution of infected air-borne particles.

The Study of Bacterial Dispersal from Individual Patients. In these tests a wooden cubicle was used with internal dimensions of 6 ft. 6 in. high, 3 ft. wide and 2 ft. 6 in. deep (48.75 cu. ft.). The door contained an observation window and could be fitted tightly by means of clamps. A Casella slit sampler was connected to the chamber by a metal hose which penetrated the side wall at the rear; in addition, the size-grading sampler was placed inside the front right-hand corner of the chamber.

A standard procedure was adopted for tests on individual patients. Immediately before the patient entered the cubicle, the slit sampler was operated for two minutes to obtain the residual air count. The patient was then asked to enter the cubicle, remove his dressing gown and hand this outside the cubicle. Male patients also removed their pyjama jackets. The door was closed, and the patient, who was seated on a stool for a period of five minutes, went through the motions

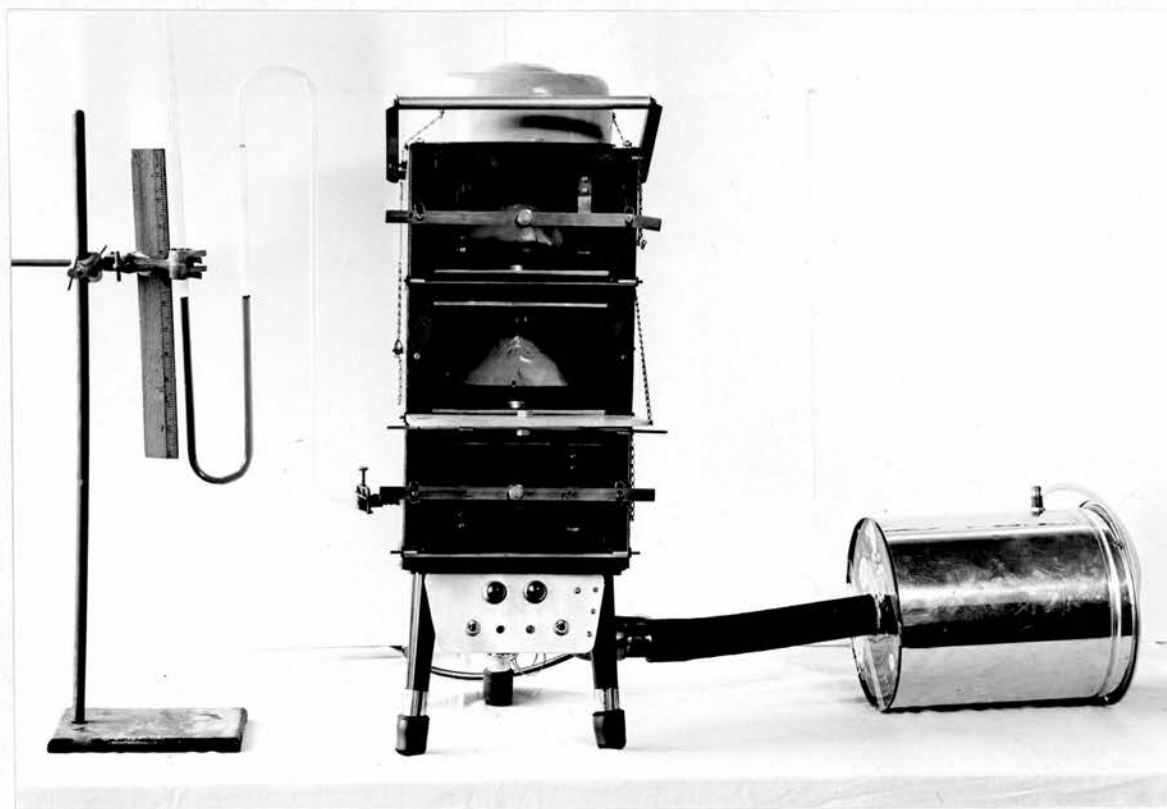


FIGURE 25. THE FOUR-STAGE SIZE-GRADING IMPACTION SAMPLER.

A simple manometer is attached on the left-hand side and the pump motor is connected to the sampler on the right-hand side. The top stage collects the largest particles ($>18\mu$ diameter) and the bottom stage the smallest ones ($<4\mu$ diameter).

of slowly putting on and removing his clothes. The slit sampler was operated for the last two minutes of the period of activity, and thereafter at two intervals of five minutes after the patient had left the cubicle. The size-grading sampler was operated for the last minute of the period of activity. The cubicle was used only once each day. A few hours before use the ward maid removed all visible dust from the interior by means of a vacuum cleaner. The internal surface was then lightly smeared with spindle oil to minimise any subsequent dust raising. At infrequent intervals the whole interior was washed with a freshly-prepared mixture of detergent and Chlorox as recommended for baths by Boycott (1956). To obtain comparable results, each patient was examined approximately one hour after the daily bath and before any skin dressings had been applied. Night-clothes were usually changed every few days, but the ward dressing gowns were changed and washed at very irregular intervals (approximately once each month in the case of long-stay patients).

Tests to Identify the Vehicle of Air-borne Infection. While the investigation was in progress, Davies and Noble (1962) reported the presence of numerous epidermal scales in the air of general hospital wards. These fragments had been collected by impaction on to grease-coated slides which were then treated with stains. However, when this procedure was attempted in the present study, it was found that the grease films were either damaged or entirely detached during

subsequent staining, and the unstained preparations could not be stored satisfactorily. After examining a number of possible alternatives to grease, the epoxy resin 'Araldite' (Ciba) was found to be ideally suitable. Clean glass slides were coated on one side with the same mixture of resin, 'hardener', 'catalyst' and 'accelerator' as that recommended for embedding tissues in electron microscopy*. The slides were placed on the four stages of the size-grading sampler which was operated both in the occupied cubicle and in the ward. After their removal from the air sampler, the slides were incubated for 48 hours at 56°C in closed boxes thus avoiding dust contamination. When the transparent resin had hardened the films were stained by the method of Pressley as described on p. 94 .

The Isolation and identification of Bacteria

Swabs from lesions were inoculated onto blood agar and salt-milk agar, and were finally broken off and incubated in nutrient broth containing 10 per cent sodium chloride. Milk agar was used both for hand impressions and for plating out nasal swabs. Also, as before, blood agar and salt milk agar were used in parallel as settle plates and in the slit sampler. Blood agar was used alone, however, in all tests upon individual patients.

All cultures were incubated and examined as described

* in the proportions 10: 10:10.4 respectively.

on p.100 et seq. after 72 hours' incubation. Salt-broth cultures showing turbidity were subcultured onto blood agar in those cases where the primary cultures on solid media were negative for pathogenic bacteria. The results of these enrichment cultures were recorded as 'scanty' growths.

The methods already given were used for the identification of pathogenic bacteria; but in the case of Staph. aureus bacteriophage typing was performed according to the modified technique of Blair and Williams (1961). The bacteriophage filtrates were supplied by the Cross-infection Reference Laboratory, Colindale. Strains of Proteus spp. were differentiated on the basis of their interaction when swarming on the same plate, as described by Dienes (1946). Bacteriocine typing was later carried out on representative strains (p.384.).

Anti-bacterial Measures introduced in the Wards

Following the initial period of observation (Stage I) which was February to mid-October 1962, certain anti-bacterial procedures were applied in the two main wards. During the second phase (Stage II) which extended from mid-October 1962 to March 1963 all skin lesions in the main male ward were treated with 'Rikospray Antibiotic.'¹ This is a pressurised aerosol containing 500,000 units of neomycin sulphate, 37,500 units of zinc bacitracin and 300,000 units of colistin sulphate in each canister, suspended in an inert chlorofluoro-

¹ Generously supplied by Riker Laboratories, Loughborough.

hydrocarbon propellant to a total weight of 110 gm. The spray was operated evenly from a distance of between 6 in. and 9 in., and was used before the standard dermatological dressings were applied each morning. During this stage all patients in the female ward carried out nasal disinfection twice daily under the supervision of the ward sister or her deputy. For this purpose 'Soframycin' nebulizers¹ were issued to each patient. The nebulizers contain 1.25 per cent framycetin sulphate and 0.005 per cent gramicidin in an isotonic solution together with the nasal decongestant phenyl-:ephrine hydrochloride (0.25 per cent). The soft plastic container was squeezed to project into each nostril a spray of about one second's duration. In addition to nasal disinfection, the two baths adjacent to the female ward were disinfected and cleansed between each period of occupation using one ounce of concentrated hypochlorite solution ('Chloros', I.C.I.) mixed with the same volume of liquid detergent ('By-prox', I.C.I.) in a gallon of hot water. The method was essentially that of Boycott (1956).

During Stage III (early October to late December, 1963) all lesions in the female ward were treated with the antibiotic aerosol. No special measures were applied in the main male ward.

In the final stage (IV), which extended from the end of December 1963 to May 1964, no special procedures were carried

¹ Generously supplied by Roussel Laboratories, London.

out. This phase therefore corresponded to Stage I, with observations being made in an unmodified environment.

When antibiotic spraying was in progress, carry-over of active substances was avoided by swabbing immediately before the spray was applied. Moreover, when no growth was obtained from both the solid and liquid media, minimal inocula (< 100 cells) of a sensitive strain of Staph. aureus were introduced into the salt broth tubes. Following re-incubation, growth occurred in all cases.

Special studies Arising out of the Main Investigation

- (a) The Application of Bacteriocine-typing to the Identification of Proteus
- (b) The Evaluation of Polynoxylin in Nasal Carriers of Staph. aureus.

The methods used in both of these studies are given in the Appendix (pp.384-90).

- (c) The Use of Hexyl-resorcinol for the Disinfection of Air in a Dermatology Department.

Several investigators have found hexyl-resorcinol vapour to be a satisfactory disinfectant against artificially generated clouds of air-borne bacteria (e.g. Mackay, 1952; Darlow, et al., 1958). Because of its reported non-toxicity and rapidity of action, studies were carried out to assess the effect of hexyl-resorcinol on the air contamination which is produced by dermatological patients.

For these tests a room was set aside measuring 15 ft. long, 12 ft. wide and 12 ft. high (2,160 cu. ft.). This room was preferred to the small cubicle as being a more realistic model of the volume of air that an individual disperser will contaminate in his immediate environment. The room was rendered free from draughts, and settled dust was kept to a minimum by the same means as in the case of the special cubicle.

The standard procedure adopted in the studies using the

cubicle were also applied in these tests on air disinfection. All four sets of air samples were, however, taken by means of the size-grading sampler. Immediately after the patient's period of activity, 0.25 ml. of an alcoholic solution of hexyl-resorcinol (40 mg./ml.) in an aluminium capsule was vapourised on the top of a small electric hotplate. This produced in less than one minute an air concentration of approximately 5 μ g. of hexyl-resorcinol per cu. ft. of air. Relative humidity readings were taken with a hair hygrometer; the disinfection tests were carried out only when values of above 50 per cent were recorded. On several occasions a pan of water was boiled in the room to obtain a satisfactory humidity. The room was allowed to remain unused and was freely ventilated for at least one day between tests.

Each alternate test was carried out without the use of air disinfection. In this way further data were also accumulated on the spontaneous decline in bacterial counts following contamination of the air.

(d) Laboratory Tests on Chemical Disinfectants used in the Hospital.

Several chemical agents of unknown activity were in use in the Dermatology Department, for the disinfection of drinking glasses and other ward utensils, as well as for baths and surfaces such as trolley tops and floors. The unrealistic nature of the standard tests for disinfectants (Report, 1965c) led to an exploration of alternative methods for assessing the

bactericidal and virucidal activity of these agents. The methods used and the results obtained are summarised in the Appendix (pp. 391-9).

Part III

STUDIES IN A DERMATOLOGY DEPARTMENT

(111) RESULTS

III(111) Studies in a Dermatology Department:

Results

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¹Details given in the Appendix

RESULTS

Bacterial Infections of the Skin Lesions of Out-patients

The incidence of bacterial infection in the skin lesions of 331 unselected new out-patients was studied clinically and bacteriologically. The results of the two independent methods of examination are compared in Table XXVII. Positive cultures are included in the Table only when 'moderate' or 'profuse' growths of pathogenic bacteria were obtained. As shown, a clinical diagnosis of infection was made in 31 cases, and, of these, 23 yielded significant cultures. The discrepancy here may be partly explained by the presence of antiseptic dressings on the lesions of several of the clinically infected patients. In the remaining 300 cases a firm diagnosis of infection could not be made on clinical grounds, and yet the lesions of 83 of the patients (27.6 per cent) yielded significant bacterial cultures. Subclinical infection was particularly common in the large group of patients with eczema; and significant cultures were obtained from rather more than one-third of those who showed no clinical evidence of infection.

Staph. aureus predominated in 90 of the 106 infected cases. Twelve of the remaining 16 cases yielded profuse growths of non-haemolytic streptococci. Heavy growths of Proteus vulgaris were obtained from the lesions of three patients whose dermatological diagnoses were squamous cell carcinoma, extensive naevi and post-traumatic infective eczema,

TABLE XXVII. CLINICAL AND BACTERIOLOGICAL DIAGNOSES OF INFECTION IN THE SKIN LESIONS OF NEW OUT-PATIENTS.

DERMATOLOGICAL DIAGNOSIS	NO. OF CASES	CLINICAL ASSESSMENT OF INFECTION (SIGNIFICANT BACTERIAL CULTURES IN PARENTHESES)		
		'INFECTED'	'DOUBTFUL INFECTION'	'NON-INFECTED'
Eczema	115	9(8)	39(21)	67(23)
Naevi	18	0	0	18(2)
Psoriasis	16	0	0	16(1)
Acne	15	2(0)	7(1)	6(1)
Warts	14	1(1)	0	12(1)
Pityriasis rosea	12	0	1(0)	11(2)
Alopecia	11	0	0	11(1)
Impetigo	10	9(7)	0	1(0)
Rosacea	10	0	3(1)	7(1)
Besnier's prurigo	9	1(1)	1(0)	7(4)
Skin carcinoma	9	1(0)	5(2)	3(2)
Dermatitis *	8	0	1(0)	7(2)
Sebaceous cysts	6	0	0	6(1)
Herpes simplex	5	3(1)	1(1)	1(0)
Drug eruption	5	0	1(0)	4(1)
Eczematide	5	0	2(1)	3(2)
Molluscum contagiosum	4	0	0	4(1)
Lichen planus	4	0	0	4(0)
Tinea	4	1(1)	1(0)	2(1)
Scabies	3	0	0	3(1)
Paronychia	3	0	2(0)	1(0)
Lichen simplex	3	0	0	3(0)
Urticaria	3	0	0	3(0)
Fibroma	3	0	0	3(0)
Furunculosis	3	3(3)	0	0
Miscellaneous [†]	33	1(1)	2(1)	30(8)
TOTALS	331	31(23)	66(28)	234(55)

* Including neurodermatitis, traumatic dermatitis and dermatitis artefacta.

† Conditions encountered on one or two occasions only.

respectively. A profuse culture of Esch. coli was obtained from another case of eczema.

Antibiotic sensitivity tests were carried out on 115 strains of Staph. aureus, including 25 that were obtained from lesions as scanty growths only. Although the strains were isolated from a non-hospital population 46 per cent were resistant to penicillin, 13 per cent were resistant to tetracycline, and 7 per cent were resistant to streptomycin. Of the 90 strains from 'significant' cultures, 47 were in bacteriophage group III, 19 in group II and 7 in group I (the remaining 17 could not be typed with the standard set of filtrates). The well-known association between impetigo and Staph. aureus of bacteriophage group II (p.49.) was observed in only four of the seven cases from which the organism was isolated.

Bacterial Contamination of the Ward Environment.

Air-borne Bacteria. The mean morning air counts of Staph. aureus in the three wards and in the main bathrooms are represented in Figures 26 - 28. Total bacterial counts are not depicted in the histograms and were less subject to fluctuation than were the levels of Staph. aureus. A large proportion of the total counts usually consisted of saprophytic bacteria, notably spore-bearing bacilli and micrococci, many of which were probably derived from non-human sources. Although Staph. aureus generally constituted between 2 and 5 per cent of the total counts, higher percentages were frequently encountered, and there were several occasions in the bathrooms when over 40 per cent of the total air count consisted of Staph. aureus.

In the absence of anti-bacterial measures, the morning air counts of Staph. aureus were consistently high. This was the situation in the small ward throughout the study (Figure 28), and in the main wards and bathrooms before mid-October 1962 and after December 1963 (Figures 26 and 27). It was found, however, that the levels of air-borne Staph. aureus - but not of saprophytes - fell markedly during the periods when the skin lesions were receiving anti-bacterial treatment (Stage II in the male ward, and Stage III in the female ward). In contrast, the intensive application of nasal disinfection in the female ward during Stage II produced no significant changes in the levels of air-borne Staph. aureus.

Unusually high, transient air counts of individual phage

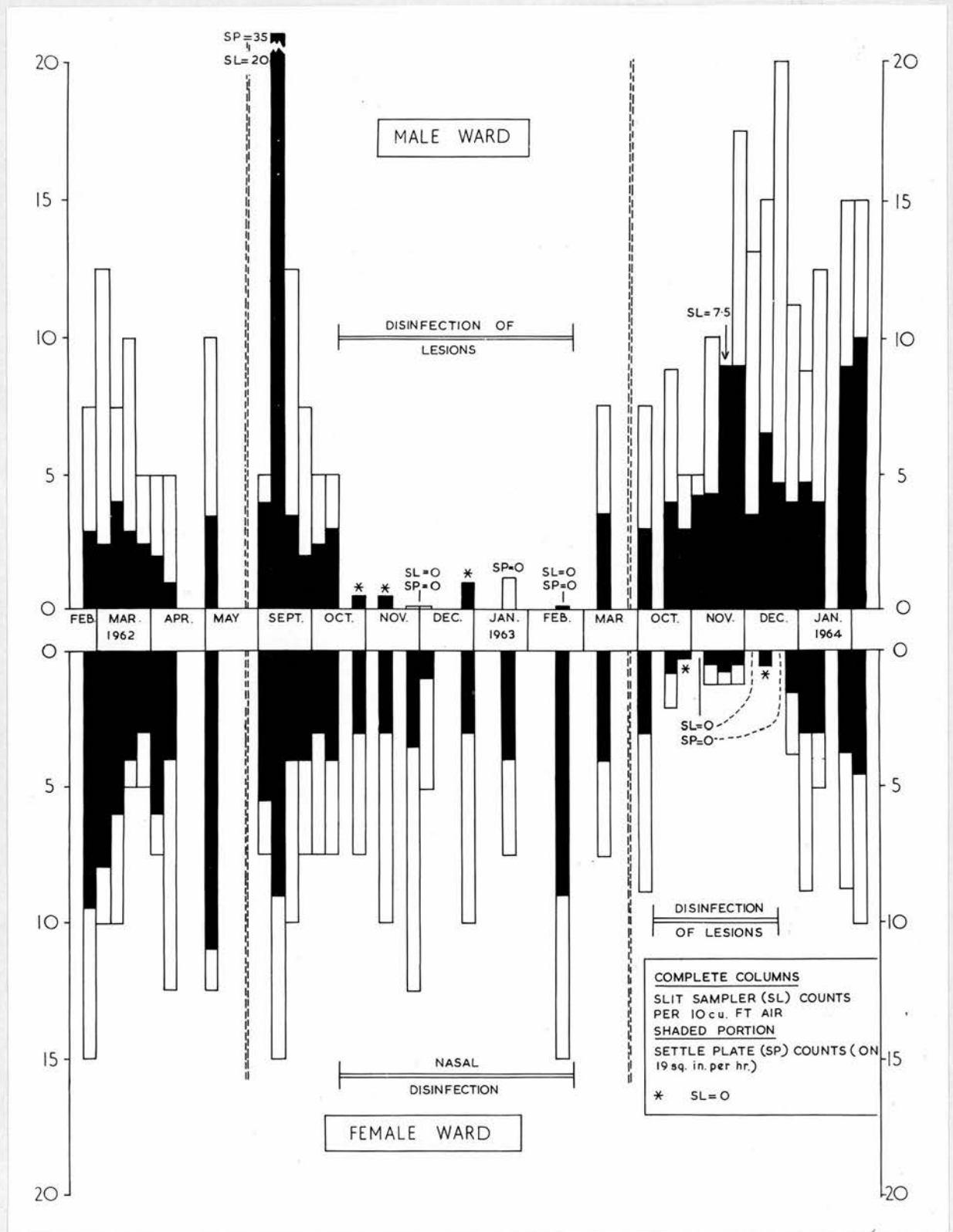


FIGURE 26. THE TRENDS IN THE MEAN MORNING AIR COUNTS OF STAPH. AUREUS IN THE TWO MAIN WARDS.

The counts were persistently high for the remainder of the observation period (i.e. until late May 1964).

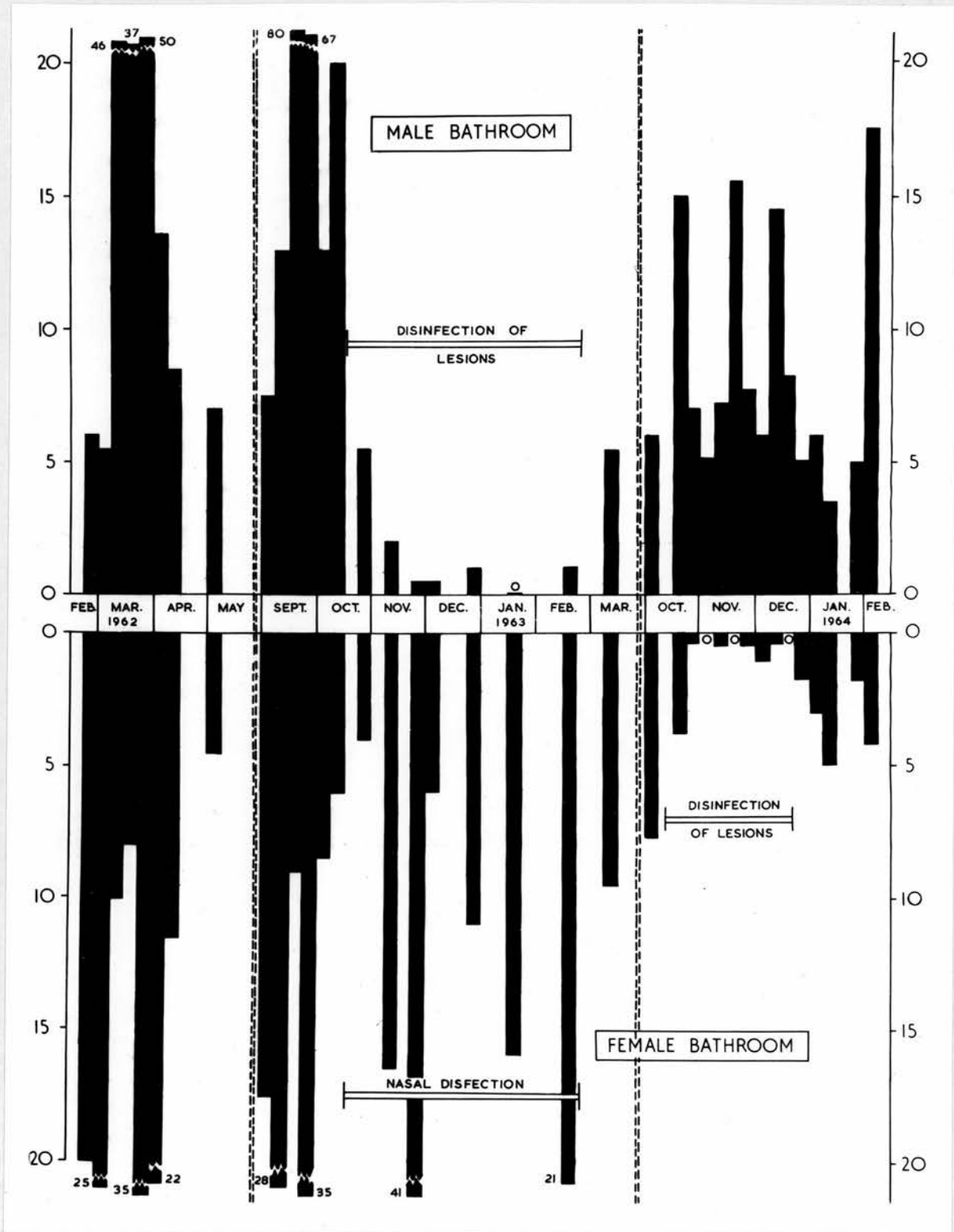


FIGURE 27. THE TRENDS IN THE MEAN MORNING AIR COUNTS OF STAPH.AUREUS IN THE MAIN BATHROOMS.

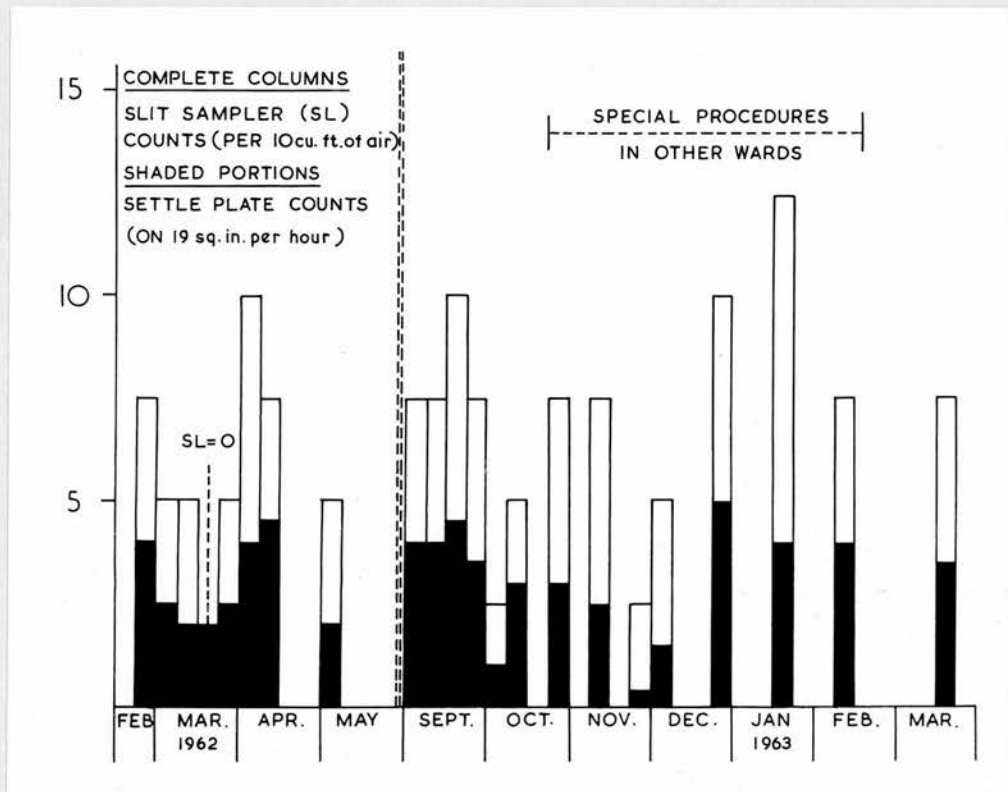


FIGURE 28. THE TRENDS IN THE MEAN MORNING AIR COUNTS OF STAPH. AUREUS IN THE SMALL WARD.

(This ward was not in continuous use after March 1963).

types of Staph. aureus were frequently encountered, particularly in the bathrooms (Figure 29). These 'broadcasts' were probably caused by individual dispersers of infection; in retrospect the episodes could often be correlated with the presence, during the sampling period, of individual patients known to have had infected lesions at the time.

Other potentially pathogenic bacteria were isolated from the air intermittently. They included coliform bacilli, Pr. mirabilis, Ps. pyocyanea and non-haemolytic streptococci. Once again the bathrooms were the richest source (e.g. Figure 30). These miscellaneous bacteria, when present, constituted up to 10 per cent of the total air count.

The diameters of air-borne particles carrying Staph. aureus were estimated after determining the Petri ratios (Lidwell, 1948). By this method the diameters were found to range from 4μ to over 50μ during individual air sampling periods. The mean particle diameter in the female ward was 11.1μ ; in the main male ward it was 10.7μ ; and in the small ward it was 10.0μ . The wide scatter in individual samples was confirmed by direct observations using the size-grading sampler (Figure 31). The largest number of colonies was usually obtained in either the second or third fractions ($4 - 10\mu$ and $10 - 18\mu$); but substantial counts of Staph. aureus as well as of non-pathogenic bacteria were also obtained in the other two fractions (i.e. $<4\mu$, and $>18\mu$).



FIGURE 29. SETTLE PLATE (SALT-MILK AGAR) FROM THE MALE BATHROOM.

(The central area of the plate is shown,x2. Staph.aureus which was in the majority on this plate was of two phage types — corresponding to the pale and more deeply-pigmented colony types).

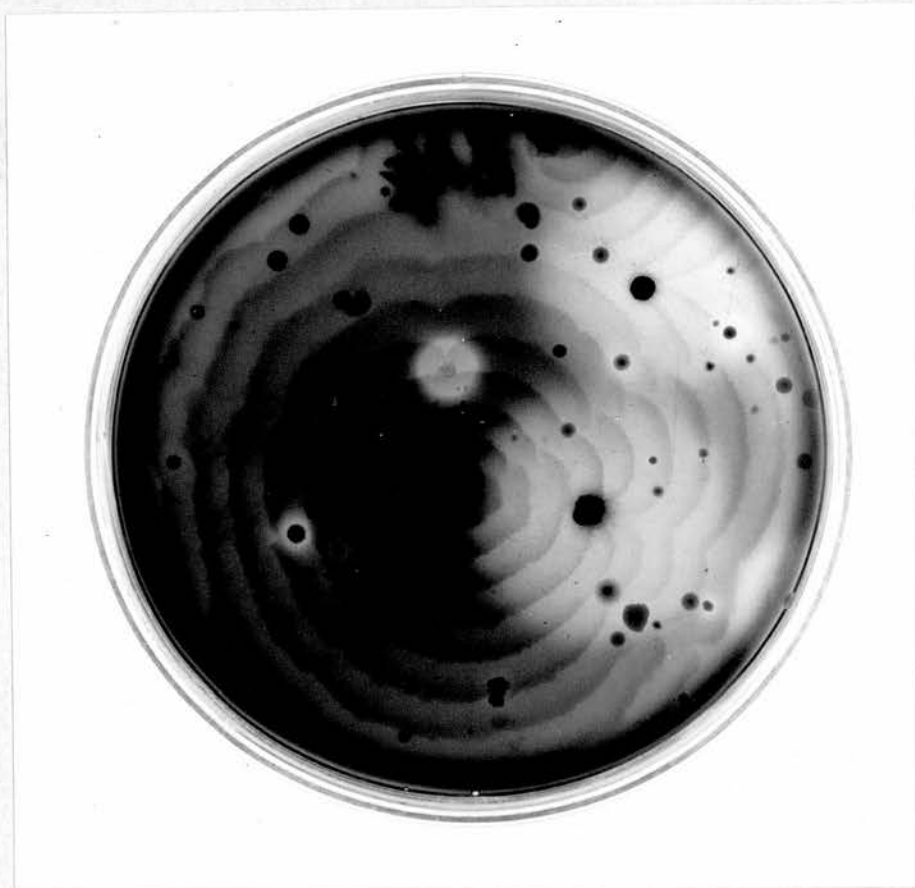


FIGURE 30. SETTLE PLATE (BLOOD-AGAR) FROM THE FEMALE BATHROOM.

(Two colonies of Pr.mirabilis have swarmed over staphylococci and other organisms).

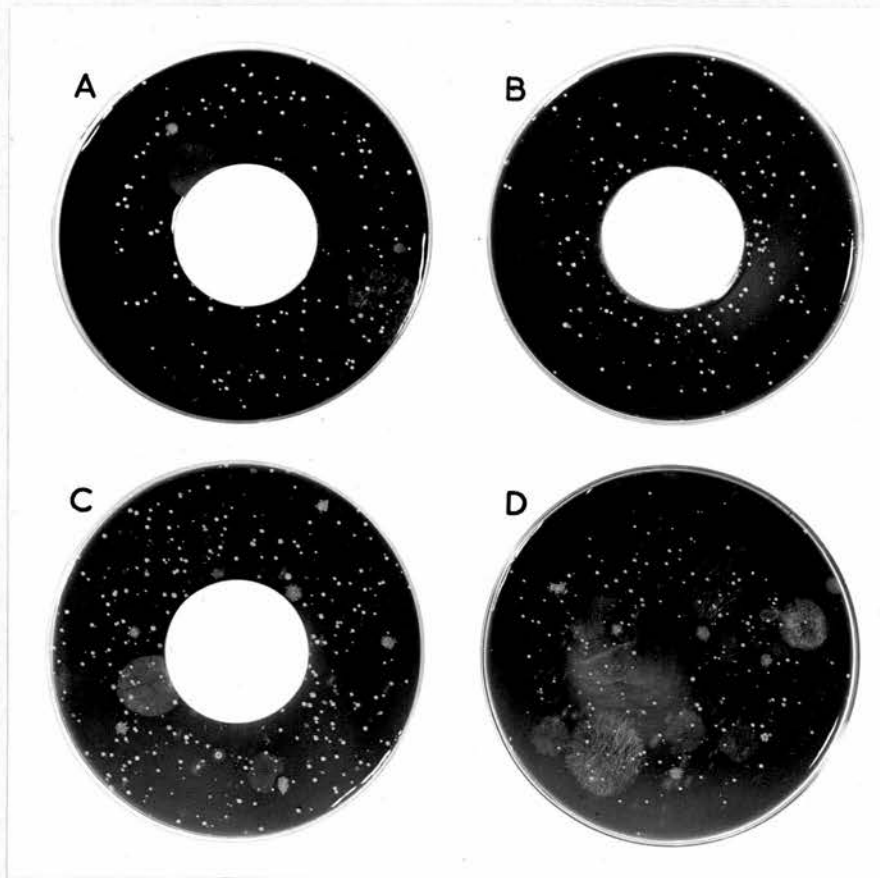


FIGURE 31. A SET OF BLOOD AGAR PLATES OBTAINED FROM THE SIZE-GRADING SAMPLER AFTER OPERATING IT FOR ONE MINUTE IN THE MALE WARD.

(Fraction A = $>18\mu$ particle diameter; B = $10 - 18\mu$;
C = $4 - 10\mu$; D = $<4\mu$).

Ward Surfaces. Heavy growths of Gram-negative bacilli were obtained from settled dust in the wards. Counts of both Ps. pyocyanea and coliform bacilli reached the order of 10,000 organisms per ml. of broth washings on several occasions; but only two samples yielded Proteus spp. (Pr. mirabilis) and these gave counts of less than 100 per ml. The predominant pathogen in almost all samples was, however, Staph. aureus. The maximum count of this organism was 600,000 per ml. of washings, and the mean count was 15,000 per ml. in dust from the two main wards during the stages when lesions were not receiving antibacterial treatment. In contrast, eight days after the introduction of such treatment the counts of Staph. aureus were found to be 5 per ml. in Stage II, and 20 per ml. in Stage III. The levels of non-pathogenic bacteria, however, remained relatively constant around a mean count of 40,000 per ml. throughout the two-year period from February 1962 to February 1964.

Specific staining of the dust samples revealed a predominance of cellulose fibres amongst the formed material. The dust was, however, mainly composed of amorphous protein material which resembled desquamated epidermal debris. When ignited in a crucible the dust always produced a strong odour of burning keratin.

During the periods when the air and settled dust were contaminated with Staph. aureus, this organism was readily isolated from such varied objects as taps, dressing trolleys, door handles and television set controls, all of which were frequently handled by patients or members of staff.

In connection with ward outbreaks of upper respiratory tract infections (p.281.), 30 drinking glasses and 30 water carafes were examined bacteriologically before they were issued to patients in the female ward. Six of the glasses had a dried film around each of their rims. Moist swabs rubbed over these yielded, in 4 cases, scanty growths of Strep. viridans, accompanied in two of the cases by diphtheroid bacilli. The rims of 3 other glasses yielded bacteria which were judged to be of upper respiratory tract origin. Swabs taken from the outer surface of each carafe, where it makes contact with the drinking glass, produced negative results. It was found that these utensils were washed after use by dipping them for a few seconds into a basin of tepid water containing a liquid detergent (p.395). They were then dipped into fresh water, and were usually left to dry in air.

Bedding. Once during each of the four stages the bedclothes on all occupied beds were examined bacteriologically. A note was taken in each case of the length of time since the previous change of bedding. "Positive cultures" (p.93.) were obtained from the bedding of 65 out of 104 patients whose skin lesions were not receiving anti-bacterial treatment. Two moderate growths of Ps. pyocyanea and one of Pr. mirabilis were obtained from sheets. All the other positive cultures were of Staph. aureus. In 20 cases the bedding yielded strains of Staph. aureus that were not found in the skin lesion or nose of the bed occupant.

Most of the profuse bacterial growths were derived from

sheets: pillow cases were the next most abundant source, while the woollen blankets, which yielded Staph. aureus in 42 of the tests, produced heavy cultures on four occasions only. Positive cultures, including profuse growths, were obtained from sheets and pillow cases within three hours of a change of bed-linen; sporadic tests on bedding received from the laundry were, however, negative for pathogenic bacteria.

The bedding of 29 patients was tested during periods when the disinfection of skin lesions was in progress. Scanty cultures of Staph. aureus were obtained from the blankets of three beds, and from the top sheet of one of the beds.

Among the miscellaneous items also tested, particular attention was paid to lotions and creams that were used in the wards. No pathogenic bacteria were isolated from these.

Communal Baths. As shown in Table XXVIII, significant cultures of pathogenic bacteria were obtained on 72 occasions out of 84 after the baths had been 'cleansed' during Stage I. In 18 of the cultures pathogenic Gram-negative bacilli predominated (Figure 32). This heavy contamination occurred despite the addition of 1 fl. oz. of cetrimide solution B.P. to the bath water of each patient. Serial tests on individual baths between successive patients confirmed that a cumulative process of contamination was taking place.

The cleansing of the male patients' baths was very unsatisfactory throughout the four stages. The incidence and degree of contamination was, however, much reduced during stages when

TABLE XXVIII. SIGNIFICANT CULTURES OF PATHOGENS OBTAINED FROM THE COMMUNAL BATHS.

WARD	STAGE	NO. OF TESTS	POSITIVE CULTURES*	
			BEFORE CLEANSING	AFTER CLEANSING
Male	I	42	-	37(10)
	II	30	9(5)	6(4)
	III	44	36(5)	22(4)
	IV	30	25(4)	14(0)
Female	I	42	-	35(8)
	II	30	21(1)	2(1)
	III	44	8(1)	1(0)
	IV	30	18(5)	4(0)

Figures in parentheses refer to numbers of cultures with predominant Gram-negative bacilli.

- = not done.

* Two or more colonies of Staph. aureus or pathogenic Gram-negative bacilli from a 2 sq. in. transfer strip.

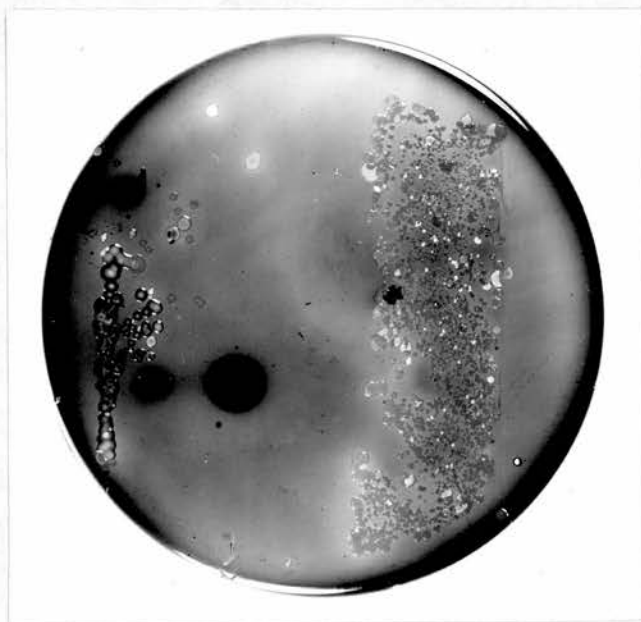


FIGURE 32. 'TAPE-TRANSFER' CULTURES ON BLOOD-AGAR FROM TWO BATHS (ADJACENT TO THE FEMALE WARD).

On the right-hand side the growth is mainly of Staph.aureus (of which there were two separate phage types). On the left-hand side coliform bacilli and 3 colonies of Ps.pyocyanea grew in addition to several colonies of Staph.aureus.

skin lesions were being disinfected. The results of tests on the female patients' baths during Stage II show the effectiveness of Boycott's method of cleansing. This procedure was voluntarily continued during stages III and IV in the female bathroom, but was not always adequately applied, as the results indicate.

Following the end of Stage IV, intermittent air sampling was carried out in connection with studies that are not described in this thesis. The air counts of Staph. aureus remained consistently high until sampling was discontinued in January 1966. Pr. mirabilis was also frequently isolated from the air during 1965.

The Acquisition of Infection by Patients

The average duration of stay was 39.2 days, and the average age of the patients was 45 years.

Skin Lesions. Table XXIX summarises the bacteriological findings in 342 patients who remained in hospital for more than one week. 'Moderate' or 'heavy' cultures of pathogenic bacteria were obtained at the time of admission from 152 of the patients (45 per cent). Staph. aureus predominated in the lesions of 129 of these and Gram-negative bacilli were predominant in 21 cases. These consisted of 6 infected with Proteus spp., 5 infected with Ps. pyocyanea and 10 infected with coliform bacilli (which grew in mixed culture with a smaller proportion of Ps. pyocyanea in 3 cases). Typical Esch. coli predominated in only 3 of these

TABLE XXIX. PRE-EXISTING AND HOSPITAL-ACQUIRED INFECTION IN SKIN LESIONS

WARD	STAGE	NO. OF PATIENTS	NO. WITH INFECTION			
			UPON ADMISSION	ACQUIRED IN HOSPITAL		
				PRIMARY CROSS INFECTION	SUPER-INFECTION	AUTO-GENOUS
Male	I	46	20(1)	11(1)	8(2)	4
	II	37	14	1(1)	0	0
	III	30	11(1)	*12(1)	4	1
	IV	37	18*	6	5(1)	3
Female	I	45	21(3)	7(3)	11(2)	3
	II	44	21+(6)	8(2)	10(6)	0
	III	28	13(4)	0	0	1
	IV	40	17(3)	12(1)	3(2)	2
Small	I	17	6(1)	4(1)	2	2
	II	18	11(2)	4	5(1)	0
TOTALS		342	152(21)	65(10)	48(14)	16

Figures in parentheses refer to numbers of cultures with predominant Gram-negative bacilli.

+ Including one case of varicose ulcer infected with Candida albicans together with Staph. aureus.

* Including one case of eczema infected with group A streptococci (Staph. aureus predominated in the remaining infections).

cases.

During their stay in hospital, 109 out of 233 patients (43 per cent) were found to have acquired infection of their lesions in the absence of specific counter-measures. Fifteen of the infections were due to strains of Staph. aureus identical with those carried in the patients' noses at the time of admission and they were classified as 'autogenous' infections.

The incidence of hospital-acquired infection of skin lesions was equally high in the female ward during Stage II. Thus despite nasal disinfection and improved cleansing of the baths the lesions of 18 out of 44 patients (41 per cent) yielded significant cultures of pathogenic bacteria that were not present on admission. None of these infections, however, could, be classified as autogenous.

In contrast, during the stages when the lesions received an anti-bacterial spray, only 2 out of 65 patients were found to have acquired infection of their lesions in hospital. In one of the cases the infection was apparently autogenous, the patient being a heavy nasal carrier of an identical strain of Staph. aureus at the time of admission. The second case was due to infection with Pr. mirabilis. Neither of these infections was present when the lesions were next examined one week later.

Out of the total of 129 hospital-acquired infections, 24 (19 per cent) were due to Gram-negative bacilli. Pr. mirabilis predominated in nine of these, and Ps. pyocyanea in eight; the remaining infections were due to coliform bacilli (three were typical Esch. coli and four were classified as Klebsiella spp.).

'Negative' swabs from both in-patients and out-patients were rarely sterile. In most cases they yielded moderate or profuse mixed growths of pigmented micrococci (mainly Staph. epidermidis albus) and diphtheroid bacilli; but occasionally scanty growths were obtained. These wide variations in the counts of normal flora were confirmed in many of the patients by means of 'skin maps' prepared using the sticky-film method. Small numbers of the organisms usually persisted in patients receiving antibiotic sprays. Occasional colonies of Staph. aureus, coliform bacilli and aerobic spore-bearing bacilli were also frequently noted, and these organisms were common in enrichment cultures from swabs.

A comparison between the clinical and bacteriological diagnosis of infection is given in Table XXX. As shown, on 13 occasions a clinical diagnosis of infection made at the time of admission to hospital was not confirmed by the bacteriological examination of the lesion. Nine of these cases were of varicose ulceration and four were of acne. Conversely, a clinical diagnosis of infection was made in only 37 per cent of patients whose lesions yielded significant cultures of pathogenic bacteria on admission. Moreover, out of the 129 cases of hospital-acquired infection diagnosed bacteriologically, only 23 (18 per cent) showed clinical evidence of the infection. The incidence of subclinical infection was particularly high in patients with psoriasis - the commonest dermatological condition in this series. Typical 'skin maps' from one such patient are shown in Figure 33.

In addition to the cases of acquired infection listed in

TABLE XXX. CLINICALLY AND BACTERIOLOGICALLY DIAGNOSED INFECTIONS AMONGST IN-PATIENTS WITH SKIN DISEASES

DIAGNOSTIC GROUPS	NO. OF CASES	NUMBER WITH INFECTION			
		ON ADMISSION		HOSPITAL-ACQUIRED	
		CLINICAL DIAGNOSIS	CULTURE	CLINICAL DIAGNOSIS*	CULTURE
Psoriasis	114	2	39(2)	1	40(2)
Eczema	113	24	56+(7)	15	+49(7)
Varicose ulcer	34	30	21 ^x (10)	2	21(12)
Besnier's prurigo	22	2	12	1	7(1)
Acne	113	4	0	0	1
Drug eruption	7	0	3	0	0
Pityriasis rosea	7	1	3	0	2
Dermatitis herpetiformis	5	0	3	0	0
Mycosis fungoides	5	1	1	2	3
Disseminated lupus	3	0	2	0	1
Dermatomyositis	3	0	2(2)	0	2(1)
Lichen planus	3	0	2	1	1(1)
Impetigo	3	3	3	0	1
Furunculosis	2	2	2	0	0
(Miscellaneous)	8	1	3	1	1
TOTALS	342	70	152(21)	23	129(24)

* Number of previously "clean" cases with signs of infection.

+ Including one case infected with Strep. pyogenes.

x Including one case infected with C. albicans.

(Numbers in parentheses denote infections with predominant Gram-negative bacilli; other cultures predominantly Staph. aureus.)



FIGURE 33. 'TAPE-TRANSFER' SKIN MAPS FROM A PATIENT WITH PSORIASIS.

On the right-hand side the transfer culture is from an area of healthy skin: several colonies of normal skin flora and of Staph.aureus have grown. On the left-hand side the culture is from an adjacent patch of psoriasis, and an almost confluent growth of Staph.aureus has been obtained.

Table XXX, two patients with psoriasis in the male ward developed furunculosis during Stage I; and a patient with eczema in the female ward developed abscesses of the buttocks during Stage II. The prevalent ward strains of Staph. aureus were isolated from these lesions.

The only other clinical infections with a bacterial aetiology that were acquired by patients in the wards were urinary tract infections. These occurred in 4 female patients, none of whom had been catheterized. Two of the infections were during Stage II, and were due to Esch. coli (sensitive to sulphonamides and streptomycin); one in Stage III was due to a sulphonamide-resistant strain of Esch. coli, and the fourth infection was due to Pr. mirabilis. This organism was identical with a 'ward' strain on the basis of antibiotic sensitivities, Dienes' phenomenon and bacteriocine production (p.309). Apart from these cases, there were several small outbreaks of coryzal illness in both of the main wards, affecting a total of 37 patients. Throat swabs were taken from each but no pathogenic bacteria were isolated on blood agar or crystal-violet blood agar. Virological investigations were not performed.

During the two-year period of ^{the} main investigation, 19 patients died in the wards. Ten of the patients were included in the study, and the remaining 9 had been in the Department for less than one week, but in none of the fatal cases was infection an aetiological factor.

Clinical Effects of Spraying Lesions. Although during stages II

and III the spraying of lesions with antibiotics was not designed to provide an objective clinical evaluation of topical antibiotic therapy, it was noteworthy that none of the 65 patients who received the spray developed clinical signs of newly-acquired infection. In comparison, of the 277 patients whose lesions were not sprayed 23 developed clinical infection. A further clinical observation was that in the treated patients signs of infection present on admission had disappeared by the end of the first week. It was felt by the medical staff that this contrasted very favourably with the progress of infected lesions in the larger group of untreated patients.

At the end of Stage IV, ten patients with extensive infected skin lesions were chosen for preliminary tests upon a new anti-bacterial spray. This contained a synthetic chemical agent, oxymethylene-methyl-thiourea ('Noxyflex', Geistlich), which is chemically related to polynoxylin (p.390). The material was supplied as a 0.3 per cent suspension in a pressurized aerosol canister. The spray was applied to lesions on the right-hand side of the midline, and the antibiotic aerosol ('Rikospray') was applied to those on the left-hand side. Swabs were taken daily from a representative area on each side. The sites chosen for swabbing were on the arms or legs, since sprays may reach areas of skin across the midline of the trunk despite careful application. The results are given in Table XXXI. As shown, both sprays appeared to produce satisfactory clearing of pathogenic bacteria within six days, although in four out of the ten cases the synthetic agent acted rather more slowly than the antibiotic mixture. The patients

TABLE XXXI. A COMPARISON OF THE ANTI-BACTERIAL ACTION OF 'RIKOSPRAY ANTIBIOTIC' AND 'NOXYFLEX' SPRAY IN TEN PATIENTS WITH INFECTED SKIN LESIONS.

DIAGNOSIS	PATHOGEN CULTURED	NO. OF POSITIVE DAILY CULTURES FROM	
		RIGHT+	LEFT*
Psoriasis	<u>Staph. aureus</u>	2	2
Psoriasis	<u>Staph. aureus</u>	2	2
Psoriasis	<u>Staph. aureus</u>	3	3
Psoriasis	<u>Staph. aureus</u>	3	3
Psoriasis	<u>Staph. aureus</u>	3	3
Psoriasis	<u>Staph. aureus</u>	5	3
Eczema	<u>Staph. aureus</u>	6	4
Eczema	<u>Staph. aureus</u>	5	4
Eczema	<u>(Pr. mirabilis & coliforms</u>	5	3
Eczema	<u>(Ps. pyocyanea & coliforms</u>	5	5

+ Lesions on the right-hand side were sprayed with 'Noxyflex'

* Lesions on the left-hand side were sprayed with 'Rikospray Antibiotic'.

found both sprays fully acceptable, and there were no complaints of discomfort in this series or in the larger group of patients who received the antibiotic spray during stages II and III.

Nasal Carriage. The incidence of staphylococcal nasal carriage during the four stages is shown in Table XXXII. In the absence of nasal or skin disinfection, 51 out of 233 patients after admission became carriers for the first time or acquired a new strain of Staph. aureus in their noses. During Stage II when antibiotic nebulizers were in use in the female ward, only one patient - who was 82 years of age - out of 44 became a nasal carrier of Staph. aureus. However, during the periods of skin disinfection only one of 65 patients became a nasal carrier, although established carriers usually retained their nasal staphylococci.

In only three patients was nasal colonization by Staph. aureus observed to precede infection of the skin lesions with the same strain. On admission, 150 patients were nasal carriers of Staph. aureus, but only 13 of these - 9 per cent - had significant staphylococcal colonization of their skin lesions during their hospital stay. In contrast, the lesions of 76 of the 192 non-carriers (39 per cent) were colonized by Staph. aureus. Cross-infection with Gram-negative bacilli was relatively as frequent in pre-existing nasal carriers of Staph. aureus as in non-carriers (10 and 14 cases respectively).

'Soframycin' nebulizers produced satisfactory suppression of nasal Staph. aureus in the 17 patients who, during Stage II,

TABLE XXXII. NASAL CARRIAGE OF STAPH. AUREUS IN PATIENTS

WARD	STAGE	NO. OF PATIENTS	NASAL CARRIAGE		
			UPON ADMISSION	ACQUIRED IN HOSPITAL	
				PRIMARY INFECTION	SUPER-INFECTION
Male	I	46	27	5	3
	II	37	17	1	0
	III	30	9	6	0
	IV	37	15	6	3
Female	I	45	26	6	3
	II	44	19	1	0
	III	28	8	0	0
	IV	40	17	6	4
Small	I	17	7	4	1
	II	18	5	3	1
TOTALS		342	150	38	15

were carriers on admission to the female ward. None of the nasal swabs from these patients taken after one week in the ward yielded a 'moderate' or 'profuse' growth of Staph. aureus, although in four of the patients scanty growths of the original strain were obtained after more than one week's application of the nasal spray.

Significant nasal carriage of pathogenic organisms other than Staph. aureus was encountered on four occasions. In one patient, Ps. pyocyanea, which had not been present on admission, was found on successive nasal swabs. Likewise two patients became nasal carriers of Pr. mirabilis, and a third patient was a nasal carrier of this organism at the time of admission. Three other patients temporarily acquired the organism during their stay. In two of the Proteus carriers, 'Soframycin' nebulizers were used but without success, despite in vitro sensitivity of both strains.

The Bacteriological Findings in Members of the Ward Staff.

Persistent nasal carriage of Staph. aureus was found in 21 out of the 49 members of staff who were examined on more than one occasion during the four stages. Nasal carriage developed in four who were initially free from Staph. aureus; these were the only members of staff who were found to be persistent nasal carriers of prevalent ward strains. However, two nurses who were already nasal carriers of other strains became transient carriers of one of the endemic staphylococci.

The Senior House Physician developed severe sycosis barbae from which a strain of Staph. aureus was isolated that differed from those present in the wards at the time, but was identical with the doctor's nasal strain. The only other bacterial infection encountered amongst the staff was in a nurse who developed subacute paronychia. The lesion yielded a profuse growth of Pr. mirabilis which appeared, on the basis of Dienes' phenomenon and bacteriocine production, to be identical with a strain that had been isolated on several occasions in the ward.

A total of 320 hand impressions were taken during the stages of the work when counter-measures were not in use. Two or more colonies of pathogenic bacteria were isolated from 190 (60 per cent) of the plates. Staph. aureus was the predominant organism in most cases, but mixed cultures of coliform bacilli and Ps. pyocyanea, as in Figure 34, were frequently obtained in addition to Staph. aureus.

The incidence of hand contamination remained high during



FIGURE 34. HAND IMPRESSION CULTURE (ON MILK AGAR) FROM A NURSE (x 1 $\frac{1}{2}$).

At the points of contact of finger tips and palm there has grown a mixed culture of Staph.aureus (3 phage types), coliform bacilli and Ps.pyocyanea, together with Staph.albus.

Stage II in the female ward, with 26 positive plates out of a total of 45. During the two stages when disinfection of skin lesions was being carried out, 82 hand impressions were taken; these yielded 4 positive cultures.

Throughout the entire period, the nurses washed their hands with soap and water enthusiastically, but 15 minutes or even longer would elapse between each hand-washing operation; this afforded ample opportunities for contamination from patients, bedding and other sources. As already noted, the tap handles (and towels) were themselves, often contaminated.

Pathogenic Bacteria Prevalent in the Wards.

Staph. aureus. Although during the course of the investigation very many different bacteriophage types of Staph. aureus were isolated from human sources and from the environment, three strains predominated in the Department. As shown in Table XXXIII, the majority of cases of cross-infection in the male ward were due to a single strain. This was a group III organism that underwent confluent lysis with the routine test dilutions (r.t.d.) of phages 47 and 75, and gave a weaker reaction with phage 53 at r.t.d. The organism was resistant to sulphonamides, penicillin and tetracyclines, but was sensitive to streptomycin, chloramphenicol, erythromycin, fusidic acid, neomycin and the related antibiotic, framycetin ('Soframycin'). This strain constituted a large proportion of Staph. aureus isolates obtained from the environment during stages I, III and IV. Its re-establishment in the ward following its apparent absence during most of stage II may have been due to the re-admission of a patient whose skin lesions were found to be still subclinically infected with this organism, after he had been out of hospital for more than five months.

Two strains were endemic in the female ward: 'type i' (Table XXXIII) which was a strain possessing multiple antibiotic resistance and was lysed only by group III phages at 1000 times r.t.d., and 'type iii' which was resistant only to sulphonamides and tetracyclines and was lysed by a wide range of group III phages at r.t.d.

TABLE XXXIII. SIGNIFICANT CROSS-INFECTION OF SKIN LESIONS WITH THREE ENDEMIC STAPHYLOCOCCI.

WARD	TOTAL CROSS- INFECTIONS	NUMBER WITH <u>STAPH. AUREUS</u> OF TYPE			
		i.	ii.	iii.	OTHER
Male	47	0	24 ⁺	3	13
Female	51	13	1	17*	6
Small	15	0	1	0	12

'Type i' lysed by undiluted phages 6/7/47/54/77; resistant to penicillin, streptomycin, tetracycline and erythromycin.

'Type ii' lysed by diluted phages 47/53/75; resistant to penicillin and tetracycline.

'Type iii' lysed by diluted phages 6/7/42E/47/54/75; resistant to tetracycline. All strains sensitive to methicillin and fusidic acid.

+ 2 additional patients developed furunculosis due to this strain.

* an additional patient developed abscesses of the buttocks due to this strain.

The three strains were isolated very occasionally and in scanty cultures from the environment of the small ward, but, except in one case that became infected with the endemic male ward strain, the organisms were not acquired by patients or staff.

When grown on 1 per cent glycerol monoacetate agar (Willis and Turner, 1962) types 'i' and 'ii' were both found to produce yellow pigment. However, the penicillin-sensitive strain, 'type iii', was cream-coloured.

Table XXXIV gives a comparison between strains of staph aureus present in significant cultures on admission and those acquired in the wards. It can be seen that few of the strains brought into the ward were acquired by other patients.

Other Pathogenic Bacteria. In the female ward six patients developed Ps. pyocyanea infection of their lesions. Five of these infections were due to phage type 'J', and in each case the organism was resistant to sulphonamides, penicillin, tetracyclines and erythromycin, and it was relatively resistant to streptomycin and chloramphenicol. The sixth infection was due to an organism of phage type 'V' - the only occasion on which this type was isolated. Five out of seven representative strains of Pseudomonas isolated from the ward environment proved to be of phage type 'J' and had the same antibiotic sensitivities as the lesion strains.

In the male ward two cases of cross-infection due to Ps. pyocyanea were encountered, and, from each, phage type 'M' was isolated. This organism was resistant to sulphonamides and to all the principal antibiotics except polymyxin and colistin

TABLE XXXIV. BACTERIOPHAGE GROUPS AND ANTIBIOTIC SENSITIVITIES OF STAPH. AUREUS ISOLATED IN SIGNIFICANT CULTURES FROM SKIN LESIONS.

PHAGE GROUP	SENSITIVITY	W A R D					
		MALE		FEMALE		SMALL	
		(a)	(b)	(a)	(b)	(a)	(b)
I	PS	8	1	10	2	0	2
I	PR	9	4	9	1	2	3
II'	-	9	0	8	0	2	0
III	('type i')	0	0	0	13	0	0
III	('type ii')	3+	24	0	1	0	1
III	('type iii')	0	3	0	17 ^x	0	0
III	others PS	7	1	14	1	4	5
III	PR.TS	13	4	6	0	0	0
III	others PR.TR	5	0	2	0	1	0
NT'	-	6	3	7	2	5	2
TOTALS		60	40	56	37	14	13

(a) = Strains cultured from swabs taken on admission.

(b) = Strains cultured from swabs taken subsequently (cross-infections).

' Mainly 'PS'. NT = non-typable with routine phages.

+ Two of these isolates were from patients who were re-admitted.

x Two strains were isolated from mixed cultures in which Gram-negative bacilli predominated.

'PS' = penicillin-sensitive; 'PR' = penicillin-resistant; 'TS' = tetracycline-sensitive; 'TR' = tetracycline-resistant.

('Colomycin'). Identical organisms were isolated from the ward environment, although two other phage types were also obtained from this source.

The skin lesions of five female patients became infected with Pr. mirabilis. Three of these appeared to be identical on the basis of Dienes' phenomenon and antibiotic sensitivities. Strains that were indistinguishable from these were isolated from the air and from baths on several occasions. The identity of these strains was later confirmed by bacteriocine typing (p.389). The strains obtained from the other two cases were apparently unrelated, as were other strains isolated from the environment.

The skin lesions of three patients in the main male ward developed Pr. mirabilis infections after admission to hospital. Two of the causative organisms, and the strain which was isolated from a nurse (p.287) who worked in the ward were found to be identical. The same organism was isolated from the nose of another patient a month later, and was also found intermittently in the baths and in the ward dust. The organism differed from the prevalent one in the female ward, and, as in the female ward, several different strains were also encountered in the environment. By bacteriocine typing it was later found that some of these miscellaneous strains were identical with organisms brought into the ward by infected patients.

The two types of Pr. mirabilis most commonly isolated were sensitive to streptomycin, kanamycin and chloramphenicol, and were resistant to penicillin, tetracycline and colistin.

The predominant type in the female ward was, however, resistant to sulphonamides, while the prevalent male ward organism was always sensitive to these agents.

Six patients in the female ward and two in the small ward developed infected skin lesions from which profuse cultures of coliform bacilli were obtained. Precise characterization of these strains and of similar ones isolated from urinary tract infections (p.281.) and from the environment was not possible, although biochemical reactions and antibiotic sensitivity tests indicated that at least two different organisms were present in the female ward. One was a typical Esch. coli which was sensitive to sulphonamides, streptomycin and chloramphenicol, and the other was a non-lactose fermenting coliform bacillus which was resistant to chloramphenicol. The atypical organisms, however, were not all equally sensitive to sulphonamides or streptomycin, and may have been a heterogeneous group. In the case of the coliform infections, therefore, the distinction between cross-infection and autogenous infection could only be very tentatively made. In Table XXIX (p.276.) the eight infections due to coliform bacilli are entered under the headings of 'primary cross-infection' or 'super-infection' according to whether the lesions were originally free from infection or not.

Dispersal of Pathogenic Bacteria by Individual Patients

Tests were carried out on 48 patients whose extensive lesions were infected with Staph. aureus, and on 30 patients who were nasal carriers of Staph. aureus but whose lesions were free from infection at that time. Table XXXV shows the extent to which these 78 patients contaminated the air of the special cubicle.

Clinical infection was present in only 7 of the 48 patients whose lesions yielded significant primary cultures of pathogens. The heaviest dispersal was, however, found amongst the patients with psoriasis, none of whom showed clinical signs of infection. The nasal carriers of Staph. aureus with uninfected lesions produced relatively little staphylococcal contamination of the air.

Representative colonies of Staph. aureus obtained in air samples were submitted to phage typing and antibiotic sensitivity testing to establish their identity. Strains that did not correspond to the patients' own lesion or nasal strains were detected on only four occasions. These anomalous isolates have been excluded from Table XXXV.

Two additional patients who were examined are not included in the Table. They both had widespread eczema with crusted lesions, and swabs taken on admission from the lesions of each patient yielded profuse growths of Strep. pyogenes (one of the patients stayed in hospital for less than one week and so is excluded from tables XXIX and XXX). During the period of activity in the cubicle, 2 cu. ft. of air yielded 100 colonies of Strep. pyogenes in the case of one of the patients, while the

TABLE XXXV. DISPERSAL OF STAPH. AUREUS BY PATIENTS WITH SKIN DISEASES

DIAGNOSTIC GROUPS	NO. OF CASES	NASAL CARRIERS	NUMBER WITH INFECTED LESIONS		STAPH. AUREUS COUNT*	
			CLINICAL DIAGNOSIS	CULTURE	MEAN	RANGE
Psoriasis	20	6	0	20	40	0 ⁺ -135
	16	16	0	0	3	0-20
Eczema	17	7	5	17	18	0-65
	14	14	0	0	2	0-10
Besnier's prurigo	5	2	0	5	10	0-15
Lichen planus	2	1	1	2	57	5-110
Mycosis fungoides	2	1	1	2	32	20-45
Pityriasis rosea	2	2	0	2	12	10-15

* Per 10 cu. ft. of air, using the slit sampler.

+ One patient only.

second patient produced relatively little contamination of the air (3 colonies of Strep. pyogenes were obtained from 2 cu. ft. of air).

A relatively rapid decline in bacterial counts occurred after patients with psoriasis had left the cubicle whereas a more gradual fall in the air counts was usually seen after eczema cases. Figure 35 compares the trends in the counts of total bacteria. In contrast to the total bacterial counts in the wards, those in the cubicle were closely correlated with the counts of Staph. aureus and were derived almost entirely from the occupants of the cubicle. The total air counts before the patients entered the cubicle were always low, ranging from 1 to 7 organisms per cu. ft. (mean count 2.8 per cu. ft.). A typical series of slit sampler plates from one of the cubicle tests is shown in Figure 36.

Air samples taken with the size-grading sampler confirmed that there were differences between the average size of particles bearing bacteria in the two main groups of patients. The size distribution of the air-borne particles carrying Staph. aureus is shown in Table XXXVI. The maximum bacterial count from the eczema patients was usually in the second fraction (particles of 10 - 18 μ in diameter), but the first and third fraction also contained substantial numbers of Staph. aureus. From the psoriasis patients, however, the first fraction (particles of above 18 μ in diameter) usually contained most ^{of} the air-borne bacteria. Patients with crusted eczema or lichen planus gave similar particle distributions to those from the psoriasis cases.

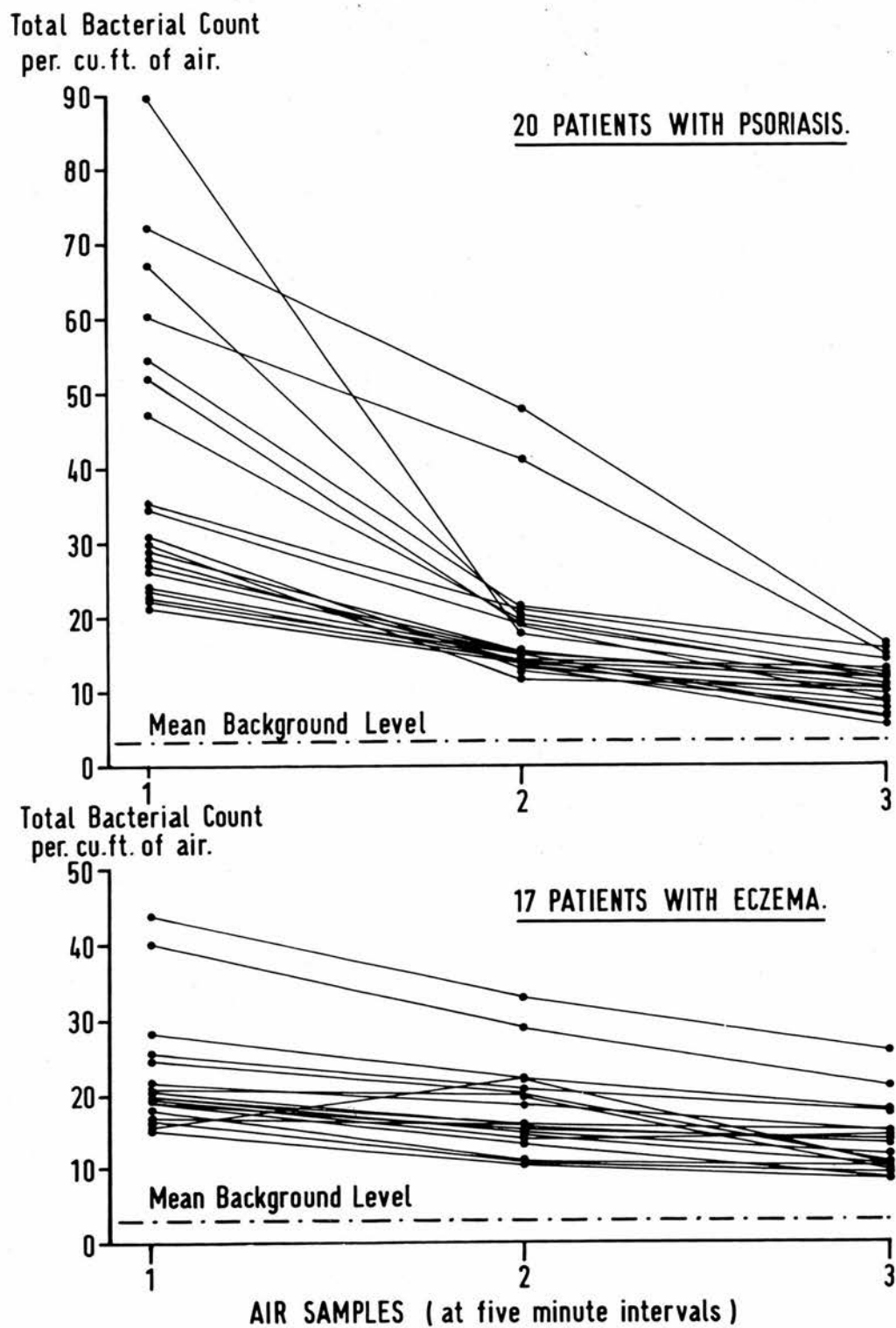


FIGURE 35. DECLINE IN BACTERIAL AIR COUNTS DURING THE FIRST TEN MINUTES AFTER PATIENTS HAVE LEFT THE TEST CUBICLE.
(two groups of unselected, consecutive patients).

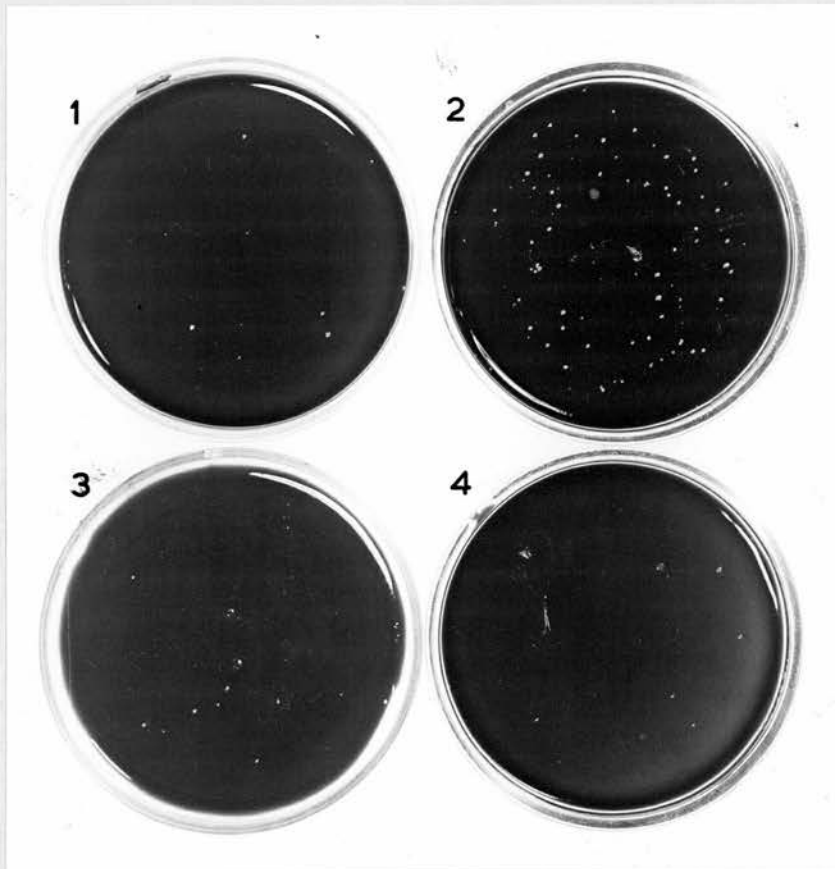


FIGURE 36. A SET OF BLOOD AGAR PLATES FROM THE SLIT SAMPLER DURING TESTS ON A PATIENT WITH PSORIASIS.

Plate 1 was exposed before the patient entered the cubicle, plate 2 was exposed during occupation of the cubicle, and plates 3 and 4 at five-minute intervals after he had left the cubicle. The rapid decline in the air count is a notable feature.

TABLE XXXVI. SIZE GRADING OF PARTICLES CARRYING STAPH. AUREUS SHED BY PATIENTS WITH INFECTED SKIN DISEASES.

SKIN DISEASE	NO. OF CASES	MEAN COUNTS OF <u>STAPH. AUREUS</u> [*] IN FRACTION			
		>18 μ	10-18 μ	4-10 μ	<4 μ
Psoriasis	16	94(78%)	20(17%)	5(4%)	1(1%)
Eczema	14	5(24%)	7(39%)	6(30%)	1(7%)
Other Diagnosis	10	30(53%)	17(30%)	8(14%)	1(3%)

* In approximately 20 cu. ft. of air.

Figures 37 and 38 illustrate typical sets of cultures obtained in these tests. Figure 39 shows a complete series of plates from one test period.

When slides coated with 'Araldite' were exposed in the size-grading sampler the size-distribution of the impacted particles coincided with that of the bacteria-carrying particles. As shown in Figures 40 and 41 most of the microscopic material on the slides stained as protein and resembled epidermal scales. A small proportion of the particles, however, were fibrous fragments, the majority of which were composed of cellulose.

Culture plates after exposure on the first stage of the size-grading sampler were frequently found to be covered with a layer of 'dust' visible to the unaided eye, particularly following tests on patients with psoriasis. Under the plate microscope the large dust particles were seen to consist almost entirely of skin debris; the smaller particles could not be identified at this low magnification. As there was no provision made for the rotation of plates on the first stage during sampling, the particles were usually distributed on the surface in an uneven fashion. Photographs taken of the plates before and after incubation showed that the bacterial colonies which grew followed the same irregular distribution as the dust (Figures 42 and 43). On further magnification of the cultures, the colonies were seen to be arising from the epidermal fragments, thus providing direct evidence of the vehicle of air-borne infection.

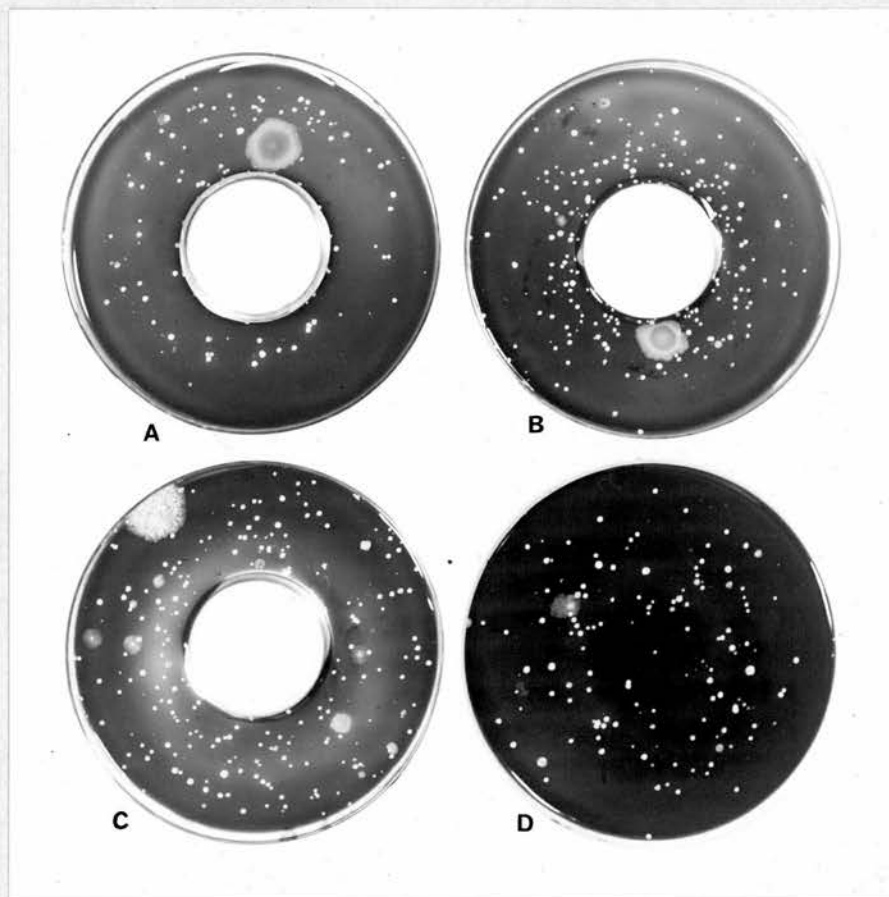


FIGURE 37. SET OF BLOOD-AGAR PLATES FROM THE SIZE-GRADING IMPACTION SAMPLER.

The special cubicle was occupied by a patient with clinically infected eczema.

(Particle diameter in fraction A = $>18\mu$; B = $10 - 18\mu$; C = $4 - 10\mu$; D = $<4\mu$).

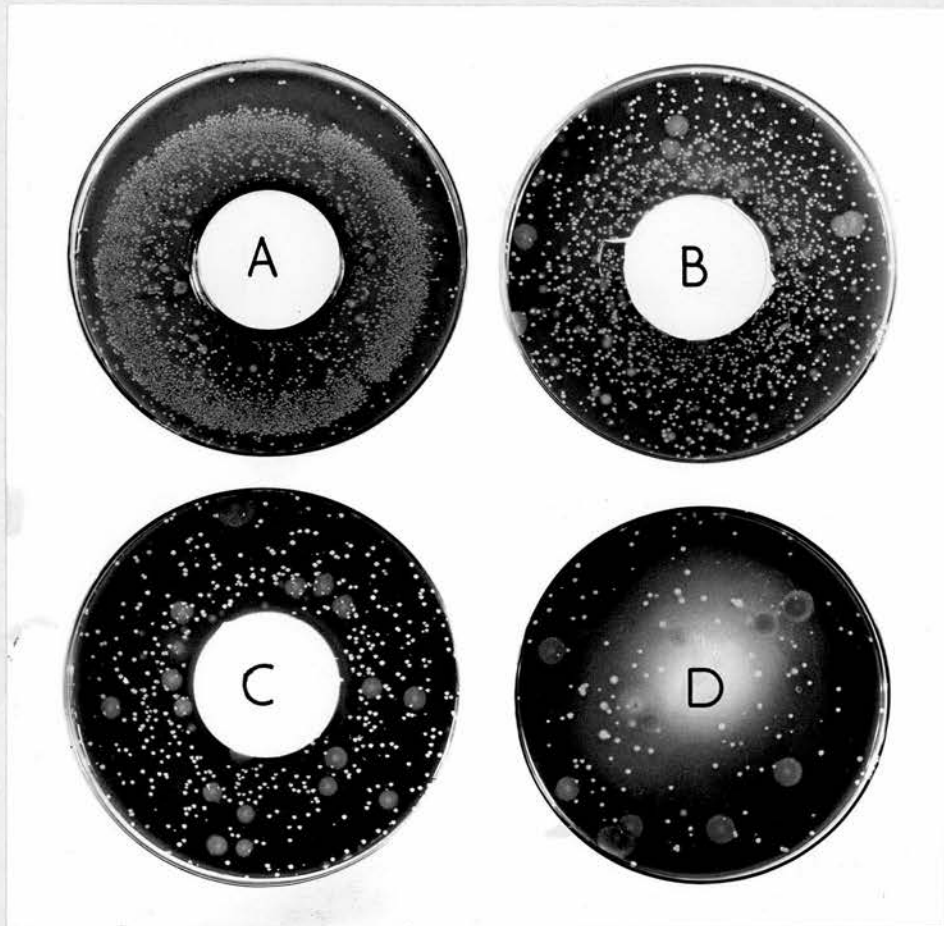


FIGURE 38. SET OF BLOOD-AGAR PLATES FROM THE SIZE-GRADING IMPACTION SAMPLER.

The special cubicle was occupied by a patient with sub-clinically infected psoriasis. Staph.aureus of one phage type constituted the majority of the smaller colonies.

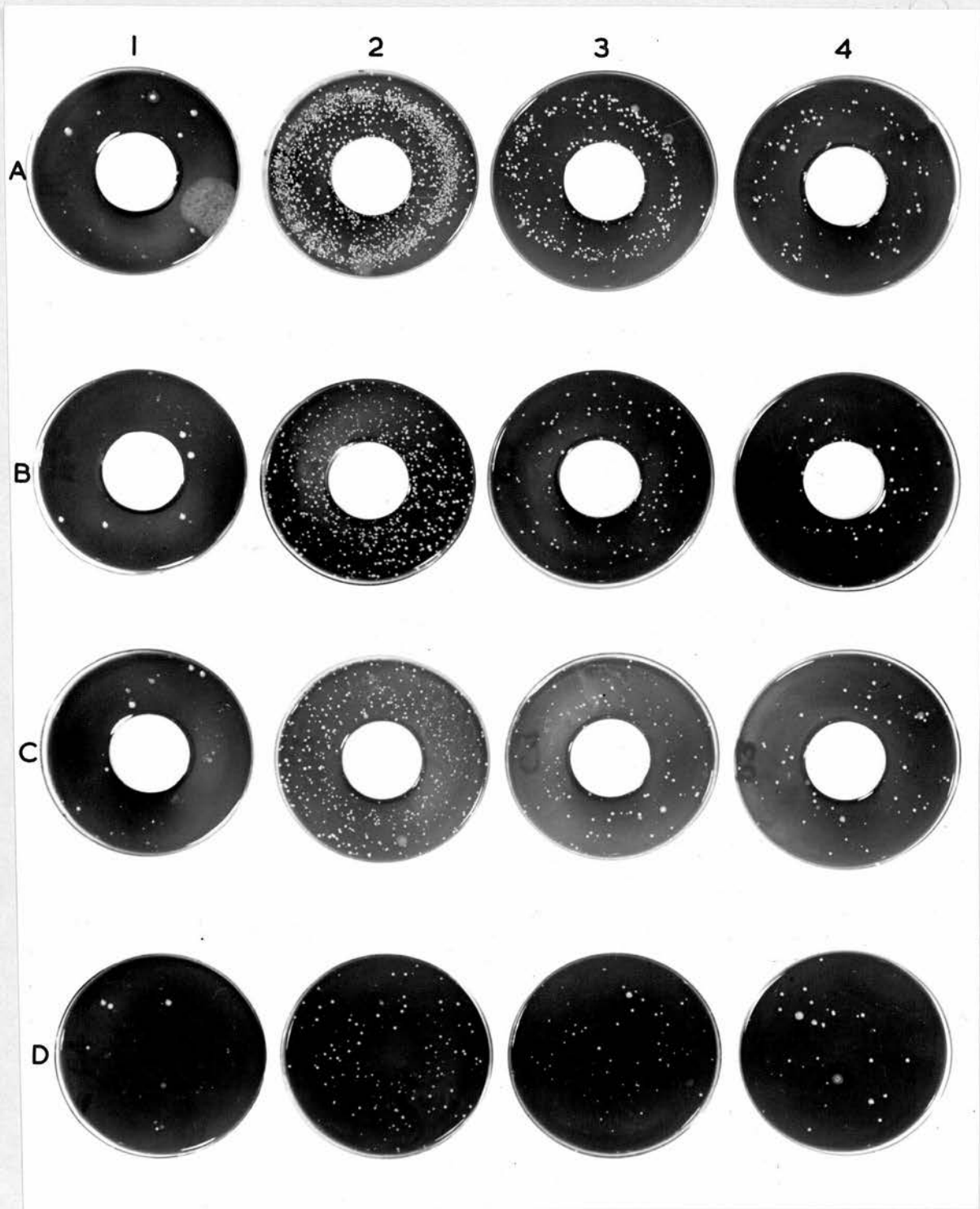


FIGURE 39. A COMPLETE SERIES OF PLATES EXPOSED IN THE SIZE-GRADING IMPACTION SAMPLER DURING ONE TEST PERIOD.

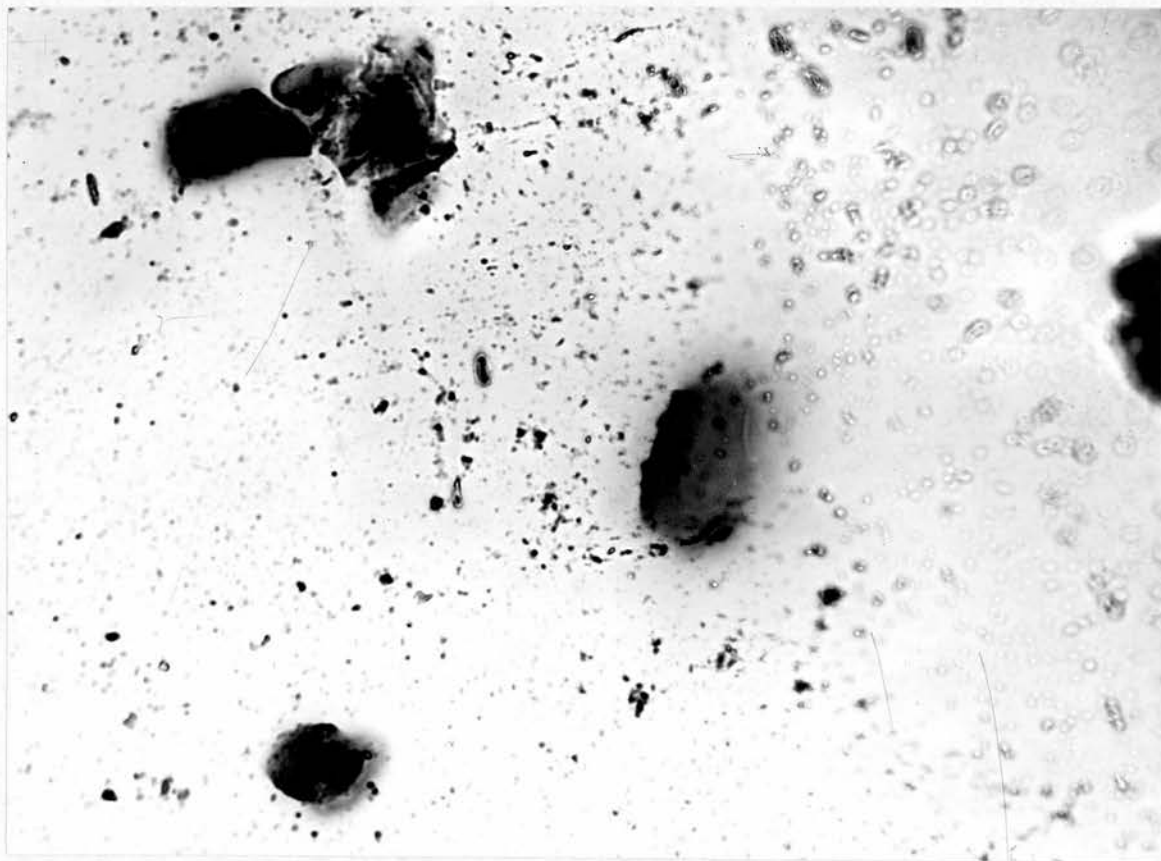


FIGURE 40. PARTICLES FROM THE AIR OF THE SPECIAL CUBICLE TRAPPED ON A COATED SLIDE PLACED ON THE FIRST (TOP) STAGE OF THE SIZE-GRADING IMPACTION SAMPLER (x600).

Using Pressley's method, almost all particles stained blue (protein). While small particles are also present, this was the only fraction to trap the large epidermal scales (> 18 μ diameter).

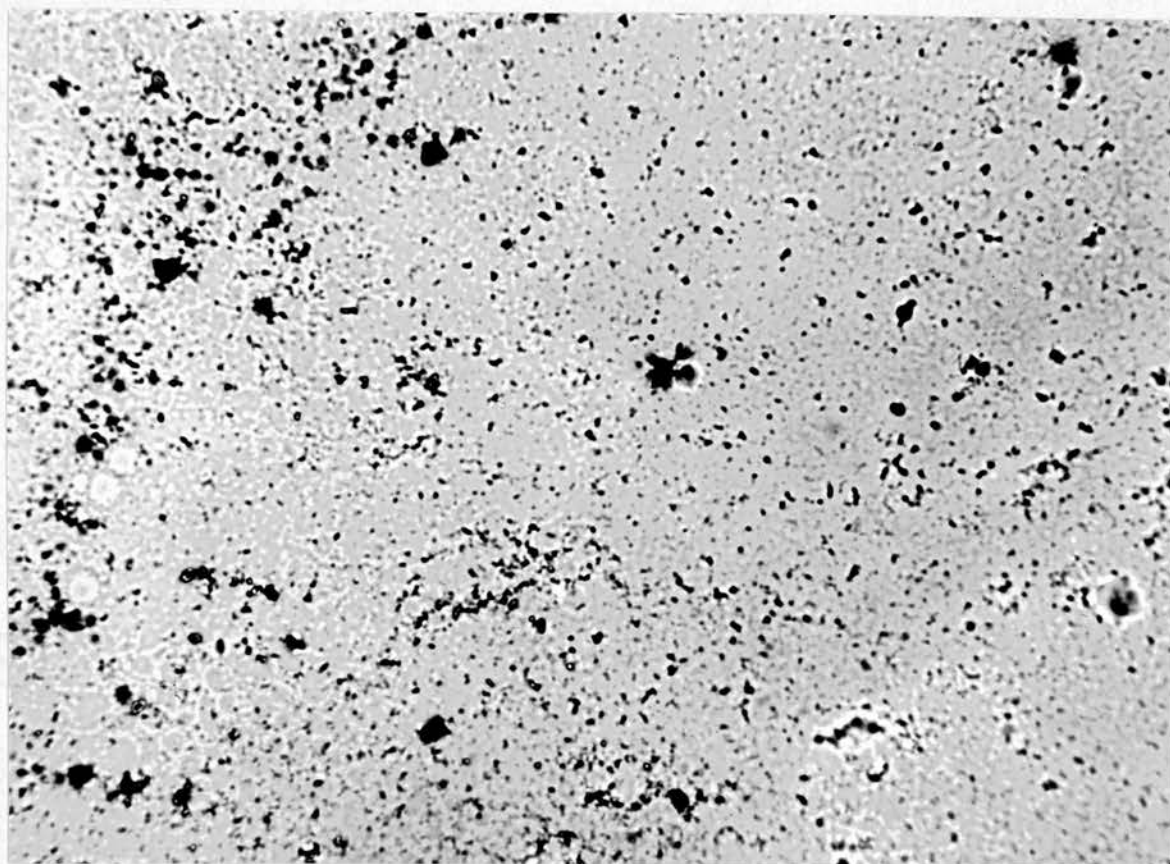


FIGURE 41. PARTICLES FROM THE AIR OF THE SPECIAL CUBICLE TRAPPED ON A COATED SLIDE PLACED ON THE FOURTH (BOTTOM) STAGE OF THE SIZE-GRADING IMPACTION SAMPLER. (x600).

Almost all particles stained as protein. All the particles are small, and most are $< 4 \mu$ in diameter.



FIGURE 42.

PLATE FROM THE TOP STAGE OF THE IMPACTION SAMPLER (FROM A PATIENT WITH PSORIASIS). Figure 42 shows the plate before incubation; the fine dust seen consists of skin scales. Figure 43 shows the same plate following incubation; Staph.aureus predominates.



FIGURE 43.

Bacteriocine Typing of Proteus Species

On the basis of bacteriocine production, most of the strains of Pr. mirabilis isolated in the female ward were placed in group 'a'; in contrast, two-thirds of the strains from the male ward were placed in group 'f' as described in the Appendix (p. 389). The majority of the remaining strains, however, could not be identified, as they did not inhibit the growth of the 'indicator' strains used in the tests, nor were they themselves inhibited by any of the collection of 'producer' strains.

Polynoxvlin Cream in Nasal Carriers of Staph. aureus

The histograms in Figure 44 compare the effects of polynoxvlin cream and placebo cream on persistent nasal carriers of Staph. aureus. After one week's application of the active cream the number of carriers had fallen from 36 to 11, of whom 10 yielded only scanty cultures. The incidence of carriage in this group continued to fall during the next two weeks. However, three weeks after the cessation of nasal disinfection, the incidence had risen again to a peak of 22 out of 36 (16 of whom yielded scanty cultures). Thereafter the numbers of carriers remained relatively constant. A comparison was made between the phage types of the original staphylococci and the strains which reappeared after treatment. In 20 out of the 22 cases the pair of strains was identical.

In contrast, little change occurred in the incidence of

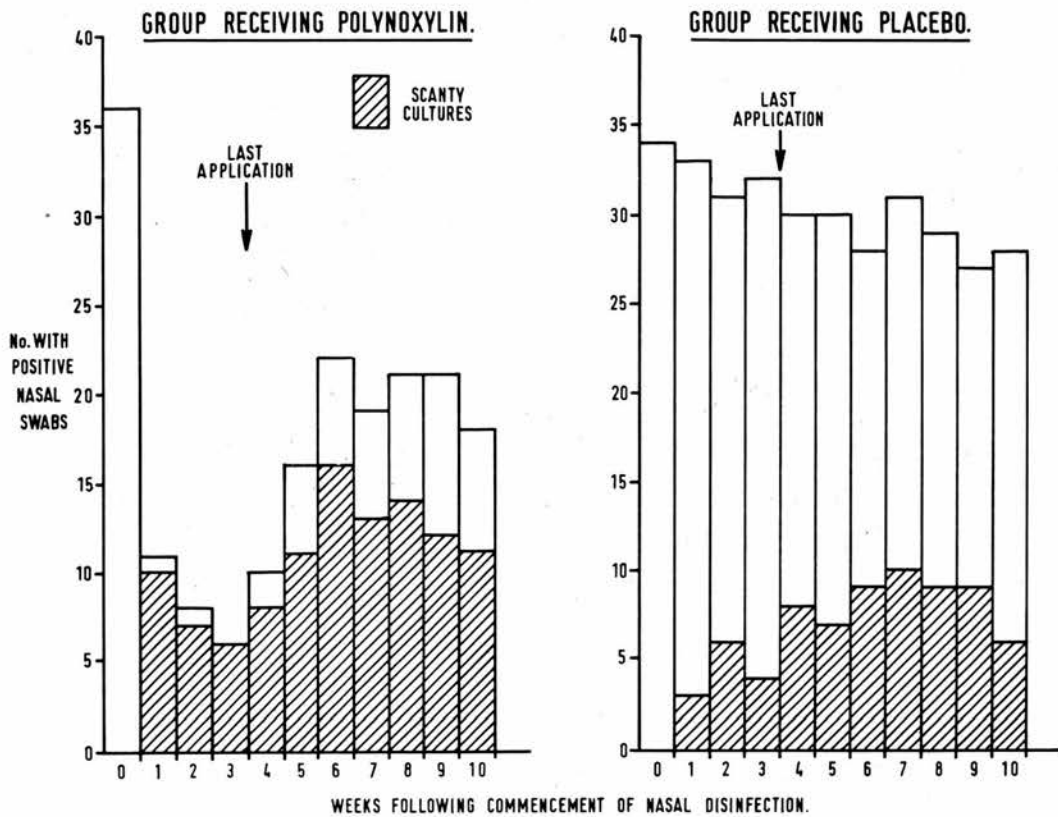


FIGURE 44. RESULTS OF THE NASAL APPLICATION OF POLYNOXYLIN CREAM AND PLACEBO IN TWO GROUPS WHO CARRIED STAPH.AUREUS IN THE ANTERIOR NARES.

nasal carriage amongst the placebo group. After three weeks there remained 32 carriers out of the original 34, although three of these yielded only scanty growths of Staph. aureus. At the end of the ten-week period the number of carriers had fallen to 28.

The Efficacy of Hexyl-resorcinol as an Air-disinfectant in a Dermatology Department

Figures 45 and 46 represent the decline in the total bacterial air counts, sampled as four fractions, after each patient's period of activity in the room. The rate of decline appeared to be proportional to the initial air count, and was not perceptibly influenced by hexyl-resorcinol vapour.

Figure 47 depicts a set of plates exposed following the period of activity of a patient with crusted eczema whose lesions yielded a mixed culture of Pr. mirabilis and staphylococci. Hexyl-resorcinol was vaporized on this occasion. Swarming colonies of Proteus are seen on most of the plates. During the course of these tests, two patients with eczema whose lesions were colonized by coliform bacilli produced air contamination with these organisms; the growth obtained was relatively scanty, however, in both cases.

(The results of tests upon chemical disinfectants used in the Hospital are given in the Appendix (on p.395 et seq.)

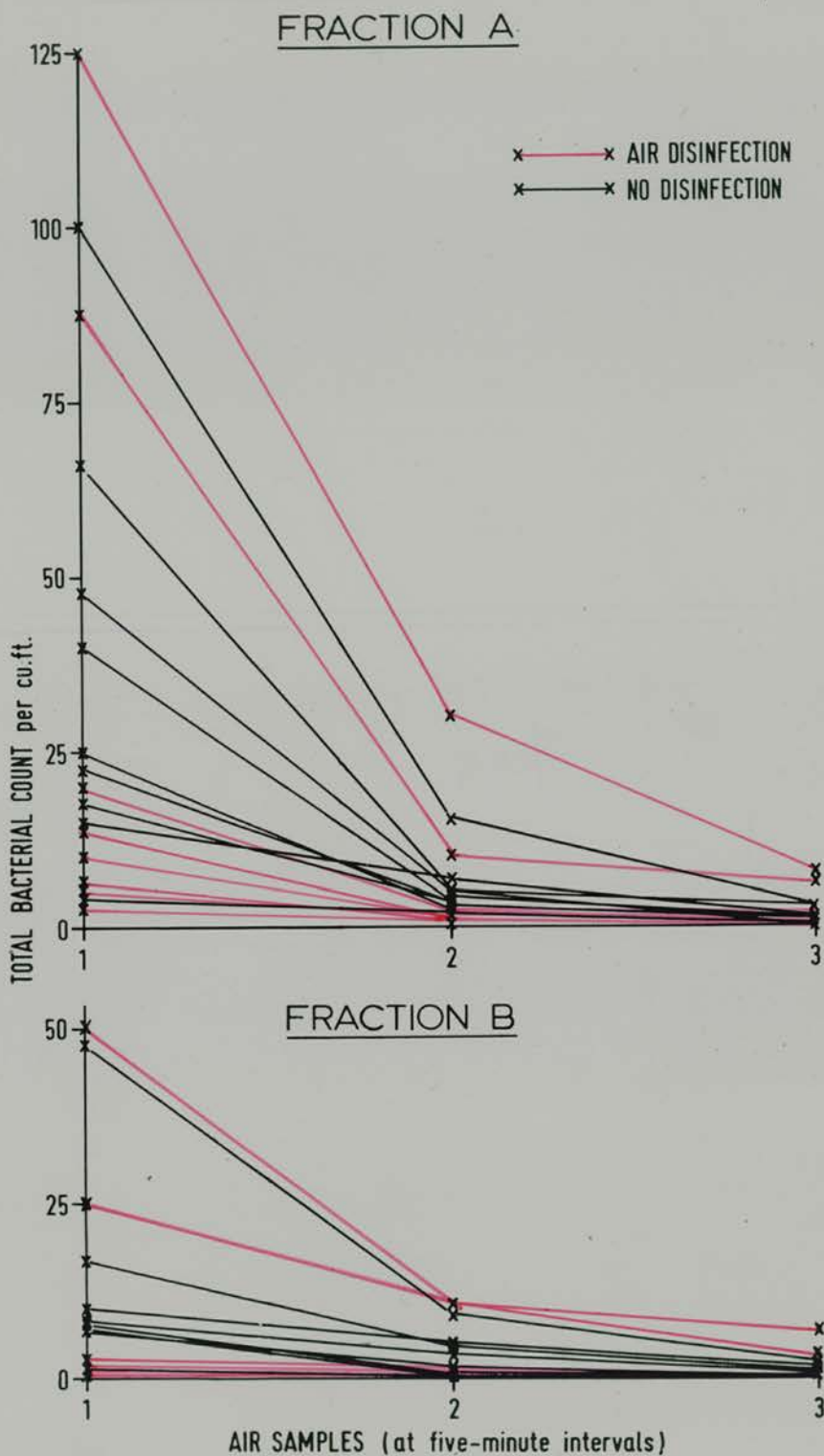


FIGURE 45. THE INFLUENCE OF HEXYL-RESORCINOL VAPOUR ON THE DECLINE IN BACTERIAL AIR COUNTS AFTER PATIENTS HAD LEFT THE SPECIAL ROOM.

Fractions A and B collected in the size-grading sampler (see footnote to Figure 37, p.303).

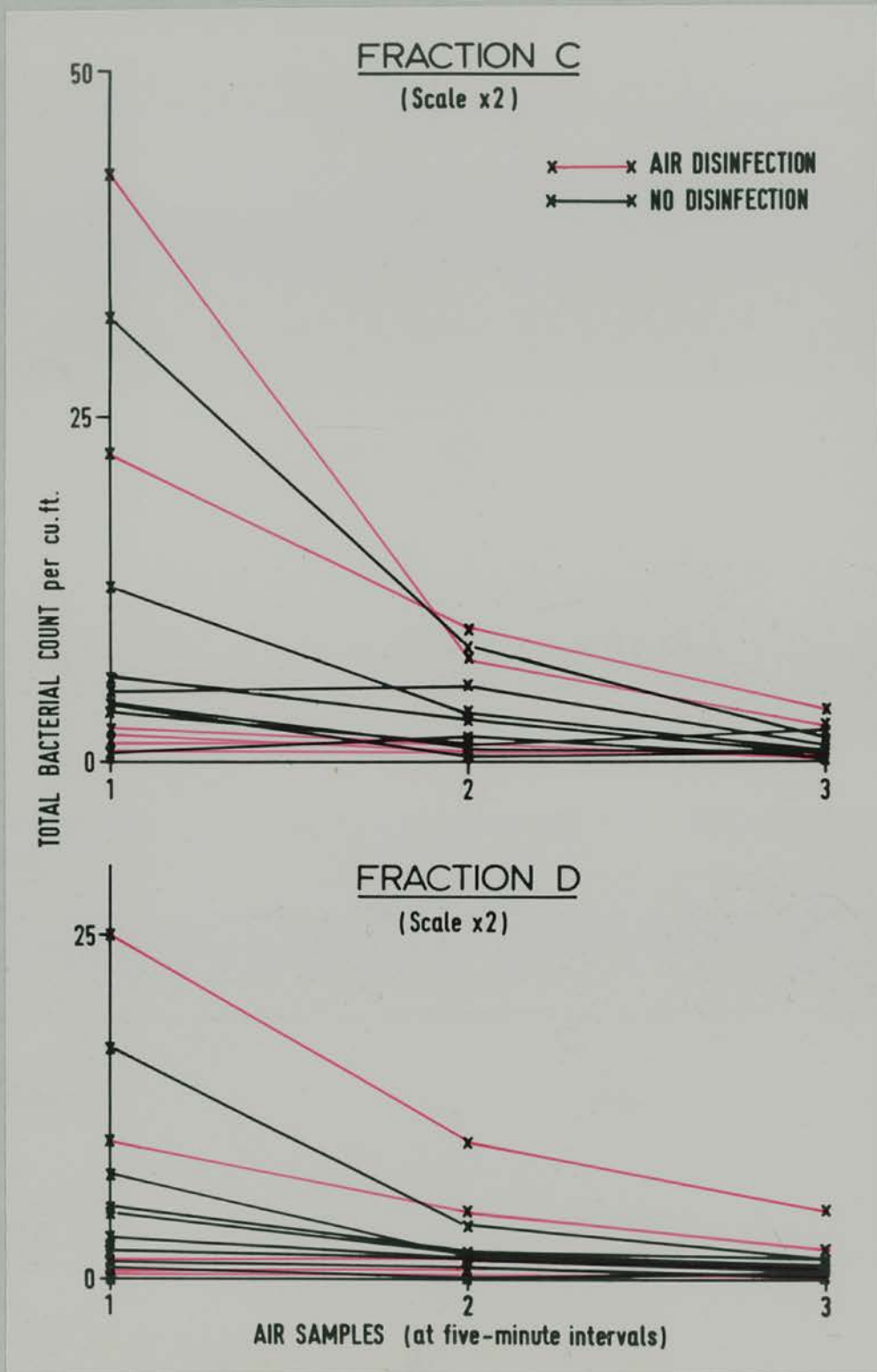


FIGURE 46. THE INFLUENCE OF HEXYL-RESORCINOL VAPOUR ON THE DECLINE IN BACTERIAL AIR COUNTS AFTER PATIENTS HAD LEFT THE SPECIAL ROOM.

Fractions C and D collected in the size-grading sampler (see footnote to Figure 37, p.303.).

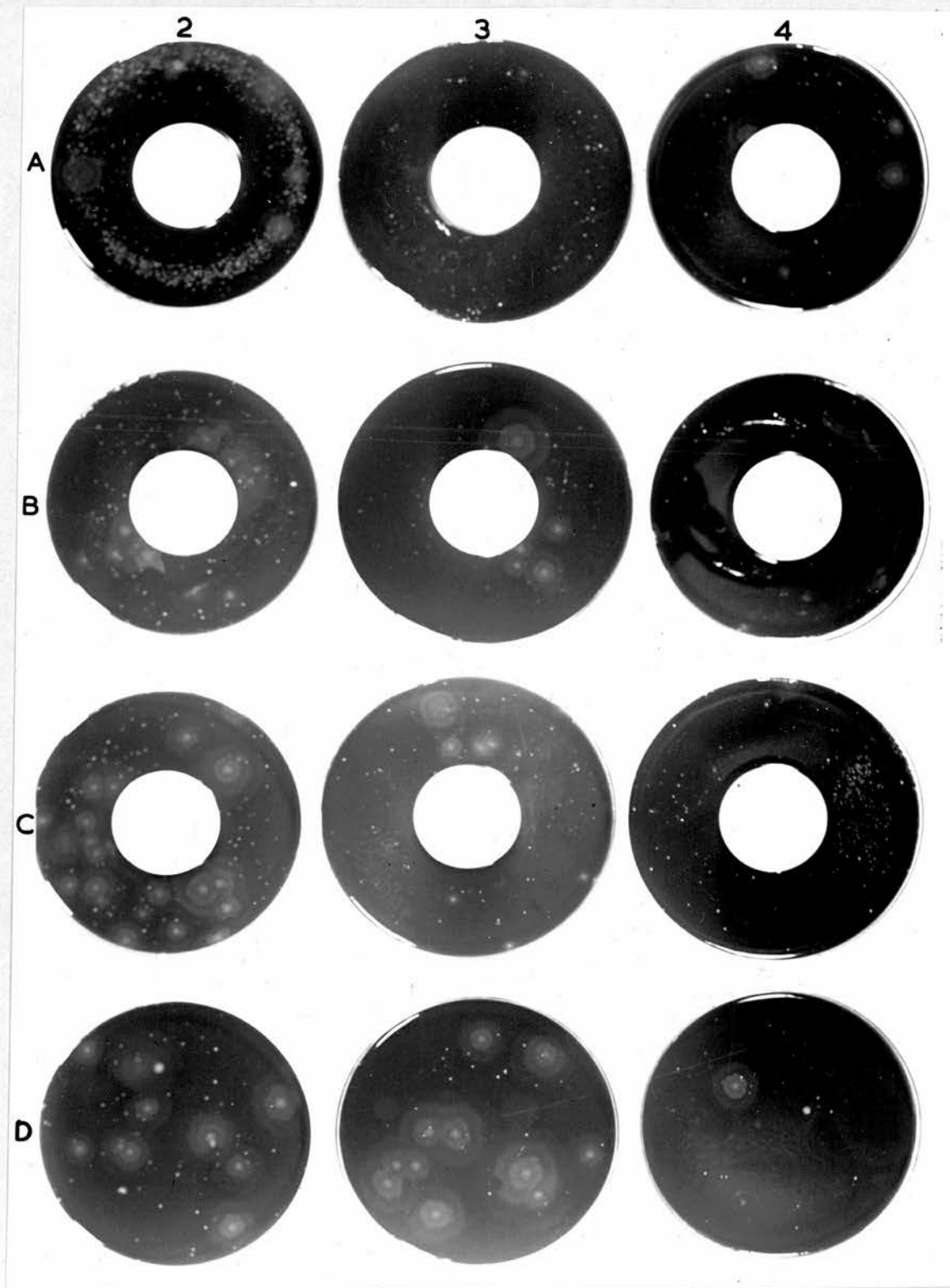


FIGURE 47. A COMPLETE SET OF PLATES EXPOSED IN THE SIZE-GRADING SAMPLER DURING A TEST ON HEXYL-RESORCINOL AIR DISINFECTION.

Pr. mirabilis has grown on most of the plates.

Part III

STUDIES IN A DERMATOLOGY DEPARTMENT

(iv) DISCUSSION

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The Bacterial Flora of Skin Lesions in the Population outside
Hospital

Scanty growths of Staph. aureus and other pathogenic bacteria which were obtained from skin lesions have been disregarded throughout the investigation. These organisms may, in small numbers, form part of the normal 'transient' flora of the skin. Thus, by sampling a relatively large area of skin, using the broth-enrichment method, Williams (1946) obtained Staph. aureus from 70 per cent of normal individuals. Persistent carriage of the organism on healthy skin is, however, uncommon over most of the body surface, and seems to be mainly restricted to the axillae and perineum in those cases where it is observed. In a study of 50 normal males, Ridley (1959) found that the axillae of 6, and the perineum of 13 yielded varying numbers of Staph. aureus on a single occasion; but perineal carriage persisted in less than half of the positive subjects. More recently Bøe et al. (1964) reported a perineal carriage rate among hospital patients of 13 per cent, but did not distinguish between persistent and transient carriage or between results from direct cultures and those from enrichment cultures. It is noteworthy that almost all axillary and perineal carriers are also nasal carriers of Staph. aureus; Bøe and his colleagues reported that only 3 per cent of patients yielded the organism from the perineum alone. The anterior nares must still be regarded as the principal site of superficial colonization in the normal individual; and carriage at this site is not only more than twice as frequent as it is on the perineum

but it is also more stable (Ridley, 1959).

Gram-negative intestinal bacilli are surprisingly uncommon on healthy skin, even in moist, flexural areas (Kligman, 1965). The only members of the group isolated with any regularity are Aerobacter (Klebsiella) spp., small numbers of which may occur in the axillae of about 20 per cent of normal individuals. Kligman (1965) has also commented on the extreme rarity of streptococci, including those of group A, on human skin; and this may be partly due to the presence of fatty acids which are highly active against organisms of this genus.

In the present study, the skin lesions of 28 per cent of the out-patients, who were free from clinical infection, yielded significant cultures of potential pathogens. The incidence of subclinical infection was 38 per cent among patients with eczema - the commonest diagnosis. Swabs from the lesions of the remaining patients usually yielded moderate cultures of coagulase-negative staphylococci and diphtheroid bacilli; these organisms together constitute almost the entire flora of healthy skin (Kligman, 1965). The variable concentration of normal flora revealed by swabbing the lesions may be related to the wide variations which are known to exist in the bacterial populations at different sites on healthy skin. Williamson (1965) used a quantitative rinsing method to obtain bacterial suspensions from normal skin; he found that counts in the axilla were almost twice as high as those on the scalp, but were twelve times higher than on the forehead, and 10,000 times higher than on the back or forearm.

Staph. aureus predominated in 85 per cent of the significant cultures obtained from lesions: 46 per cent of the strains were resistant to penicillin and 13 per cent were resistant to tetracycline. The incidence of penicillin-resistance was the same as that reported from a general practice in Manchester by Kay (1962); it was, however, more than three times higher than the rate among the non-hospital population observed several years earlier in Edinburgh by Gould and McKillop (1954). None of the strains isolated by Gould and McKillop were tetracycline-resistant. Kay (1962) did not report sensitivities to antibiotics other than penicillin; but two years earlier, a large survey of staphylococcal infections in Australian general practices showed that the incidence of tetracycline-resistance was only 2.3 per cent (Johnson et al., 1960). The present observations, which demonstrate a growing incidence of antibiotic resistance outside hospital, emphasise the importance of laboratory services for general practitioners. The empirical use of antibiotics, which is particularly common outside hospital, is likely to be increasingly unsuccessful. This undesirable practice can be avoided only where facilities are available for rapid bacteriological diagnosis - and are used.

Dermatological Wards as Models for the Study of Hospital Infection

There are very few departments in which the various facets of hospital infection can be investigated adequately over a long period of time. A maternity nursery meets some of

the requirements, but the infants remain in it for a relatively short time, and, consequently, studies on individuals cannot usually be continued for longer than one week. Moreover, the specialised conditions in a nursery, and the unique nature of its occupants make it inadvisable to apply findings from such studies to other branches of hospital practice. Most of the work carried out in adult wards has either been centred upon sporadic outbreaks of infection - usually retrospectively - or, as in the case of surgical units, has involved the investigation of endemic sepsis usually occurring at a low incidence. The drawbacks of each situation are obvious, and in neither case is it easy to assess the value of any counter-measures which may have been introduced.

The present investigation has confirmed the hypothesis that was formulated at the outset. Dermatological wards possess almost every feature that is required for an intensive study of the problems of hospital infection and hospital hygiene. Many of the patients when admitted to hospital are extensively, but in the main subclinically infected. Their lesions are extremely sensitive indicators of bacterial contamination of the environment, having a susceptibility to colonization by pathogens - from endogenous and exogenous sources - which is probably equalled only by the comparable lesions of burns. Dissemination of bacteria from dermatological lesions is frequently heavy, and the close investigation of this and other phenomena is facilitated by the long periods of hospital treatment required by many of the patients. The average duration

of stay was, indeed, twice as long as in the general medical wards studied in Part II, and three times as long as in the general surgical wards. Moreover, the methods of prevention which may be studied, such as modifications to dressing techniques, and to nursing and other routine procedures, are relevant not only to dermatological practice but also to surgical and other fields.

The Susceptibility of Skin Lesions to Colonization by Pathogens

Significant cultures of pathogens were obtained from the lesions of 32 per cent of all out-patients and 45 per cent of in-patients at the time of admission; yet few of the skin conditions were due to primary infection (4 per cent and 1.5 per cent, respectively). The higher incidence of positive cultures among new in-patients is probably because their lesions tend to be more extensive and chronic in nature than those of out-patients. In both series, however, the high frequency and intensity of colonization by potential pathogens is in sharp contrast to the findings on healthy skin.

The ease with which dermatological lesions become colonized is further demonstrated by the results of serial observations upon the in-patients. During their stay in the wards, 38 per cent of all patients acquired bacteriologically significant infection of their lesions. Super-infection was involved in more than one-third of these cases, and usually a pre-existing strain of Staph. aureus was replaced by a different type.

Although the second strain was generally one of the prevalent group III organisms, the types they replaced were diverse and belonged to the three main bacteriophage groups. It is evident, therefore, that while the concept of 'bacterial interference' as a means of preventing staphylococcal cross-infection may be valid in maternity nurseries (vide p.218.) its validity elsewhere in hospital is doubtful. Experiments on the controlled colonization of skin lesions in adults would, however, be of great interest. Such work could proceed along similar lines to the studies carried out on the newborn by Shinefield et al. (1965).

As well as lack of knowledge about the ways in which members of the same species interact on the skin, little is yet known of the factors that determine which one of a variety of different species reaching the skin will multiply and become predominant. The relative and absolute numbers of viable organisms, and their 'infectivity' must be very important in this connection (vide p.223.), but many other factors are involved.

The comparatively low moisture content of the normal stratum corneum seems to be partly responsible for the failure of most bacteria to survive and grow on healthy skin (Kligman, 1965). Following the use of occlusive dressings over normal skin, Marples (1965) observed large initial increases in the resident staphylococcal population. After about two days, diphtheroid bacilli, and to a lesser extent Gram-negative intestinal bacilli (with the exception of Esch. coli) almost entirely replaced the staphylococci. Although Marples concluded

that increasing hydration was mainly responsible for these findings, simultaneous increases in epithelial debris and secretions - especially of lipids, organic acids and possibly lysozyme - together with decreases in oxygen tension must also be considered. Moreover, Staph. aureus, which has a very limited ability to colonize healthy skin possesses moisture requirements for growth which are very similar to those of the micrococci normally resident on the skin (Blank and Dawes, 1958). The possibility that mutual antagonism between bacterial species is also of importance in maintaining the normal skin flora receives support from Shehadeh and Kligman (1963). They found that after suppressing the normal Gram-positive bacterial flora in the axilla, Gram-negative bacilli freely colonized the area.

Observations that are particularly relevant to the present work on the bacteriology of diseased skin have been made by Colebrook, Lowbury and Hurst (1960). These investigators reported that small inocula of Staph. aureus and Strep. pyogenes grew well in fresh human serum, while Esch. coli did not survive. Variable results were obtained with Ps. pyocyanea and Proteus. In the fluid from the blisters of burns Esch. coli once again did not survive, whereas the other bacteria grew readily. However, in the sloughs obtained from burns all the bacteria grew well; and similar results were obtained with serum that had been treated with trypsin or heated at 56°C for one hour. This suggests that complement, 'properdin' or other relatively unstable serum proteins, which selectively inhibit the Gram-

negative bacilli, are absent from slough material.

In the present investigation, it was found that the skin lesions of 10 out of 34 patients admitted to the ward with varicose ulceration - in which sloughing and serous crusting is a regular feature - yielded significant cultures of Gram-negative bacilli. Staph. aureus predominated in a further 10 of these cases, and Candida albicans in one other case. During their stay in hospital, 12 of the patients acquired infection due to Gram-negative bacilli, and 9 due to Staph. aureus. These very high incidences of pre-existing and hospital-acquired infection with Gram-negative bacilli (29 per cent and 35 per cent, respectively) were not found in any other group of patients. The nearest approach to these rates was in the large group of eczema cases, in which exudation and crusting were not infrequent. Gram-negative bacilli predominated in 6.2 per cent of the lesions at the time of admission, and a similar proportion of lesions yielded significant cultures of these organisms for the first time on subsequent examinations. In this group, heavy colonization by Staph. aureus was, however, more than seven times as common as colonization by Gram-negative bacilli. Almost all of the remaining patients who were investigated, notably the large group with psoriasis, had dry skin conditions without exudation or crusting; and significant growths of Gram-negative bacilli were rarely obtained from the lesions.

Although Esch. coli must be one of the commonest contaminants of the skin from the bowel, this organism was less

frequently isolated from lesions than were Pr. mirabilis, 'atypical' coliforms and Ps. pyocyanea. However, this paradoxical finding receives support from the observations of Marples (1965), mentioned above, and is in keeping with the in vitro work of Colebrook and his colleagues which has already been discussed.

The Consequences of Hospital Infection in Dermatological Patients

Clinical Infection of Skin Lesions. Despite its high incidence, hospital-acquired infection fortunately did not lead to serious disease in any of the patients. Heavy subclinical infection of skin lesions was a very frequent finding throughout the investigation. In the out-patient study, although the lesions of 106 patients (32 per cent) yielded significant cultures, infection was diagnosed clinically in only 31 cases (9 per cent). Similarly, among in-patients at the time of admission, 45 per cent of the lesion swabs yielded significant cultures, but the lesions of only 20 per cent of patients were judged to be clinically infected. Moreover, only 18 per cent of the patients whose skin lesions became heavily colonized in the wards showed clinical signs of their infection. Heavy colonization of skin lesions in the absence of clinical sepsis was also observed by Cooke and Buck (1963) during their study of self-contamination among 36 dermatological patients; but data on cross-infection were not included in their report.

Non-dermatological Sepsis. The low incidence of cross-infection

other than of dermatological lesions and of the anterior nares was a striking finding in the present investigation. Three patients developed primary staphylococcal skin lesions due to 'hospital' staphylococci; a nurse contracted paronychia due to a ward strain of Pr. mirabilis, and one of the four cases of urinary tract infection in the female ward could be confidently attributed to a 'hospital' strain of pathogen.

As in the case of the maternity wards studied in the second part of this work, the reasons for the low clinical sepsis rate in the presence of heavy environmental contamination - and colonization - must be sought both in the parasite and the host (vide p.222).

The Pathogen. The three staphylococci prevalent in the wards were all of group III. One of them further resembled the strain which was endemic in the general hospital for it was resistant to all the standard antibiotics except chloramphenicol.

Apart from the sprays, which contained non-absorbable antibiotics that are rarely used systemically, the only antibiotic administered in the wards was tetracycline; and this was used infrequently. The possession of resistance to penicillin, streptomycin, erythromycin and tetracycline could therefore have been of very limited survival value to the prevalent staphylococci. The three strains which caused most of the infections in dermatological patients were, like the endemic strain in the general hospital, evidently of low virulence although possessing a high 'communicability.'

Apart from Staph. aureus, 'typing' was carried out on strains of Ps. pyocyanea and Pr. mirabilis isolated in the Dermatology Department. Strains of Ps. pyocyanea were examined by Dr. J.C. Gould for bacteriophage susceptibilities (Gould and McLeod, 1960), and by this means most of the isolates from the two main wards were clearly differentiated. It is possible, however, that epidemiologically useful sub-grouping of these strains could have been accomplished by pyocine typing (R.R. Gillies, personal communication).

The increasing importance of infection due to Ps. pyocyanea in surgical and medical wards has been discussed in the Introduction. The organism was responsible for 7 per cent of the cross-infection in the Dermatology Department; and more recently its importance in dermatological patients has also been indicated by Noble and Savin (1966). These investigators mentioned that in one ward an 'epidemic strain' - apparently identified solely on the basis of antibiotic sensitivities - was responsible for a mounting incidence of 'minor but clinically apparent infections.' No further details of these infections were given, but presumably they involved dermatological lesions, as in the present study.

Pr. mirabilis was also responsible for 7 per cent of the cross-infection among the dermatological patients, and in addition it produced clinical infection in a nurse. The infections were not severe, however, and although significant cultures of Staph. aureus were also obtained in three of the cases, and in the lesions of two out-patients in whom Pr.

vulgaris predominated, there was no evidence in these mixed infections of the synergism described by Arndt and Ritts (1961).

Typing of Proteus was initially carried out by means of Dienes' phenomenon (p.57.) and antibiotic sensitivity patterns. Although Dienes' phenomenon provides a very sensitive method of establishing identity between Proteus strains (Story, 1954) the results are not always easy to interpret. Moreover, the procedure is not readily standardised, and no reference cultures are available. Consequently, the results cannot easily be communicated to other investigators. There is, therefore, a great need for an alternative typing method in this group. The experiments on bacteriocines carried out in the course of the present investigation gave encouraging results that were of practical value, but, as described in the Appendix (p.386.), unusual problems evidently exist in connection with production and demonstration of bacteriocines in the Proteus group. These difficulties must be overcome before bacteriocine typing of Proteus spp. can be recommended for general use.

The Host. The average age of the patients - 45 years - was rather lower than the average usually found in present-day medical wards (p.126.), and the general health of most of the patients was good. Very different findings were noted among the dermatological patients included in the recent Public Health Laboratory Service enquiry (Report, 1965b). The general results of that enquiry have already been discussed (p.199.), but perhaps the most striking observation made was that the ill

patients with skin diseases had the highest incidence of hospital-acquired infection in the entire survey - 17.1 per cent. The majority of the infections were staphylococcal but no further details were given of these patients, apart from the comment that 'few of them, however, were strictly dermatological patients; most also suffered from other serious medical diseases.'

Similarly, a clinical investigation carried out in a New York general hospital showed that patients in a dermatological ward had a rate of staphylococcal infection (8.8 per cent) which was higher than that found elsewhere in the hospital (Biro, Gibbs and Leider, 1960). The investigators gave no data on cross-infection or environmental contamination. Further analysis of their results, however, shows that the increased susceptibility to infection existed only among those patients receiving systemic cortico-steroid or antibiotic therapy; and 4 of the 5 deaths from generalised infection occurring in the nine-month period of the study were in patients who suffered from the very serious condition of pemphigus vulgaris. On the other hand, only 2.6 per cent of patients who received neither steroids nor antibiotics developed staphylococcal sepsis at sites other than their original skin lesion. This was said to be a lower rate than that found among general medical patients elsewhere in the hospital, and it approximated to the rate observed in the present investigation.

Two remarkable paradoxes are, therefore, encountered in dermatological wards: the skin lesions of a large proportion

of patients are heavily colonized by pathogenic bacteria with apparently no serious consequences; and, despite the presence of formidable environmental and skin contamination by pathogens, the incidence of clinical infection at sites remote from the skin lesions is relatively low among these patients. However, several investigators have assigned important indirect roles to the bacteria present in skin lesions.

Immunological Theories. Blood levels of staphylococcal alpha-antitoxin have been found to be raised in many cases of 'complicated' psoriasis - notably when associated with arthropathy (Mustakallio and Lassus, 1964). This syndrome could be due to an 'immune' process in which the products of Staph. aureus may form part of the antigenic system together with tissue factors. Similarly, Haxthausen (1954) has supported the hypothesis that eczema is the result of a delayed hypersensitivity reaction, in which the sensitizing agent may be composed of bacterial products in association with skin components. He presented findings which suggested that 'the staphylococci present on eczematous skin may act as an adjuvant in the formation of "protigens" in the skin, besides very possibly exerting an antigenic effect by themselves.'

In this connection, the work of Storck (1954) is of great interest. He performed 'patch tests' on patients with eczema, applying to the skin, bacteria isolated from the individual's own lesions. Positive eczematous reactions were obtained with Staph. aureus in the majority of patients whose lesions yielded

the organism. In contrast, patients yielding Strep. pyogenes and Esch. coli gave positive reactions with these organisms in less than one-quarter and one-fifth of cases respectively. Normal controls experienced few reactions; and positive reactions were very uncommon with other organisms isolated, including normal skin commensals. Live cultures and bacterial filtrates produced similar results, whereas killed, washed bacteria usually gave very weak reactions. Storck was satisfied that the effects were due to hypersensitivity and not to toxic action. More recently, Rook (1961) has elaborated the theory of a bacterial role in autosensitization to skin, particularly in cases of disseminated eczema; while the part played by hypersensitivity to the staphylococcus at the site of the initial skin infection has been emphasised by Cluff (1965).

The immunological activity of pathogens which have colonized skin lesions need not be entirely detrimental to the host. It is, for example, conceivable that Staph. aureus in the lesions may actively reinforce specific antitoxic immunity or bring about 'desensitization' to the products of the staphylococcus. The value of toxoid in the prevention of staphylococcal infection seems established (Parish and Cannon, 1960), although there is much conflicting evidence in the literature, including a recent adverse report by Harrison (1963). The development of antitoxic and other forms of anti-bacterial immunity may, therefore, be an additional factor which, apart from the general health of the host and the virulence of the staphylococcus, underlies the relative freedom of dermatological

patients from the common forms of staphylococcal cross-infection.

The Direct Role of Bacteria in the Pathogenesis of Skin Lesions.

Apart from immunological considerations, the presence of large numbers of toxigenic bacteria in dermatological lesions is undesirable to the individual. In addition to the possible risks of hypersensitivity phenomena, the liberation of toxic bacterial products into tissues that are already devitalised must interfere with resolution and healing of the lesions. Lawrence (1959) has demonstrated the damage produced by staphylococcal alpha-toxin in mammalian skin cells growing in culture, and Liu, Abe and Bates (1961) have reported similar findings with products of Ps. pyocyanea.

While the present work was not designed to include an investigation of the clinical effects of topical antibiotics, the medical staff and the ward sister were impressed by the rapid improvement of clinically infected lesions which received the antibiotic spray. To determine whether bacteria play a significant part in the pathogenesis of subclinically infected skin lesions it will be necessary to carry out double-blind trials of topical anti-bacterial agents. Ideally, these would be applied using the 'half-body' technique, and clinical progress could be recorded objectively by means of colour photography.

The Development of Staphylococcal Nasal Carriage in Hospital

At the time of admission to hospital, the incidence of nasal carriage of Staph. aureus among the dermatological patients (43 per cent) was similar to that in the non-hospital population (p.64.). Nasal colonization by prevalent strains of Staph. aureus subsequently occurred in 22 per cent of the patients who were not participating in the trials of nasal or skin disinfection. In 15 of the 53 patients who became colonized in this way, strains of Staph. aureus present on admission were replaced by prevalent ward strains. The relative ease with which nasal super-infection occurred casts further doubt on the general validity of the findings of Shinefield et al. (1965) in relation to 'bacterial interference' (vide p.322.).

The comparatively high colonization rate in 'unprotected' dermatological patients is in contrast to the position among adult patients in the maternity wards of the general hospital (p.224.). As already mentioned, the strains of Staph. aureus prevalent in both departments had similar bacteriophage susceptibilities and multiple resistance to antibiotics, and were all evidently of low 'virulence'. However, the average length of stay of patients differed widely in the two departments; the dermatological patients, on the average, remained in hospital more than four times as long as the maternity patients. The importance of duration of hospital stay in relation to the acquisition of nasal staphylococci has

been accepted for many years, but has only recently been fully demonstrated on a statistical basis (Noble et al., 1964).

An additional factor that has generally received inadequate attention is the environmental load of Staph. aureus to which individuals are exposed. Although the mean air counts of Staph. aureus were higher in the Maternity Department than in most other parts of the general hospital, the counts were less than half as high as those in the Dermatology Department. In keeping with these differences was the finding that whereas no members of the Maternity Department's staff were identified as nasal carriers of the endemic group III staphylococcus, four nurses became carriers of prevalent strains in the Dermatology Department, and the pre-existing nasal staphylococci of two other nurses were temporarily replaced by ward strains. But the size of the infecting dose alone cannot explain these observed differences in nasal colonization for, as described on p.224, recent attempts by Shinefield and his colleagues to establish nasal carriage in adults by inoculating large numbers of Staph. aureus usually failed, unless antibiotics were administered first. The possibility that the vehicle of transmission of air-borne bacteria influences the establishment of infection is discussed later (p.350).

Of the 44 patients who used the framycetin-gramicidin nasal spray, only one became a nasal carrier: the single failure occurred in a patient aged 82 who, despite nursing supervision, might well have applied the spray inefficiently. The general success of this form of nasal disinfection in the prevention and treatment of nasal carriage among hospital

patients confirms the report of Stratford et al. (1960) and is in contrast to the experience of Porter et al. (1963).

Nasal staphylococci were acquired at an even lower rate during the periods when skin lesions were being disinfected. This was probably due to the marked decrease which occurred in air contamination. However, a direct anti-bacterial effect on the anterior nares, due to the inhalation of antibiotic aerosol particles, cannot be ruled out. Such an effect was deliberately produced by Elek and Fleming (1960) and, more recently, by Goldfarb and James (1963) who atomised methicillin solution in the air of hospital wards; this resulted in a suppression of nasal staphylococci. In the present investigation, however, aerial dissemination of antibiotic is believed to have been minimal (vide p.343.).

Nasal Carriers of Staph. aureus as Sources of Hospital Infection

Autogenous Infection. Sixteen of the 105 staphylococcal infections of skin lesions acquired in hospital were due to strains of Staph. aureus identical with those cultured from the patients' anterior nares at the time of admission. These were regarded as autogenous infections, and they indicate an important consequence of nasal carriage. Earlier work on the prevention of autogenous staphylococcal sepsis by means of nasal disinfection has already been reviewed (p.66.). During the present investigation, this form of infection was not encountered among

the 44 patients who participated in the trial of framycetin-gramicidin nasal sprays; nor, however, was it found among the 37 male patients whose skin lesions were disinfected.

As shown by Duguid and Wallace (1948) and later investigators (e.g. Hare and Thomas, 1956) nasal staphylococci are spread mainly by dust from contaminated clothing, although fingers may also play an important part in self-infection. Dermatological patients who lie for long periods of time in self-contaminated nightclothes and bedding are at particular risk from autogenous infection. It is perhaps surprising, therefore, that this form of infection occurred in only 15 out of the 106 patients who were nasal carriers on admission but who were not subsequently protected either by nasal or skin disinfection. Further, it was found that staphylococcal (but not Gram-negative) cross-infection of skin lesions was more than four times as common in patients who were not staphylococcal nasal carriers when admitted to hospital as compared with those who were carriers on admission. Of interest in this connection is the paradoxical finding of Moore and Gardner (1963) that surgical patients who were staphylococcal nasal carriers on admission to hospital had a lower sepsis rate than non-carriers, although carriers of type 80/81 had a higher incidence of sepsis than other carriers.

The hypothesis that the comparatively low incidence of staphylococcal disease observed in dermatological patients has an immunological basis has already been discussed (p.331.). Similarly, nasal carriers of Staph. aureus who enter hospital

with skin lesions free from infection with this organism might, during the course of their chronic disease, have already had extensive colonization of their lesions with Staph. aureus. Cellular or humoral immune processes may subsequently render the skin lesions of the established carrier relatively resistant to staphylococcal infection. This interesting possibility requires further study.

Cross-infection. No significant change occurred in the incidence of cross-infection during the period when efficient nasal disinfection was carried out in the female ward; and on only three occasions during the remainder of the investigation was colonization of a patient's anterior nares found to have preceded colonization of his skin lesions with the same staphylococcus.

Until 1962, there was wide acceptance of the view that patients who enter hospital carrying Staph. aureus in their noses, or who become nasal carriers after admission play a central role in hospital cross-infection. Many investigators since then have cast doubt on this concept (vide p. 66.). Thus Henderson and Williams (1963) considerably modified their interpretation of earlier work (e.g. Williams et al., 1962) which had appeared to indicate that nasal carriage was an important precursor of staphylococcal wound sepsis.

Several investigators, however, still emphasise the importance of nasal carriage as a source of cross-infection. Following the suggestion of Williams et al. (1962) that attention

should be concentrated upon carriers of tetracycline-resistant staphylococci, Stokes et al. (1965) introduced a policy of early detection and anti-bacterial treatment of such carriers in a variety of hospital wards. They believe that this brought about a reduction in the cross-infection rates. Similarly, Goldfarb and James (1963) appear to have greatly reduced the incidence of cross-infection among thoracic surgical patients by suppressing nasal carriage. As already mentioned in connection with antibiotic aerosols, the method used by these investigators was to spray methicillin into the hospital air, and it is possible that the results they obtained were due to the reduction in environmental contamination rather than to any effect on nasal carriage.

Environmental Contamination. Just as nasal disinfection had no influence on the rate of cross-infection in the present investigation, so also it produced no apparent change in staphylococcal contamination of the environment. Further evidence of the minor role played by nasal carriers in the contamination of a dermatology department was obtained more directly by studying individuals in the special cubicle.

Although Duguid and Wallace (1948) demonstrated the aerial dissemination of Staph. aureus by healthy nasal carriers of the organism, the bacterial air counts obtained were relatively low, and most of their data referred to non-pathogenic staphylococci. Later investigators who have emphasised the importance of nasal carriers as sources of staphylococcal air contamination

have usually based their views on work of a less strictly quantitative nature than that of Duguid and Wallace. More recent studies by Hare and his colleagues (Hare and Thomas, 1956; Hare and Ridley, 1958; Ridley, 1959; Hare and Cooke, 1961) have elucidated the routes by which staphylococci spread from the nose to the surroundings; but their air studies were limited to the use of settle plates. They concluded, however, that nasal carriers produce far less contamination than perineal carriers or individuals with infected skin lesions.

The results of the quantitative studies of White (1961) suggest that, as in the case of Strep. pyogenes, the extent to which a nasal carrier of Staph. aureus contaminates his clothing and bedding is governed by the bacterial count in the anterior nares; but even in the presence of relatively high nasal counts, many carriers produce little or no contamination of their surroundings. The analogy with streptococcal carriage may not, however, be entirely valid. The profuse streptococcal dispersal demonstrated in nasal carriers by Hamburger et al. (1945) may be related to extensive colonization of the nasal and adjoining mucous membranes by the streptococcus. Comparable dispersal by staphylococcal nasal carriers has not been demonstrated, except possibly in 'cloud babies' who have simultaneous viral disease of the respiratory tract (Eichenwald et al., 1950).

White's results also suggest that nasal carriers of the 'epidemic type' 80/81 may shed larger numbers of staphylococci

than carriers of other types. It is possible, too, that the systemic administration of antibiotics may - paradoxically - increase the dispersal of staphylococci by nasal carriers. Ehrenkranz (1965) reported that two nasal carriers of a tetracycline-resistant staphylococcus of type 52/52A/80/81 became 'spreaders' of the organism following tetracycline therapy. Solberg (1965), however, confirms the effectiveness of topical antibiotics to which the nasal strains are sensitive. He used the nasal spray employed in this investigation, but in contrast to the present findings he reports that although the sprays were applied for only a few days in a medical ward they brought about a decrease in air contamination. It is difficult to evaluate his results in view of the short duration of the experiment, but the initial air counts were relatively low before the introduction of spraying.

The importance of staphylococcal nasal carriers as sources of cross-infection has undoubtedly been over-emphasised in the literature. After studying the subject for many years, Hare was of the opinion that 'nasal organisms do not contribute very much towards the contamination of the patient or his environment' (Hare and Cooke, 1961). The findings in the present work support this view.

The Indications for Nasal Disinfection. While little or no reduction in the incidence of cross-infection or environmental contamination is likely to be achieved following the widespread

use of nasal disinfection, the procedure may be justified as a method of preventing autogenous infections. If it had been used routinely in the present investigation, infection might have been prevented in 16 patients and one member of staff. The value of nasal disinfection in patients with chronic furunculosis has been demonstrated on many occasions (p. 67.) and confirmed recently by Tulloch, Alder and Gillespie (1960), although they recommended also the use of baths containing hexachlorophane. Nasal disinfection may be of value, too, in members of the medical or nursing staff who are carriers of a hospital strain that is causing sepsis in patients (Lowbury, 1963b).

Although the framycetin type of nasal spray is a very efficient method of nasal disinfection, an alternative non-antibiotic substance would be preferable to avoid the possible hazards of bacterial resistance and sensitization to the neomycin group of compounds (vide p.372.). For this reason polynoxylin cream was tested in nasal carriers. Although the cream suppressed nasal carriage in all cases, it acted more slowly than did the framycetin-gramicidin spray. Re-establishment of the carrier state occurred in many cases - as it does after all forms of nasal disinfection. Stratford et al. (1960) suggested that recolonization is due to exogenous staphylococci, but they did not 'type' the organisms in their investigation. The results of the present study indicate that staphylococci which reappear after treatment are mainly of endogenous origin, being usually identical with the original strains. In several

of the subjects, small numbers of Staph. aureus were found to persist in the nose during treatment, while in others Staph. aureus presumably recolonized the anterior nares from remote carrier sites in the same individual. The combined approach recommended by Tulloch, Alder and Gillespie (1960) seems therefore to be justified. It should bring about a greater reduction in the staphylococcal load of the individual, and may even totally eradicate the carrier state.

Dermatological Lesions as Sources of Hospital Infection

The results obtained in the Dermatology Department provide abundant evidence for the view that infected skin lesions are prolific sources of hospital infection. Although it is now widely accepted that dermatological lesions which are clinically infected constitute a serious menace in hospital, very little attention has been paid to the dangers associated with skin lesions which show no signs of infection. Bacterial dispersal from such lesions was demonstrated both indirectly and directly in the present investigation.

Indirect Evidence of Bacterial Dispersal. Over a period of four years consistently heavy bacterial contamination was observed in the wards and associated rooms used by dermatological patients. During the periods when detailed sampling was carried out, the

presence of active dispersers of Staph. aureus and Gram-negative bacilli was clearly demonstrated by the 'broadcasts' of airborne bacteria which were detected - especially in the bathrooms. These episodes could often be ascribed to patients who were subclinically infected. Further evidence was obtained by observing the cumulative bacterial contamination of bedding, baths, settled dust and the hands of members of staff.

Following the introduction of disinfection of skin lesions, the environmental contamination declined rapidly, but no appreciable change was found during the trial of nasal disinfection. Likewise, cross-infection of skin lesions and the anterior nares was virtually eliminated during the periods of skin disinfection, whereas nasal disinfection suppressed the carriage of Staph. aureus in the anterior nares but did not influence the rate at which skin lesions were colonized.

The possibility that the reduction in environmental contamination was due not to the suppression of skin colonization but to direct air disinfection by the skin spray must, however, be considered - as must the possibility that the prevention of nasal colonization was due to inhalation of the spray. The antibiotic spray was projected as a conical mist on to the skin lesions from a distance of between 6 and 9 inches; and the aerosol impinged on an area of about 3 square inches. Although some of the aerosol was presumably scattered into the air following impact with the skin, the amount that was disseminated in this manner was insufficient to affect the

counts of saprophytic micro-organisms in the air and in settled dust. Moreover, the amount of the antibiotic mixture that was inhaled was inadequate to suppress pre-existing nasal carriage in patients or members of staff.

Direct Evidence of Bacterial Dispersal. Dermatological lesions which were judged to be free from infection on clinical grounds frequently yielded very heavy, and almost pure cultures of pathogenic bacteria; these contrasted sharply with the scanty mixed cultures obtained from neighbouring areas of healthy skin. Such differences were most clearly revealed by the 'skin mapping' technique - as shown in Figure 33 (p.280.). In contrast to normal skin, therefore, the widespread skin lesions were evidently sites at which Staph. aureus and other pathogens were actively growing.

The significance of this enormous but inapparent breeding ground as a source of air-borne contamination was demonstrated during the tests on individuals in the cubicle. Nasal carriers of Staph. aureus with uninfected skin lesions produced relatively low staphylococcal air counts, whereas many of the patients whose skin lesions were infected - usually subclinically - were responsible for very considerable air contamination.

The skin lesions of patients studied in the main series of tests were colonized by Staph. aureus or, in two cases, by Strep. pyogenes. The dispersal of Gram-negative bacilli was, however, demonstrated during the subsequent tests on air disinfection, although most of the evidence for the dissemination

of Gram-negative infection was derived from the more indirect studies discussed above.

Variations in the Intensity of Bacterial Dispersal. Neither the nasal carrier status of the patients nor the degree of clinical infection or activity of the skin lesions, could be correlated with the amount of bacterial dispersal observed in the direct studies. On the other hand, marked differences were found in the extent to which patients with different skin diseases contaminated the environment.

The most profuse dispersal was from patients with psoriasis - the commonest disease in the dermatological wards. Considerably less air contamination was produced by patients with infected eczema; and yet while the dangers associated with such patients have been duly recognised by several investigators (vide p.364.), psoriasis and other desquamating diseases have been almost entirely ignored by students of hospital infection.

The dry scaly lesions of psoriasis might perhaps appear to be unlikely sites for the prolific multiplication of pathogenic bacteria when compared, for example, with the exudative lesions of acute eczema. The bacteriological differences between normal skin and the lesions of psoriasis could be due mainly to biochemical factors. The scales in psoriasis contain higher concentrations of phospholipids and free cholesterol than are found in normal skin (Carruthers, 1962), and there are also higher concentrations of soluble

proteins, nucleic acid components, pentose sugars and mucopolysaccharide sub-units (Flesch and Esoda, 1964). The possibility that these constituents are at least partially responsible for the ready colonization of the psoriasis lesion by Staph. aureus merits detailed investigation.

The extensive dispersal from those lesions which have become colonized is undoubtedly due to the unusually active cellular proliferation in psoriasis. As shown by Van Scott and Ekel (1963) epidermal cells in normal skin have a turnover rate of from 26 to 28 days and desquamation takes place imperceptibly, whereas the turnover rate in psoriasis is from 3 to 4 days and the greatly accelerated process of desquamation is usually evident from the amount of 'skin dust' in the vicinity of the patient.

An analogous situation is found in individuals with dandruff who freely shed 'scurf' particles. These differ from the scales in psoriasis for they usually have a low cellular content and are principally composed of inspissated sebaceous material. But this form of debris, too, could be an important vehicle of infection, particularly if it can be confirmed that the scalp and hair in 20 per cent of individuals form a reservoir for Staph. aureus (Summers, Lynch and Black, 1965).

In this connection, a point of ecological interest arises from the studies of Smith and Marples (1965). They found that Staph. aureus, mainly of 'human' phage types, was frequently present in the dry scaly patches that occur on the skin of hedgehogs. More than 85 per cent of the staphylococci were

penicillin-resistant, and Smith and Marples believed that this was due to selective pressure from penicillin-producing dermatophytes which were also usually present in these areas. It is noteworthy that in man colonization of the skin by dermatophytes and other fungi is far more common than is generally realized (Dineen and Hildick-Smith, 1965). Little is known of the mutual interaction of micro-organisms on the human skin (p.322.), yet without such knowledge the processes underlying the natural selection of bacteria and dispersal from the skin will not be fully elucidated. The common dry dermatoses and the seborrhoeic conditions may prove not only to be leading sources of hospital infection but also ideal systems for investigating the fundamental problems of skin ecology.

Air-borne Vehicles of Infection in Dermatological and
Other Wards

In his review of air-borne infection published just after the present series of investigations had begun, Williams (1960) stated:

'We know practically nothing of the size distribution of the particles carrying pathogenic bacteria or viruses and we can only guess at the probable frequency with which any infective particles are dispersed at all, from our knowledge which is largely qualitative, of the distribution of bacterial pathogens in infected people.'

As shown above, and in the remainder of the present discussion, remarkable progress seems to have been made since

1960 in our understanding both of bacterial dispersal and of the physical and chemical nature of the particles which carry pathogenic bacteria.

Particle Size. On the basis of Petri ratios (Lidwell, 1948), the average diameters of air-borne particles bearing Staph. aureus were found to vary between 11.5μ and 17μ in the different departments of the General Hospital. The air of the Dermatology Department yielded particles with a narrower range of diameters - from 10μ to 11.1μ in the three wards. These values are similar to the diameters calculated by other investigators, and the validity of this order of size has been confirmed recently using the size-grading impaction sampler (Noble and Lidwell, 1963; and the present work, p.266.). It has not been possible to substantiate the report by Eichenwald et al. (1960) that the air-borne particles bearing Staph. aureus in maternity wards are approximately 5μ in diameter; but in their investigation the 'cloud babies' present in the wards had respiratory infections and might have been disseminating organisms on small droplet-nuclei rather than on the particles more commonly encountered in hospital air.

During the present investigation consistent differences in the size-distribution of staphylococcal particles were observed in the main groups of skin disease. The particles shed in the cubicle by staphylococcal dispersers with psoriasis were mainly above 18μ in diameter, whereas those from patients with eczema were predominantly in the fraction with equivalent diameters ranging from 10μ to 18μ . These

results obtained with the size-grading sampler were in keeping both with the observed rates of decline in air counts in the different groups and with the direct observations on impacted particles trapped on solid media and coated slides.

The Nature of the Air-borne Particles. The principal vehicle of air-borne infection in the Dermatology Department was undoubtedly the skin scale. The possible significance of desquamated epidermal debris was appreciated by several observers in the Nineteenth Century (pp.34 and 368), and Smart (1883) provided an accurate illustration of this important component of hospital air in the diagram reproduced on p.35 of this thesis. Attention has only recently, however, been redirected by Davies and Noble (1962; 1963) to the possible role of skin scales in the transmission of hospital infection. These investigators suggested, on the basis of their air studies in general wards, that dangerous dispersers of Staph. aureus 'may have a heavier skin carriage of staphylococci, or they may desquamate more skin than do the non-dispersers.' In the present investigation, both of these features were found to be highly developed in patients with psoriasis and certain other skin diseases.

Most of the particles from cases of psoriasis, although accompanied by smaller epidermal fragments, are relatively large and sediment rapidly. Yet they are not necessarily less dangerous than smaller particles, for they may frequently be resuspended in the air by ward activities such as bedmaking,

and they may become further fragmented each time such disturbance occurs. Moreover, they will convey many more pathogenic bacteria than the few that were estimated by Lidwell, Noble and Dolphin (1959) to reside on unspecified air-borne particles of about 13μ equivalent diameter. There is consequently an increased danger of infection ensuing should the microscopic debris from psoriasis land upon susceptible tissues such as surgical wounds or dermatological lesions.

Whilst epidermal debris was identified as the main vehicle of transmission of air-borne bacteria in the wards, smaller numbers of fibrous fragments - chiefly cellulose - were also present in most air and dust samples both in the General Hospital and in the Dermatology Department. These fragments were called 'fibre nuclei' by Rubbo et al. (1960) who regarded them as one of the principal vehicles of air-borne infection in hospital.

It is possible that though 'fibre nuclei' are numerically less important than skin scales, they may, in their role as foreign bodies, be significant factors in the initiation of infection. Work reviewed earlier (p.224.) has shown that a relatively small infecting dose of Staph. aureus can produce sepsis in the presence of thread and other foreign material. Human epidermal scales, on the other hand, are unlikely to provoke foreign body reactions and they probably have, therefore, a passive role in the transmission of infection.

As already noted, the present data concerning dispersal relate mainly to Staph. aureus; but evidence of the air-borne

transmission of Gram-negative bacilli was also obtained by means of air studies on individuals as well as by general air sampling and the occasional observation of the nasal acquisition of these organisms. Some of the most striking bacteriological features of the environment were the relatively large intermittent air counts of Pr. mirabilis and Ps. pyocyanea. The latter organism together with coliform bacilli also abounded in settled dust. Other investigators have reported that large numbers of salmonellae survive for long periods in hospital dust (e.g. Bate and James, 1958). It is possible that the Gram-negative bacilli, which do not usually survive natural desiccation, obtain protection as a result of their intimate contact with proteins, such as those constituting epidermal debris. It is relevant to recall that, in the case of Staph. aureus, Rountree (1963) found only a slight loss in viability and infectivity over a period of 50 days for organisms dried on the protein fibres of wool, whereas a rapid decline in viability occurred on cotton fibres.

Air Disinfection in a Dermatology Department. Ultra-violet irradiation and vapours such as tri-ethylene glycol and hypochlorite have been used for air disinfection in various types of hospital ward and in operating theatres. Some of this work has already been described (pp. 81 and 233). Although reductions in bacterial air counts have usually been achieved, there has not always been a comparable effect on cross-infection rates, and undesirable side effects have often occurred. In the

present investigation, the high air counts of Staph. aureus in the Dermatology Department provided an opportunity for tests to be carried out on one of the most active and least toxic of the disinfectant vapours, hexyl-resorcinol.

In view of the demonstration by Darlow et al. (1958) of an extremely rapid 'initial kill' against artificially produced clouds of air-borne bacteria, the present series of tests was upon 'single bursts' of hexyl-resorcinol vapour. Although relatively few tests were carried out, the negative results obtained despite control of the relative humidity and the air concentration of the agent suggest that bacteria conveyed in the dried state on skin scales are protected from the action of this potent bactericidal vapour. Because of the likely importance of skin scales as vehicles of transmission outside dermatological wards the prospects of adequate air disinfection in other parts of the hospital by means of hexyl-resorcinol vapour are not favourable. Nevertheless, it would be interesting to investigate the effects of long-term air disinfection in dermatological wards.

Holland (1961) working in a children's ward which was divided into cubicles reported a reduction in the bacterial air counts following one week's use of hexyl-resorcinol air disinfection. He did not proceed to study cross-infection but suggested that the vapour should prove most useful in open wards. More recently, Meenan (1963) has reviewed 14 years' experience of this form of air disinfection in a monkey house. He recorded a very great reduction in respiratory infections

including tuberculosis among the animals, as compared with the preceding period. On the other hand, Lidwell and Williams (1954) carried out a controlled trial with hexyl-resorcinol vapour in offices, and reported that there was 'no great effect on the bacterial content of the air, on the number of colds or on the number of days of sick absence' in the offices receiving this vapour. There were obvious difficulties here, however, in avoiding errors due to the acquisition of infection while personnel were outside their offices. If, in a dermatology department, reduced air counts of Staph. aureus can be maintained during a long-term controlled trial using a low-grade vaporizer¹, it should be possible to assess the relative importance of the air-borne route of infection in dermatological patients.

¹ e.g. the 'Aerovap' apparatus manufactured by Shepherd Aerosols Ltd.

Other Routes of Infection in a Dermatology Department

Infection via Hands. 'Impression prints' taken on milk agar plates from the hands of members of staff regularly yielded cultures of the prevalent pathogenic bacteria - often even shortly after handwashing. Serial hand impressions showed that the organisms were members of the transient skin flora, and when Staph. aureus was isolated from the hands of a nasal carrier it was almost always of a different phage type from the nasal strain. Repeated contamination of nurses' and doctors' hands was clearly taking place at every contact with patients, their bedding and the objects in the ward environment.

Handwashing with soap and water did little to alleviate the situation, and even the tap handles, wash basins and towels were often heavily contaminated. However, pathogenic bacteria virtually disappeared from the staff's hands during the periods when skin lesions were being disinfected.

That the hands constitute an ideal vehicle for the transmission of infection to patients was appreciated in the ancient Talmud (p.12.) and by many of the early students of cross-infection, notably by Alexander Gordon and Semmelweis (p.25 et seq.). It was Semmelweis who first demonstrated the value of hand disinfection in the prevention of puerperal fever, and, twenty years later, Joseph Lister's insistence upon the disinfection of the surgeon's hands as well as the patient's skin probably played an important part in reducing the incidence of surgical sepsis. Moreover, surgery took a

significant step forward with the introduction of sterile rubber gloves in 1889 (Halsted, 1913).

In recent years, several investigators (e.g. Rammelkamp et al., 1964) have shown that the use of hand disinfection by maternity nursery personnel leads to a reduction in the rates of colonization and cross-infection among infants, but equivalent work has apparently not been carried out in adult wards except as part of a combined programme (e.g. Gillespie et al., 1961).

Although skin lesions were undoubtedly the principal source of infection among dermatological patients in the present investigation, the hands of members of staff could well have been an important means of spread to other patients. Proof of the part played by hand contamination can come only from a controlled trial of hand disinfection in these wards.

Hexachlorophane and chlorhexidine preparations have been widely used as skin antiseptics (Lowbury, 1965), but they act slowly and are relatively ineffective against Gram-negative organisms and fungi (Miller, Jackson and Collier, 1962). Since such organisms may be present in large numbers in a dermatological ward, alternative preparations are preferable to avoid the dangers of selecting resistant flora (vide p.219.). A promising application for the hands is composed of dequalinium acetate and cetylpyridinium acetate in ethanol (Dineen and Hildick-Smith, 1965). However, the high incidence of bacterial contamination both of patients and the environment in a dermatology department will necessitate frequently repeated hand

disinfection. The risk of infection via hands will be removed by nothing short of surgical asepsis, involving amongst other things, hand disinfection and the wearing of sterile gloves before the skin lesions of each patient receives nursing or medical attention. It would probably be more rewarding to concentrate upon the sources of infection - notably the skin lesions themselves.

Infection from Bedding. As in the case of the hands of members of staff, heavy bacterial contamination of bedding was found in the majority of tests, except during periods when skin lesions were receiving anti-bacterial treatment. In a number of cases strains of Staph. aureus other than those colonizing the bed-occupant were found in bedding. The rapidity with which staphylococci spread from bed to bed in an open ward has been demonstrated experimentally by Anderson, Coulter and Looke (1960), and by Rubbo, Stratford and Dixon (1962).

The bedding in the Dermatology Department was, therefore, a depot for staphylococci derived from the patients, and it constituted a potential source of secondary dispersal in the wards. Sheets, though, changed frequently, were found to be more heavily contaminated than blankets; this has also been the experience of Rubbo (1963). The cotton fragments from sheets can readily become air-borne, carrying with them Staph. aureus, whereas wool from blankets cannot produce particles small enough to remain suspended in air. Rubbo, Stratford and

Dixson (1962) have, however, demonstrated an alternative route of air contamination from blankets for, when these are covered by a counterpane, friction causes the transfer and dissemination of bacteria from the blanket into the air. A similar mechanism probably underlies the dispersal of some of the bacteria from skin via the clothing (Hare and Thomas, 1956), and is an alternative route to transmission on epidermal scales.

Rubbo (1963) has reviewed reports which show that the oiling of blankets and the issue of clean blankets to each patient do not result in a reduction in the incidence of cross-infection; and mention has already been made of the irrational attention which hospital blankets have recently received (p.236). In a dermatological ward, where the principal vehicle of air-borne infection is the skin scale, it is unlikely that even daily changes of bedding would greatly influence the cross-infection rate. Nevertheless, if it can be confirmed that Staph. aureus remains fully infective for long periods in the dried state (p.235), it would be reasonable to reduce the environmental load of bacteria as far as possible. Frequent disinfection of bedding will contribute towards achieving this aim.

Infection from Baths. Unlike the bedding, the baths were used in quick succession, with minimal cleansing, by a large number of patients. This sequence of events led to a rapid accumulation not only of staphylococci but also of a variety of Gram-negative bacilli. This formidable reservoir of

infection is of great potential importance both in connection with the spread of superficial infections and in relation to urinary tract infection in the female(p.198.).

Wherever possible the communal bath should be replaced in hospital by showers. Unfortunately, the nature of the dressings which are commonly used in a dermatology department necessitates the provision of baths for the patients. As shown in the present work, the combined use of a detergent and hypochlorite solution - originally employed for cleansing dairy equipment - is a simple yet efficient method of disinfecting baths: and the conditions in the present tests were particularly exacting in view of the thick greasy applications with which many of the patients were being treated. The alternative method of disinfecting baths described by Ayliffe, Alder and Gillespie (1959) consists of adding to the water before use 1 oz. of a 10 per cent hexachlorophane solution in spirit. It is unlikely that this would have proved effective under the difficult conditions prevailing; the comparable procedure of adding cetrimide to the bath water proved valueless in the Dermatology Department, and may possibly have acted selectively in favour of Ps. pyocyanea and other relatively resistant Gram-negative bacilli. The choice of efficient chemical disinfectants for hospital use is briefly discussed below.

It was disappointing to find that the incidence of cross-infection, especially with Gram-negative organisms, did not fall after the introduction of an efficient cleansing method

for baths. However, numerous alternative reservoirs and pathways of infection persisted during the period when the baths were being properly disinfected.

Miscellaneous Vehicles of Infection. Almost all the varied objects examined in the wards - taps, door and television-set knobs, towels, dressing gowns, trolley tops and numerous other surfaces - yielded pathogenic bacteria. These objects, however, were probably of limited importance as vehicles of infection in an environment heavily charged with pathogens. In contrast, the creams, ointments and lotions applied directly to the patient's skin lesions were potentially of great importance. These medicaments are readily contaminated by attendants' hands and dust. Bacteria can persist in most of them and may even multiply - especially in the case of Ps. pyocyanea. In the recent outbreak of Pseudomonas infection in a dermatological ward (p.327) cortico-steroid cream dispensed in bulk was believed to be both the reservoir and the vehicle (Noble and Savin, 1966). Tests on a variety of dermatological preparations were, however, negative in the present study. The high turnover rate of these substances in the Dermatology Department must greatly reduce the risks of a reservoir of infection developing; but the regular bacteriological examination of such materials should be an integral part of any programme designed to reduce hospital infection.

In the present study, the drinking glass and water carafe appeared to be possible vehicles of respiratory tract infection.

They had previously attracted the attention of Walter et al. (1958), but these investigators described the transfer of unwashed carafes from one patient to another, whereas in the Dermatology Department the utensils were washed - albeit inadequately. The processes of 'sanitization' used for some crockery and other articles in hospital were of doubtful value, and the heterogeneous agents used on surfaces and baths stimulated the present work on the evaluation of chemical disinfectants.

Disinfectants for Hospitals. All of the reservoirs and vehicles of infection described above can be disinfected by means of chemical agents. Much attention has been paid to hand disinfection in recent years (p.355.), but in contrast relatively little information concerning disinfectants for use on inanimate objects is available from independent sources (Report, 1965c).

The majority of 'disinfectants' and 'chemical sterilizers' used in the General Hospital and in the Dermatology Department were found either to be inactive against a selection of bacteria and viruses or active at an unreasonably slow rate. Disinfectants of the halogen type were the only entirely suitable ones examined.

For the evaluation of bactericidal activity the modification of the 'surface' technique of Hare, Raik and Gash (1963) described on p.391 proved very satisfactory. It closely simulates the conditions under which many solid objects are

disinfected in practice. The technique devised for evaluating the virucidal activity of chemicals has similar advantages of simplicity and realism. Unlike the disk-diffusion procedure for testing anti-viral compounds on infected cell monolayers (Siminoff, 1961), the present method can be used with cytotoxic substances. Moreover, it avoids the disadvantages of the comparable 'surface' technique of Lorenz and Jann (1964) which involves a large and indeterminate dilution of the virus inoculum.

By means of the simple, direct test procedures used in the present studies it should be possible to provide a reliable assessment of the bewildering range of chemical agents now available for hospital use.

The Concept of Microbial Dispersal from Skin

Observations suggesting that the human skin is a leading source of hospital infection have been made since earliest times (vide Part I); but although knowledge of the part played by the hands in the transmission of infection came early, it was not until the mid-Nineteenth Century that the indirect modes of infection from skin began to receive attention. Since then the literature has contained scattered references to the role of the skin in the dissemination of infection. Following the discussion of results obtained in the present investigation, it

is appropriate that the diffuse literature on 'skin dispersal' should now come briefly under review - particular emphasis being placed on contributions made since 1961.

Table XXXVII outlines the curiously circular development of ideas on the mechanism of bacterial dispersal during the past hundred years. As shown, one complete cycle had been turned shortly after the start of the present investigation in the Dermatology Department. The current concept of bacterial dispersal is essentially identical with the balanced view held by Sir James Simpson. This was based on his own and other investigations carried out rather more than a hundred years ago (p. 34.). The Table, however, omits a number of investigators who continued to be aware of some aspects of skin dispersal during the intervening years.

Qualitative Observations on Dispersal from Skin. After the considerable interest shown during the third quarter of the Nineteenth Century, the subject was almost entirely ignored for more than 80 years. However, Crookshank (1886) drew attention to the dissemination of dermatophytes in the air of hospitals dealing with skin diseases (p. 62.), and twenty years later, Gordon (1903-5) re-opened the discussion of the possible role of skin 'scurf' as a vehicle of air-borne infection. But almost 30 years were to elapse before a specific pathogen was found to be associated with skin dispersal. Allison and Gunn (1932) mentioned in passing, during a review of the epidemiology of streptococcal infection, that haemolytic streptococci could be readily isolated from desquamated skin in scarlet fever

TABLE XXXVII. CYCLICAL DEVELOPMENT OF THE CONCEPT OF BACTERIAL
DISPERSAL

KEY REFERENCE ^x	ORGANISM	MECHANISM
SIMPSON, 1869	Indeterminate	<u>Skin scales</u> and other air-borne debris.
CORNET, 1889	Tubercle bacillus	Contaminated dust
FLÜGGE, 1897	" "	Respiratory droplets
(CHAPIN, 1912) [‡]	(Various)	(Direct contact)
WELLS, 1934	Respiratory patho- :gens	Droplet nuclei
HAMBURGER <u>et al.</u> , 1945	<u>Strep. pyogenes</u>	Nasal carriers, via dust
DUGUID & WALLACE, 1948	<u>Staph. aureus</u> , etc.	Nasal carriers, (quantitative)
HARE & RIDLEY, 1958	<u>Staph. aureus</u>	Perineal carriers, via dust
HARE & COOKE, 1961	" "	Skin lesions as source
DAVIES & NOBLE, 1962	" "	<u>Skin scales</u> as vehicle

x All have been reviewed in Part I and Part III (above)

‡ Represents period of eclipse for theory of air-borne infection.

wards. A few years later extensive dispersal from burns infected with Strep. pyogenes was demonstrated by Cruickshank (1935). This and subsequent observations on streptococcal dissemination are reviewed in Part I.

Four reports which were not mentioned earlier are of particular interest in the present context. Boisvert and Powers (1944) hinted that children suffering from eczema whose skin lesions became infected with Strep. pyogenes could be sources of infection in hospital wards. Subsequently, De Forest and Kerr (1945) described an outbreak of streptococcal infection among nurses in a paediatric department due to a child with clinically infected eczema. The remarkable degree of contamination which may be caused by an adult with a small infected skin lesion was shown by Colebrook and Ross (1947). They studied the aerial dissemination of Strep. pyogenes which apparently originated from a small healing abrasion wound on the elbow of a surgeon. The fourth report was made by Loosli et al. (1950) who carried out an extensive epidemiological survey of the personnel and environment of a paediatric unit following an outbreak of streptococcal infection. They emphasised the danger in hospital of individuals whom they termed 'skin dispersers' of streptococci, and they compared them to the profuse nasal dispersers described earlier by Hamburger et al. (1945).

Following the work of Loosli and his colleagues, interest in the dispersal of streptococci declined; but although, two years earlier, Duguid and Wallace (1948) had published their

report of direct studies on staphylococcal dispersal, it was not until 1956 that further progress was made in the quantitative field (p.368.). A similar period of time elapsed before relevant observations of a qualitative nature were reported. In 1955 Barber and Burston during a discussion of the evolution and spread of antibiotic-resistant staphylococci mentioned that four patients whose extensive skin lesions were infected with Staph. aureus were probably important sources, as were three patients with staphylococcal enterocolitis and three with staphylococcal chest infections. This paper, however, contains no data on environmental contamination. Three years later, Barber and Dutton (1958) described a serious outbreak of staphylococcal infection in a surgical ward which apparently originated from a patient with 'multiple septic spots and boils' whose lesions yielded a group I multiple-resistant staphylococcus. Cases of severe infection of the skin, wounds and chest ensued and the ward had to be closed. In the same report there is also a description of a less severe outbreak of infection in a medical ward. A patient admitted with infected facial dermatitis was believed to have introduced a group III erythromycin-resistant staphylococcus into the ward. This organism then infected the extensive eczema lesions of another patient who was believed to have been the source of the subsequent widespread dispersal of Staph. aureus in the ward. The causative staphylococcus was identical in phage susceptibility and antibiotic sensitivity with the endemic strain in this General Hospital and also resembled the

prevalent strains in the Dermatology Department. Like these, it was widely disseminated but produced minimal disease, in contrast to the group I staphylococcus described by Barber and Dutton which resembled the organism found in the General Medical Department (p.146.).

The dangers associated with dispersal of a virulent strain of Staph. aureus from skin lesions are also demonstrated in a paper by Vogel et al. (1959). Three patients whose dermatological lesions were heavily infected with a staphylococcus of type 52/52A/80 were believed to have been responsible for 63 cases of clinical infection, mainly of the chest, in a medical ward. Secondary spread occurred in the general community, and in all there were 14 deaths. In the same year Mitchell et al. (1959) reported a serious outbreak of post-operative sepsis in a Glasgow hospital. Once again it was due to the epidemic group I staphylococcus whose source on this occasion was a surgeon with a skin infection.

In newborn infants widespread dissemination may follow subclinical infection of the umbilical cord stump with haemolytic streptococci (Boissard and Eton, 1956; Kwantes and James, 1956) or with Staph. aureus (e.g. Jellard, 1957). The circumcised penis is also a significant source of infection until the wound heals (Hurst, 1965).

There are surprisingly few recorded observations on dispersal from subclinically infected skin lesions in adults. An interesting example of an inapparent source of dispersal is mentioned briefly by Colbeck (1962) in his monograph on the

control of hospital infection. He describes the frequent contamination of nutrient agar plates when these are poured by technicians who have 'scaly lesions' which appeared to be free from infection. More recently, Alder and Gillespie (1964) have demonstrated that the hospital environment may become heavily contaminated from subclinically infected pressure sores. Similarly, as already described, Hare and Cooke (1961) and Thomas and Griffiths (1961) have reported that dermatological patients may heavily contaminate their surroundings: but cross-infection of patients' skin lesions has attracted remarkably little attention, though the present results indicate the high incidence of such infections. One of the very few accounts of this form of cross-infection is given by Stevenson and Whittingham (1963). While describing a new form of treatment for psoriasis they mention that Staph. aureus from a case of varicose ulcer in the ward spread to the skin lesions of 15 patients suffering from psoriasis.

Skin dispersal of micro-organisms other than bacteria has rarely been reported. Almost 80 years after the observations of Crookshank (1886) on the dissemination of dermatophytes in hospital, Clayton and Noble (1963) reported similar findings in a skin out-patient clinic. An even longer period separates the observations of Sir John Pringle (1752) on the dispersal of Sarcoptes scabiei from those of recent investigators (p. 63.). In 'Norwegian (crusted) scabies' extremely profuse dissemination of the mite takes place (Herridge, 1963). As in the case of bacteria the vehicle of transmission appears to be mainly the skin scale, but the large fragments conveying the mites will

sediment rapidly after being liberated into the air.

Quantitative Observations on Dispersal from Skin. The modern quantitative work in this field began with the studies of Duguid and Wallace (1948). They investigated in detail the contamination produced in a test cubicle by four healthy men who were not carriers of pathogenic bacteria, and they later studied two nasal carriers of Staph. aureus. Their results showed that dust derived from skin and clothing during normal activity was responsible for most of the air contamination observed; direct liberation of organisms from the respiratory tract contributed comparatively little, even during sneezing. The value of specially-designed clothing in the prevention of air contamination was also demonstrated. As noted on p.338, the two nasal carriers were found to disperse relatively few staphylococci compared with the infected dermatological patients who were tested under similar conditions in the present work.

Subsequent investigations by Hare and colleagues (p.339.) on healthy carriers confirmed the findings of Duguid and Wallace, and indicated that individuals whose skin is colonized by Staph. aureus are particularly heavy dispersers. The studies were extended to patients with staphylococcal infections by Hare and Cooke (1961), and - in parallel with the present investigation - specifically to dermatological patients by Cooke and Buck (1963). The latter investigated, on a single occasion, the staphylococcal contamination produced

by each of 36 unselected patients admitted to two general medical wards. The skin lesions of two-thirds of the patients were found to be infected with Staph. aureus, and self-contamination of the patients and their surroundings was described in most cases. Proof of self-contamination was not, however, possible since phage typing was only carried out in one case. Air sampling was not performed, nor did the investigators study the spread of infection in the two wards; but they expressed the view that most of 'these strains (of Staph. aureus) had not been acquired in hospital'. Apparently none of the patients showed clinical signs of infection. It is noteworthy that although only four patients with psoriasis were included in the series, three of these seemed to have produced extremely heavy contamination.

Very recently, Noble and Davies (1965) have carried out quantitative air studies on a number of patients. These included 41 who had skin diseases, which were grouped as infantile eczema (8 cases), adult eczema (10 cases), miscellaneous skin diseases (16 cases) and staphylococcal skin diseases (7 cases). Using a curtained form of cubicle in which patients undressed, Noble and Davies found that most of the dermatological patients yielded larger numbers of skin scales and staphylococci than did the other patients. Moreover, 19 of those with skin diseases were 'dispersers' - defined by the authors as individuals in whose immediate vicinity Staph. aureus constitutes more than 1 per cent of the total air-borne bacteria. Their tests were carried out

mainly on out-patients, but some of the dispersers were in-patients and six of them appeared to be infected with the same type of staphylococcus. The report does not, however, include data on the ward environment or on cross-infection.

In contrast to his recent findings in dermatological patients, Noble (1962) detected among surgical patients over a four-year period only 8 dispersers of Staph. aureus (as judged by general air counts in the wards) in 3675 admissions. Three of the dispersers were skin carriers, but the skin was not swabbed in the remaining five patients. In no case was the surgical wound found to be a source of dispersal. Similarly, Thom and White (1962) did not detect aerial dispersal during the surgical treatment of out-patients who had septic lesions, unless contaminated dressings from these were carelessly handled.

Further evidence of the very heavy dispersal of Staph. aureus which may be produced by dermatological patients was recently provided by Solberg (1965). He investigated 15 patients who had staphylococcal sepsis of their skin lesions, and he assessed the ability of each patient to disperse Staph. aureus by transferring their beds to a special test room where a nurse carried out a standardised bedmaking procedure while air sampling was in progress. Two of the 15 patients had 'widespread pyodermias' and they dispersed more staphylococci into the air than did the remaining 13 dermatological patients, 14 other patients who were perineal carriers and 100 who were nasal carriers added together.

Finally, during the past year two groups of investigators have once again focused attention on bacterial air contamination from normal skin. Speers et al. (1965) reported that the total bacterial content of the air in the vicinity of 11 individuals increased after showers had been taken. The same team of investigators (Bernard et al., 1965) subsequently confirmed the observations of Duguid and Wallace (1948) on the prevention of air contamination by the use of suitable clothing. Similar studies were reported by Bethune et al. (1965) who tested a small group of surgical patients and staff. Men were found to disperse more staphylococci than women, and dissemination was more profuse from below the level of the waist than from above it. As shown previously by Duguid and Wallace, cotton operating clothes did not prevent the shedding of bacteria.

The Recognition and Prevention of Bacterial Dispersal
from Skin

It is evident from the present investigation that patients with skin diseases constitute a serious potential danger in hospital. Usually these patients are not segregated in special dermatological wards but are treated instead in open medical wards. Moreover, patients with dermatological lesions are often admitted to surgical and other units on account of conditions unrelated to their skin disease. Thus it has been estimated that psoriasis is present in 2 per cent of the British

population (Ingram, 1964), and minor forms of the other dermatoses, including eczema and the miscellaneous desquamating diseases, are probably even commoner when considered together. As shown in the present work, the skin lesions of many of these patients may be sites of heavy subclinical infection at the time of admission. Ideally, therefore, dermatological lesions should be located and swabbed when the patient is seen in the out-patient department or elsewhere before admission. Failing this, the lesions should be swabbed when the patient is admitted to hospital and he should be effectively isolated for one day until the initial laboratory results are available. If it is found that the patient's skin lesions are colonized by pathogenic bacteria he must not be allowed to enter an open ward. The same considerations apply also to members of staff, some of whom may well have clinically quiescent skin lesions which are heavily colonized by pathogenic bacteria.

In this investigation, a spray containing a mixture of antibiotics was found to be an efficient method of suppressing these sources of bacterial contamination. A similar mixture was shown to be effective in the treatment of overt clinical infection of the skin in a series reported by Lubowe (1963). Of the three antibiotics used in the Rikospray, neomycin and bacitracin are reserved for topical application since they are unsuitable for systemic use. Nevertheless, the value of neomycin and the related substance, framycetin is threatened by the recent appearance in other parts of Scotland of resistant strains of Staph. aureus (Robertson, 1963; Mitchell, 1964).

Fortunately resistance was not encountered in the present studies, and this might have been due to the inclusion of a mixture of unrelated bactericidal agents in the spray.

Further concern in relation to neomycin and framycetin has arisen because of recent reports that contact dermatitis may follow the topical use of this group of antibiotics (e.g. Epstein, 1963). Sensitization was not, however, experienced during the present trials of either the framycetin nebulizer or the Rikospray. The finding of Kirton and Munro-Ashman (1965) that neomycin is held in the stratum corneum for prolonged periods could explain both the tendency of the antibiotic to produce sensitization and its excellent antibacterial properties when used topically.

Colistin, the third antibiotic included in the Rikospray, has the disadvantage of being required occasionally for systemic administration; and yet the polymyxin-colistin group of antibiotics is the only one at present available which can deal adequately with Ps. pyocyanea. For this reason, preliminary tests were carried out on Noxyflex (p.282); the results were encouraging.

Skin lesions which are free from infection at the time of admission to hospital may readily become colonized during the patient's stay in the ward. It is therefore essential that dermatological lesions are examined bacteriologically at intervals while the patient remains in hospital. The prophylactic application of a non-antibiotic antimicrobial agent to the lesions should be considered in these cases -

particularly if psoriasis is present - and is certainly more justifiable in the interests of hospital hygiene than is prophylactic nasal disinfection. Other measures which should reduce the risk of skin dispersal include the application of bland dust-suppressant or occlusive dressings to the lesions, when this is dermatologically acceptable. Both colonization of skin lesions and the dispersal of infection will also be greatly reduced if dermatological dressings are changed only in a special room supplied with positive-pressure ventilation and a source of filtered air. The value of such facilities was shown by Bourdillon and Colebrook(1946) in relation to patients with burns - who are comparable in many respects with dermatological patients.

In addition to keeping individuals who are potential dispersers under scrutiny, it may be worthwhile to carry out a simple form of air sampling in open wards at regular intervals. The presence of dispersers should be suspected and further investigations undertaken when Staph. aureus counts are obtained in excess of 1 per cu. ft. of air, or when a similar number settle on 1 sq. ft. per minute. However, experience in individual wards may show that considerably lower counts than these signify unusual contamination. Routine sampling of the environment may also reveal dispersal of other pathogenic micro-organisms.

In all parts of the hospital, the recognition and suppression of bacterial dispersal from skin must form an integral part of any programme designed to prevent cross-infection. Our hospitals will not be rendered safe until these precepts are implemented.

Part III

STUDIES IN A DERMATOLOGY DEPARTMENT

(v) SUMMARY

III(V)

SUMMARY

Over a period of four years, bacteriological investigations carried out in a skin department showed that dermatological wards constitute ideal models for the planned, long-term study of hospital infection.

The skin lesions of 45 per cent of patients yielded significant cultures of pathogens - mostly Staph. aureus - on admission, but less than half showed clinical evidence of infection. The frequency of heavy subclinical infection was also high in out-patients' skin lesions, and the incidence of antibiotic-resistance was greater than had previously been observed in the non-hospital population of Edinburgh.

The average duration of stay in the wards was 39.2 days; and the skin lesions of 43 per cent of 'unprotected' in-patients acquired bacteriologically significant, but usually subclinical infection. Autogenous infection and super-infection accounted for one-seventh and one-third of these cases, respectively. Primary cross-infection occurred in the remainder. Sepsis was uncommon at sites remote from the skin lesions.

Three types of Staph. aureus caused 52 per cent of the staphylococcal cross-infection. Gram-negative bacilli were responsible for 16 per cent of all cross-infection.

Nasal carriage of Staph. aureus developed in 22 per cent of the patients who were not participating in trials of topically applied anti-bacterial agents.

In the absence of specific counter-measures, there was consistently heavy environmental contamination by Staph. aureus and Gram-negative bacilli. 'Broadcasts' of Staph. aureus were especially evident in the bathrooms, and notable sites of heavy cumulative contamination with pathogens were the communal baths, bedding, settled dust and the hands of the staff.

Nasal disinfection was successfully carried out in one of the two main wards for four months, resulting both in the suppression and prevention of nasal carriage; but no change was observed in the incidences of cross-infection or environmental contamination - even though efficient cleansing of the baths was also instituted. In contrast, the use of antibacterial sprays on skin lesions was accompanied by a striking reduction in environmental contamination, and both the acquisition of nasal staphylococci and cross-infection of the skin lesions were virtually abolished.

Direct studies upon dispersal of pathogens in a cubicle showed that patients with psoriasis who had subclinical infections generally produced higher levels of air-borne contamination than other patients, including those with clinically infected eczema. In psoriasis the majority of air-borne particles carrying bacteria had a diameter greater than 18μ , while in eczema smaller particles predominated. The probable vehicle of infection was shown to be microscopic epidermal debris. Neither the clinical assessment of the lesions nor the nasal carrier status of the patient could be correlated with the degree of dispersal; and relatively few

organisms were shed by nasal carriers of Staph. aureus whose skin lesions had not become colonized.

In addition to the main investigations, studies were also carried out on bacteriocine typing of Proteus, chemical disinfection of air, the use of a non-antibiotic nasal antiseptic and the methods of assessing bactericidal and virucidal activity of liquid disinfectants used in the hospital.

In the discussion, particular emphasis is placed on the serious potential danger of bacterial dispersal from sub-:clinically infected skin lesions, and recommendations are made for their safe management in hospital.

APPENDIX

APPENDIX TABLE I. NUMBER AND INCIDENCE OF LESIONS DUE TO STAPH. AUREUS AND OTHER BACTERIA OCCURRING IN HOSPITAL: NOVEMBER-DECEMBER 1960, JANUARY-FEBRUARY 1961

DEPARTMENT	NON-STAPHYLO- COCCAL INFECTIONS		STAPHYLOCOCCAL INFECTIONS			
	NO.	INCIDENCE ¹	NO.	INCIDENCE ¹	% OF ALL INFECTIONS	
Paediatric Medicine	(a)	11	13	5	6	31
	(b)	11	10	7	7	39
Paediatric Surgery	(a)	14	20	11	16	44
	(b)	17	23	6	8	26
Maternity Nurseries	(a)	13	5	15	6	54
	(b)	8	3	27	10	76
Maternity Wards	(a)	36	12	4	1	10
	(b)	24	12	3	2	11
Urology	(a)	26	35	4	5	13
	(b)	25	31	6	7	20
Gynaecology	(a)	14	13	4	4	22
	(b)	12	9	4	3	25
Gastro-enterology	(a)	16	30	4	8	20
	(b)	17	29	4	7	19
General Medicine	(a)	15	15	6	6	28
	(b)	17	15	10	9	37
General Surgery	(a)	15	11	6	4	28
	(b)	15	9	5	3	25
TOTALS	(a)	160	14	59	5	27
	(b)	146	12	72	6	33

¹ per 100 patients.

(a) = November-December 1960.

(b) = January-February 1961.

APPENDIX TABLE II. NUMBER AND INCIDENCE OF LESIONS DUE TO STAPH.AUREUS AND OTHER BACTERIA OCCURRING IN HOSPITAL: MARCH-APRIL 1961, MAY-JUNE 1961.

DEPARTMENT	NON-STAPHYLOCOCCAL INFECTIONS		STAPHYLOCOCCAL INFECTIONS			
	NO.	INCIDENCE ¹	NO.	INCIDENCE ¹	% OF ALL INFECTIONS	
Paediatric Medicine	(a)	11	13	8	10	42
	(b)	11	17	11	17	50
Paediatric Surgery	(a)	13	16	5	6	28
	(b)	13	13	15	15	53
Maternity Nurseries	(a)	8	5	9	6	53
	(b)	7	3	14	6	67
Maternity Wards	(a)	27	14	2	1	7
	(b)	20	7	4	1	17
Urology	(a)	28	39	3	4	10
	(b)	28	33	10	12	26
Gynaecology	(a)	14	11	4	3	22
	(b)	18	14	3	2	14
Gastro-enterology	(a)	16	28	1	2	6
	(b)	8	11	2	3	20
General Medicine	(a)	18	18	6	6	25
	(b)	14	15	2	2	14
General Surgery	(a)	16	10	6	4	27
	(b)	14	9	5	3	26
TOTALS	(a)	151	15	44	4	23
	(b)	133	11	66	6	33

¹ per 100 patients

(a) = March-April 1961.

(b) = May-June 1961.

APPENDIX TABLE III. NUMBER AND INCIDENCE OF LESIONS DUE TO STAPHAUREUS AND OTHER BACTERIA OCCURRING IN HOSPITAL: JULY-AUGUST 1961, SEPTEMBER-OCTOBER 1961.

DEPARTMENT	NON-STAPHYLOCOCCAL INFECTIONS		STAPHYLOCOCCAL INFECTIONS			
	NO.	INCIDENCE ¹	NO.	INCIDENCE ¹	% OF ALL INFECTIONS	
Paediatric Medicine	(a)	5	4	3	2	37
	(b)	10	13	2	3	16
Paediatric Surgery	(a)	12	11	12	11	50
	(b)	17	13	16	12	48
Maternity Nurseries	(a)	12	5	16	6	57
	(b)	10	4	15	6	60
Maternity Wards	(a)	28	14	4	2	12
	(b)	30	11	3	1	10
Urology	(a)	23	25	5	6	17
	(b)	21	24	5	6	19
Gynaecology	(a)	20	19	2	2	10
	(b)	18	14	3	3	14
Gastro-enterology	(a)	13	17	3	4	19
	(b)	18	25	2	3	10
General Medicine	(a)	10	10	4	4	28
	(b)	13	12	4	4	23
General Surgery	(a)	14	11	7	6	33
	(b)	13	8	7	4	35
TOTALS	(a)	137	11	56	5	29
	(b)	150	12	57	4	28

¹ per 100 patients.

(a) = July-August 1961.

(b) = September-October 1961.

Method of Recording Medical and Surgical Data on Each Patient Admitted to the Edinburgh Royal Infirmary in 1739.

This is an extract of a contemporary account which was quoted by Maitland (1753):

'There is a Journal kept, in which, in different Columns under proper Titles, opposite to the Number on the several Beds, the Clerk inserts every Circumstance of the Patient's Case, as dictated to him by the Physicians, whom he attends for that Purpose, from Bed to Bed, with his Journal lying open upon a Desk, moving on Casters; and a Note of the daily Prescriptions is also entered here.

Each Page of the Journal is divided into Seventeen Columns, containing a Diary of the Cases of the several Patients, and various Appearances of their Distempers while under Cure; the Names whereof are placed at the Heads of the several Columns as followeth, viz. The first contains the Dates of the Year, Month and Day; the second, the Number of the Bed wherein the Patient lies; third, Operation of the Medicines; fourth, intervening Symptoms; fifth, Pulse; sixth, Thirst; seventh, Appetite; eighth, Spittle; ninth, Tongue; tenth Sweat; eleventh, Urine; twelfth, Faeces; thirteenth, ordinary Symptoms; fourteenth, supervening Symptoms; fifteenth, Food; sixteenth, Drink; and the seventeenth, Medicines.

There is a Leger (sic), in which every Patient has an Opening left for them, with the Number of their Bed and their Name at the Head; Here, on their first coming to the House, the Physician dictates to him, and he enters an exact Description of the Patient's Case, and to this he subjoins daily from the Journal all that happens, and the Prescriptions for them while they continue in the House. He also keeps Books of a few Sheets of Paper stitched together, in which, under the Name of the Patients, and Number of their Bed, he daily writes the Prescriptions to be transcribed by the Surgeons Apprentices, and Directions as to Diet and Regimen are here set down, to guide the Governante and Nurses in their Management of the Sick.

At the End of the Leger there is an Index of the several Patients and Diseases mentioned in it; and a general alphabetical Index is preparing, under the proper Articles of which, all the Diseases treated in the Infirmary are to be entered: with a Reference to the particular Page of each Volume of the Leger, where the History of Patients, under such Diseases are inserted. What Improvement such an exact Register, a depositing of accurate Observations, which every one can have Access to consult, may in a little Time be to Physick and Surgery, is very obvious. It were much to be wished that all the Infirmaries in Europe would follow the same Method; but that is scarce to be hoped.'

(a) The Application of Bacteriocine-typing to the Identification of Proteus

The need for a satisfactory method of characterising Proteus spp., and the success previously obtained with bacteriocine typing in other bacterial genera (p.58.), led to an investigation of bacteriocine production and sensitivity amongst strains of Pr. mirabilis - the species of almost all Proteus organisms isolated in the two hospitals.

METHODS

In the preliminary work, 112 hospital strains of Pr. mirabilis were examined. Of these, 40 were from the dermatological wards and many were epidemiologically related; the remaining 72 were provided by Dr. T.B.M. Durie of the Royal Infirmary Bacteriology Department, and were mostly from sporadic infections occurring throughout the hospital. All the strains swarmed on nutrient agar and were biochemically homogeneous when tested for urease production, the ability to transform phenylpyruvic acid to phenylalanine, and gelatine liquefaction. None of the strains fermented mannitol or maltose, and none produced indole or grew in Koser's citrate medium.

Trays measuring 10 in. by 10 in. were filled with MacConkey's agar to a depth of $\frac{1}{4}$ in., and loopfuls of overnight broth cultures of six different Proteus strains were spread across the medium in parallel streaks on each plate. After incubating at various temperatures for differing lengths of time, the growths were scraped off with sterile glass slides, and the remaining organisms were killed by exposing the

trays to chloroform vapour for 1 hour. The trays were aired for a further hour, and then, at right angles to the initial streaks (of 'producer' strains), a second set of parallel streaks (of 'indicator' strains) was made on each tray as before. After overnight incubation the plates were examined for growth inhibition at the intersections of the lines of inoculation. By these means all the strains were tested against each other both as potential producers of bacteriocines and as indicators of bacteriocine production.

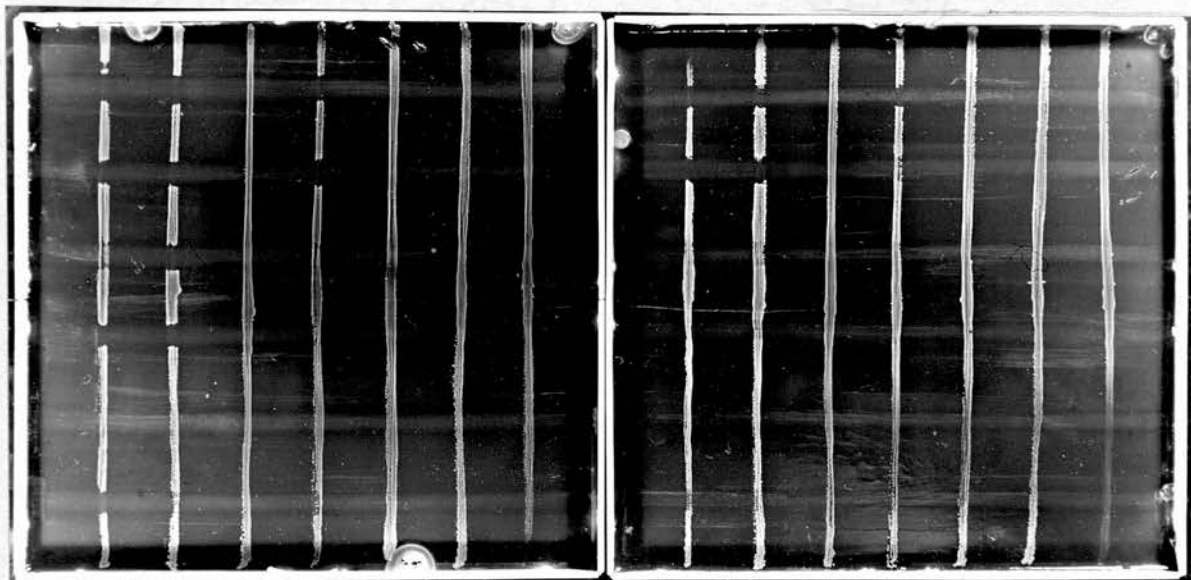
Attention was then paid to the effects of adding to the medium antagonists of proteolytic enzymes (iodo-acetic acid, sodium citrate and di-potassium hydrogen phosphate), and of adding erythromycin (to prevent overgrowth of the trays by spore-bearers). These media were compared with nutrient agar containing 0.1 per cent chloral hydrate with or without the enzyme antagonists.

Bacteria-free extracts containing bacteriocines were also prepared. For this purpose plates of nutrient agar (with or without 2×10^{-4} M. iodo-acetic and 0.2 per cent di-potassium hydrogen phosphate) were flood-seeded with producer strains; following 48 hours' incubation the bacterial growth was scraped off and the medium in each plate was subjected to a cycle of freezing at -25°C . After thawing the medium at room temperature, the extruded fluid was passed through a Seitz filter. The filtrates were then tested for activity by dropping serial dilutions on to suitable indicator strains which had been flood-seeded on solid media and then incubated at 30°C .

RESULTS:

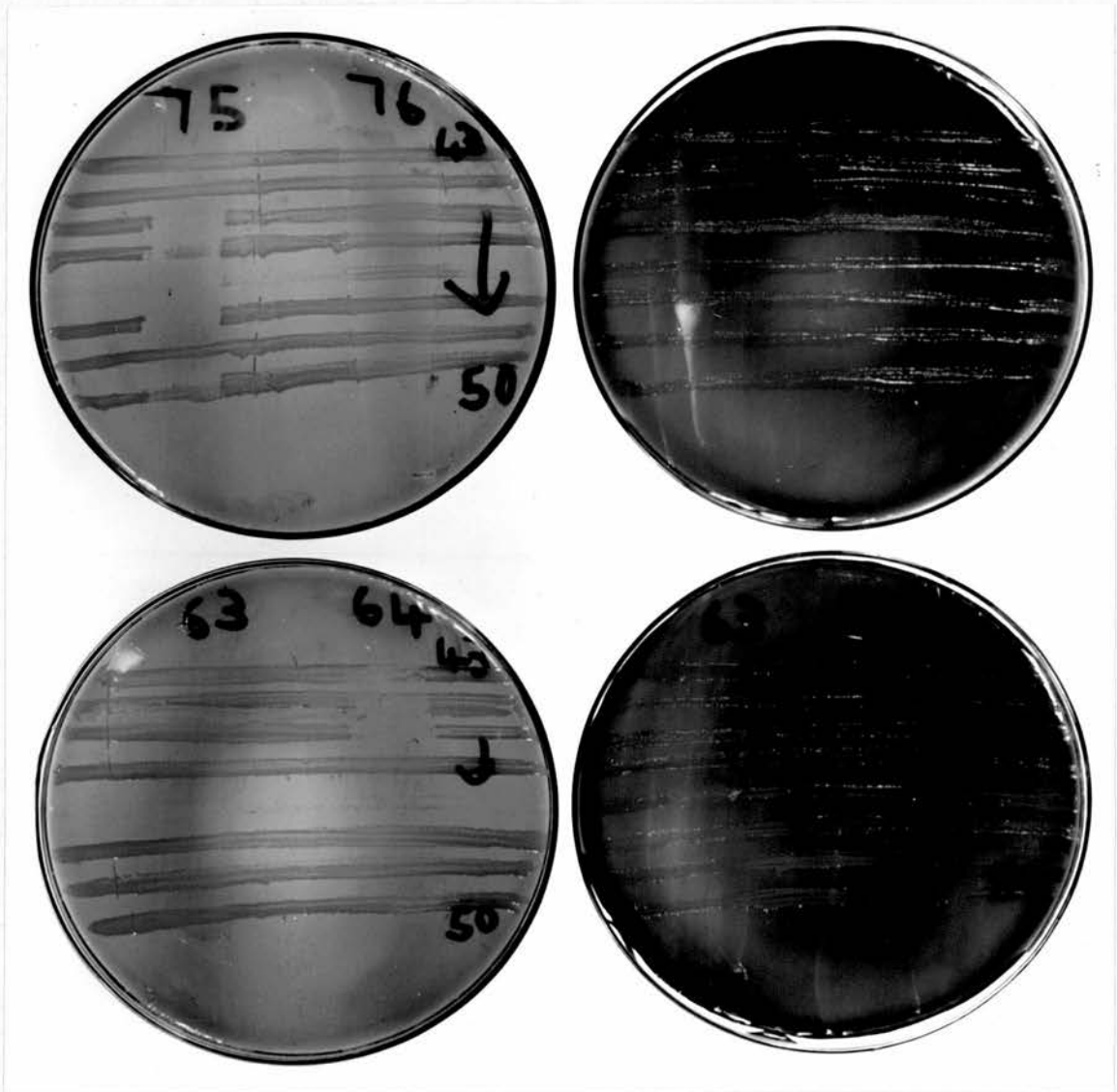
Initial tests were carried out on 15 strains chosen from the dermatological isolates and 15 strains from the 'miscellaneous' hospital isolates. As shown in Appendix Figure 1, those strains which inhibited others did so more completely on media containing the enzyme antagonists; and five strains inhibited others only when grown on the composite medium. Two other strains, however, did not grow as well on the composite medium as on plain MacConkey agar. A large number of parallel tests showed that 2×10^{-4} M. iodo-acetic acid and 0.2 per cent di-potassium hydrogen phosphate were optimal levels of the enzyme antagonists (sodium citrate was not beneficial and, indeed, in several instances it reduced the efficiency of the composite medium). The most satisfactory conditions of incubation were 48 hours at 30°C . for the first stage (i.e. producer activity), while for the second stage (i.e. indicator inhibition) overnight incubation at either 30°C . or 37°C . proved to be satisfactory. Erythromycin at a concentration of $10 \mu\text{g./ml}$. prevented the growth of spore-bearing contaminants which occasionally had been troublesome. These bacteria are not killed by the process of exposure to chloroform, and the necessity of scraping the large surface-area of the medium before the second stage serves to spread them from micro-colonies.

Chloral hydrate agar without added enzyme antagonists gave similar results to those with the composite medium, although it allowed the detection of three producer strains not evident on the composite medium. Swarming was prevented in all cases and growth was better than on MacConkey agar, but an occasional strain did not grow well (Appendix Figure 2); moreover two strains found to be 'producers' on the



APPENDIX FIGURE 1. A SERIES OF 'INDICATOR' STRAINS OF PR.MIRABILIS GROWING ON MACCONKEY'S AGAR AT RIGHT ANGLES TO THE LINES OF GROWTH OF 'PRODUCER' STRAINS.

The right-hand tray contains unmodified MacConkey's agar, the left-hand tray contains MacConkey's agar with added iodo-acetic acid (2×10^{-4} M.) and 0.2% di-potassium hydrogen phosphate.



APPENDIX FIGURE 2. A COMPARISON BETWEEN BACTERIOCINE PRODUCTION ON CHLORAL HYDRATE AGAR (LEFT-HAND SIDE) AND MACCONKEY AGAR (RIGHT-HAND SIDE).

composite medium showed no activity in the presence of chloral hydrate agar. However, on balance, a simple chloral hydrate agar seemed most convenient for further screening tests.

On testing the entire collection, it was found that 65 strains (58 per cent) produced inhibition patterns against one or more of 74 strains. The reaction patterns were grouped from 'a' to 'p', and subdivisions were distinguished in several of these 'groups'. Thus 'group a' strains all inhibited strains 13, 15 and 67, but additional activity was found according to five different patterns ('a_i' to 'a_v'). A similar variety of reactions was seen in 'group f' (basic inhibition pattern: strains 69 and 74), and 'group k' (basic inhibition pattern: strains 12 and 18).

The prevalent strains from the female ward constituted 'group a', though several were untypable. Two-thirds of the male ward strains were of 'group f', but several other patterns were found among the remainder.'

Cell-free extracts were active when derived from known 'producers' grown on nutrient agar, but there was only weak activity in extracts from cultures on MacConkey agar. The addition of enzyme inhibitors to nutrient agar in several cases resulted in higher titres of activity. The inhibitory effect was similar to that of bacteriocines from other genera, and plaques were not produced near the end-point as is the case with bacteriophage preparations.

For routine typing purposes, unknown strains could be tested for their ability to inhibit a standard set of selected indicator strains. The scope of typing could, however, be increased by testing the activity of a set of extracts from known producers against the unknown organisms.

Further work may show that the present collection of 65 producers and

'Of 12 'miscellaneous' strains in both wards, 7 were untypable.

74 indicators contains strains which are suitable for routine typing purposes. However, the ideal medium for bacteriocine production has yet to be found.

(b) The Evaluation of Polynoxylin in Nasal Carriers of Staph. aureus.

Nasal swabs were taken from 140 fourth-year medical students and 40 members of the staff of the University Bacteriology Department. Three successive swabs taken at weekly intervals yielded moderate to profuse growths of Staph. aureus in 61 of the students and in 9 of the members of staff. These individuals were regarded as persistent nasal carriers of Staph. aureus, and were accepted for the 'double-blind' trial of a new anti-bacterial agent as a nasal disinfectant. This substance, polynoxylin ('Anaflex'), is a non-toxic, synthetic chemical with a broad anti-microbial spectrum (Annotation, 1963b). The chemical was dispensed as a 10 per cent cream, and in the trial alternate volunteers received a 30 gm. or 20 gm. tube.¹ Although it was known at the outset that only one of the tubes contained the active substance, the identity of the tubes was not revealed by the manufacturer until the end of the trial.

The volunteers were instructed to apply the cream twice daily to each nostril on the tip of the little finger. This procedure was carried out for three weeks. Swabs were taken at weekly intervals for ten weeks.

The results are given on p.309.

¹ supplies were kindly provided by Geistlich Sons Ltd., Chester.

(d) Laboratory Tests on Chemical Disinfectants Used in the Hospital

METHODS:

Tests for Bactericidal Activity. The tests were carried out at room temperature (18 - 22°C) using overnight horse digest broth cultures of Staphylococcus aureus (propagating strain '75', N.C.T.C. 8354) and Escherichia coli (recently isolated from a case of urinary tract infection). Films of the cultures were prepared on the outside of flat-bottomed glass tubes which were then immersed in disinfectant, rinsed in water and finally pressed on to nutrient agar, according to the method of Hare et al. (1963). Specimen tubes (7.5 cm. x 2.5 cm.) were used, however, instead of pharmaceutical tablet containers, and were placed on parallel rows of capillary tubing which rested on the floor of large Petri dishes containing the disinfectants. Resting the films directly on the floor of the dishes interfered with the disinfection process (Hare and his colleagues did not state how their tubes were "held in a shallow layer of the antiseptic"). The tubes were moved to different positions in the dish each minute to prevent stagnation of the disinfectant. Control films were immersed in distilled water. All tests were carried out in duplicate.

The original technique makes no provision for the use of neutralizing agents to prevent carry-over of disinfectant. Preliminary tests were therefore performed using 1 per cent sodium thiosulphate and 1% Lubrol W 'stop baths' to neutralize halogens and quaternary ammonium compounds respectively. While no significant carry-over of halogens took place under the conditions of the test, films exposed to quaternaries gave higher bacterial counts after being dipped into

Lubrol W than when pressed directly onto agar. Thus appreciable transfer of quaternary compounds had occurred despite the customary immersion in running water. For this reason all films exposed to quaternaries were held for ten seconds in 1% Lubrol W before being pressed on to nutrient agar.

Tests for Virucidal Activity. Three strains of virus have been used routinely: adenovirus type 3, echovirus type 1 and vaccinia virus.

These were chosen as being representative of those viruses that resist drying for considerable periods and are therefore readily transmitted on cups and other fomites.

Films were prepared on sterile Chance round cover slips (16 mm. diameter, No. 2 thickness) using 0.2 ml. volumes of tissue culture fluids containing approximately 10^6 tissue culture doses of adenovirus or echovirus per ml. Vaccinia virus was used in the form of glycerinated calf lymph diluted in Hank's balanced saline to give a concentration of 10^6 pock-forming units per ml. of pooled lymph. The wet films were allowed to stand for five minutes before excess fluid was withdrawn with a Pasteur pipette. Drying was then accelerated with a stream of cool air from a hair dryer.

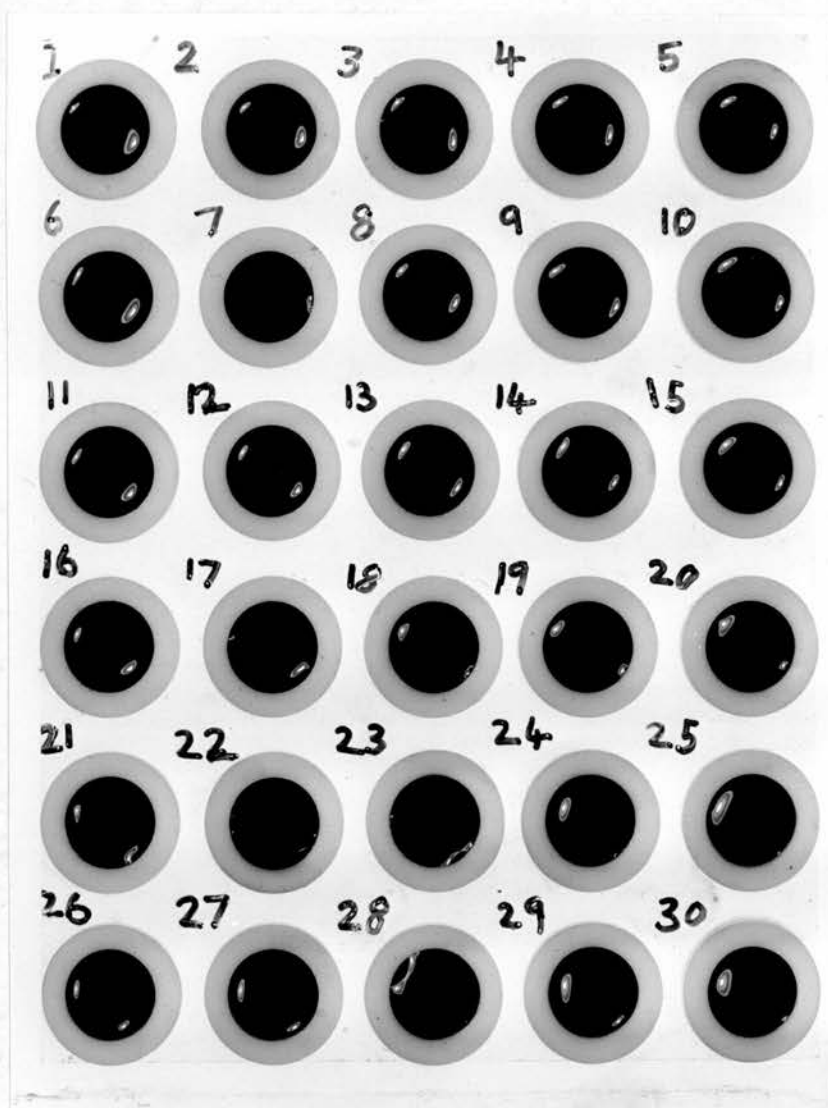
The cover slips were immersed for the required periods of time in disinfectant, with the films uppermost. The minimum period of exposure was based on results obtained in the bactericidal tests. The films were then held for 25 seconds in a beaker of running water, using forceps that had been flamed in ethyl alcohol. Following the use of quaternary compounds, films were immersed in 1% Lubrol W before the final gentle rinse. During the full period of each test control films of virus were immersed in distilled water and, as negative controls, cover slips with

dried films of sterile tissue culture medium were placed in the disinfectant.

After treatment, the cover slips were transferred face-upwards into one of the cups of the glass tray shown in Appendix Figure 3. A Perspex tray, drilled to provide cups, was used originally, but it was optically imperfect and could not be sterilized by heat. The glass trays measure 22 cm. by 16.5 cm. and consist of a base, 2 mm. thick, on to which are cemented, with Araldite, 30 rings made of a non-toxic heat resistant plastic, polytetrafluoroethylene (PTFE).¹ The rings have an outside diameter of 30 mm. and form cups 5 mm. deep and 18 mm. in diameter. Using a pipette, the cover slips were flooded with a suspension containing approximately 250,000 cells in 0.75 ml. Primary monkey kidney cells were used for films of echovirus, and cultures of the HEp-2 cell line were used for films of adenovirus and vaccinia virus. Each tray was covered with a glass plate and was then incubated at 37°C in a moist atmosphere containing 5 per cent carbon dioxide. The cover slips were examined in situ at 24-hour intervals under the 16 mm. objective of the microscope. (The inverted microscope is especially convenient, although there is sufficient working distance for standard microscopy). If advanced cytopathic changes were present, fluid was withdrawn from those cups nearest the end point, and tested for virus in suitable roller tube cultures by the neutralization technique.

Following its use, each tray was autoclaved, and the cover slips discarded. The tray was then washed and rinsed in deionised distilled water, to the standards required in tissue culture work. New cover

¹ R. Klinger Ltd., Sidcup



APPENDIX FIGURE 3. TRAY USED IN VIRUCIDAL TESTS UPON DISINFECTANTS.

(For the purposes of photography the glass plate which normally covers the cups has been removed, and excess phenol red has been added to the tissue culture media in each cup).

slips, after being placed in 1 per cent hydrochloric acid overnight, were washed and rinsed in the same way. After drying, the tray and cover slips were loosely wrapped in kraft paper and sterilized by autoclaving. The hot air oven was found to cause gradual deterioration of Araldite cement.

RESULTS AND COMMENTS:

Twelve 'disinfectants' used in the two hospitals for disinfection of baths, trolley tops and other surfaces, and for the 'sanitization' of crockery were tested for bactericidal and virucidal activity, using the two procedures. The only agents that were rapidly effective under the conditions of the tests were 'Chlorox' and 'Wescodyne'. 'Chlorox' (I.C.I.) is used routinely in the Bacteriology Department for disinfecting bench tops, and was also used for the disinfection of hospital baths as described on p.252. 'Wescodyne Surgical' (Bengue) is an iodophor which was being used for a trial period in one of the hospital wards. At dilutions of 1 in 160 both disinfectants were bactericidal within 30 seconds, and virucidal within two minutes (vaccinia virus survived for 90 seconds in 'Wescodyne', but the adenovirus and echovirus were each inactivated in one minute).

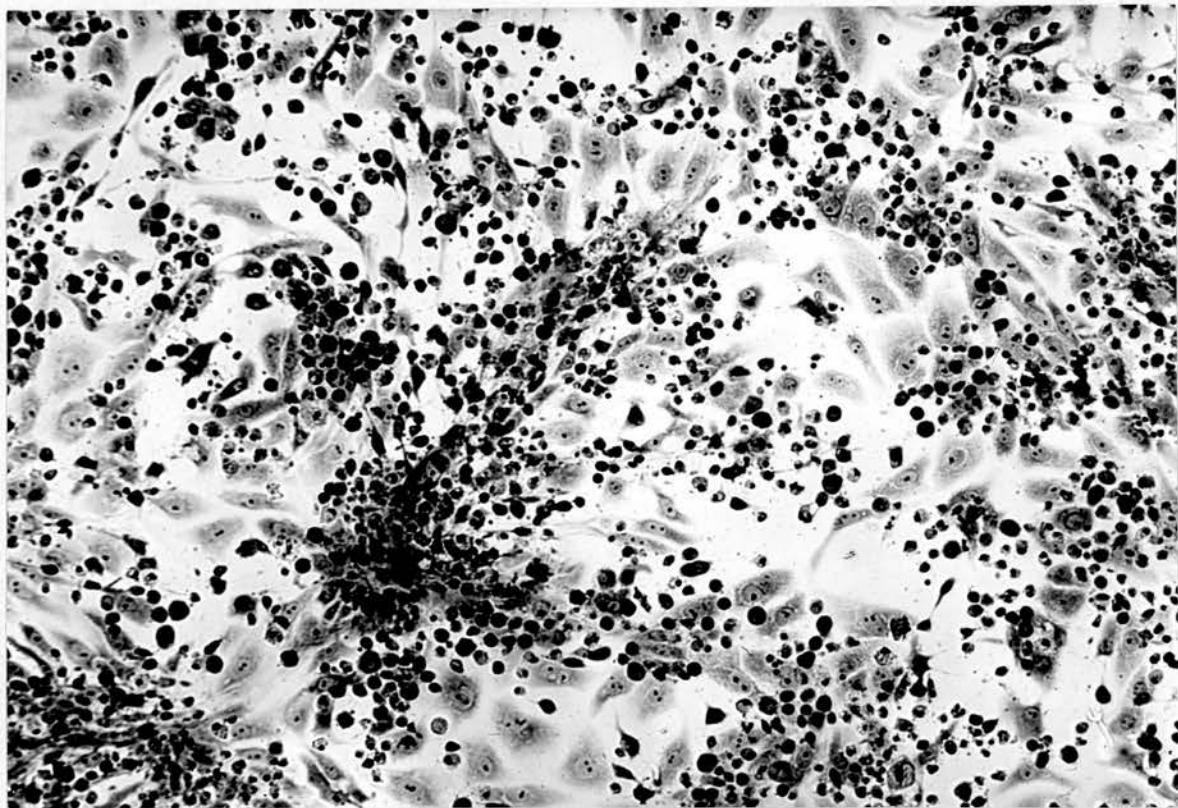
The remaining 'chemical sterilizers' consisted of five quaternary ammonium products, three simple detergents of the cationic type, and two varieties of germicidal bar-soap containing hexachlorophane and marketed for use in a special adapter to fit onto the water tap. These products were supplied with leaflets and brochures which claimed that the agents were suitable for sterilizing crockery and similar

articles. All except two of the quaternaries were devoid of germicidal activity over a period of one hour under the conditions of the test.

Sykes (1965) has criticized the procedure of Hare et al. (1963) because of their anomalous finding that 1 per cent of a chloroxylenol solution (Dettol) killed Ps. pyocyanea relatively rapidly (within 30 seconds). In the present work, however, the bactericidal end-point of this disinfectant was found to be 3 minutes against four strains of Ps. pyocyanea and 10 minutes against a fifth strain. In contrast, killing times of between 30 seconds and 1 minute were noted against Staph. aureus and Esch. coli. These results are in agreement with the findings of Calman and Murray (1956) who used a different test system.

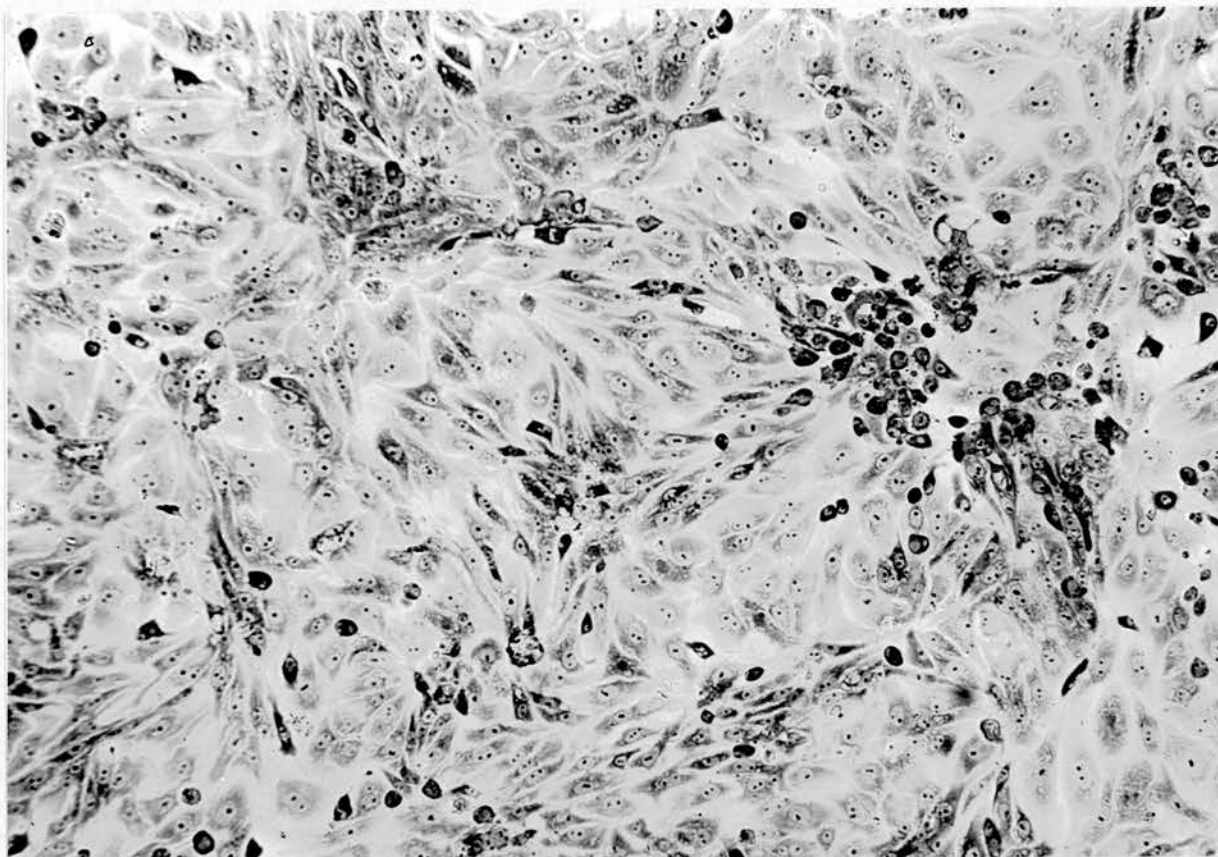
In the virucidal tests an almost complete absence of possible toxic effects on the cells was perhaps surprising. With few exceptions the cells adhered rapidly to the cover slips, and good monolayers formed beyond the virucidal end-point and in negative controls. This indicates either that carry-over of surface-active and toxic agents is avoided in the procedure, or that the serum and other organic materials in the tissue culture medium inactivate any residual amounts of disinfectant remaining on the films after processing.

The firm adsorption of the virus inoculum and its possible unavailability for subsequent infection of host cells is also of theoretical interest. However, in practice, viral films produced early and uniform cytopathic changes throughout the cell mono-layer after exposure for one hour to water or inert chemicals. Appendix figures 4 and 5 show the cytopathic effects observed on cover slips used in testing the activity of 'Chlorox' against echovirus type 1. In Appendix Figure 4, virus exposed to the disinfectant for 15 seconds



APPENDIX FIGURE 4. MONKEY KIDNEY CELL MONOLAYER ON AN ECHOVIRUS
TEST FILM WHICH WAS EXPOSED TO 'CHLOROS' (1 in 160) FOR
15 SECONDS. (x 200).

Diffuse cytopathic effect after 24 hours (i.e. virus
not inactivated).



APPENDIX FIGURE 5. MONKEY KIDNEY CELL MONOLAYER ON AN ECHOVIRUS
TEST FILM WHICH WAS EXPOSED TO 'CHLOROS' FOR 30 SECONDS.(x 200).

An occasional group of cells showing cytopathic effect
after 24 hours.

has not been inactivated, and after 24 hours' incubation a characteristic diffuse cytopathic effect is present in the monolayer. Appendix Figure 5 shows the result after exposing echovirus to the disinfectant for 30 seconds. Small islands of cells showing cytopathic effect are sparsely distributed throughout the monolayer. These changes extend and become confluent after a further 24 hours' incubation. This effect is often seen near the end-point of the test, and probably indicates the survival of relatively few intact viral particles. Support is provided for this view by the results of a limited number of tests in which the early cell monolayer was overlaid with molten nutrient agar, and the development of micro-plaques was then observed.

The numerous disinfectants were examined single-handed with ease. The actual time taken to set up and perform a full test of bactericidal activity was less than 90 minutes. The equivalent time for virucidal tests was about two hours, though this did not include subsequent examinations and any neutralization tests that were required. Together the two procedures provide comprehensive data on disinfection and should enable the busy hospital or public health laboratory to give independent advice upon examples of the bewildering variety of 'disinfectants' which are now in use.

GENERAL SUMMARY AND CONCLUSIONS

ACKNOWLEDGEMENTS

GENERAL SUMMARY AND MAIN CONCLUSIONS

The first part of this thesis contains an account of the history of hospital infection. Neglected early contributions, particularly from the eighteenth and nineteenth centuries, are reviewed; and the survey is continued up to 1966.

The second part describes investigations in a general hospital during 1960 and 1961. Their aim was to provide, over an adequate period of time, a record of environmental contamination by pathogenic bacteria and the acquisition of significant bacterial infection of all types throughout the hospital.

Of the 7,360 patients included in the investigation 1,231 (16.8 per cent) developed bacteriologically confirmed hospital infections, but only 28 per cent were due to Staph. aureus. The lowest sepsis rates were in the maternity and general surgical departments, whereas high rates were encountered in the paediatric and general medical units, and in specialized departments. Chest and urinary infections were common among debilitated adult patients.

Heavy environmental contamination with Staph. aureus and Gram-negative bacilli was frequently observed, and could be broadly correlated with clinical infections. More than one-quarter of all staphylococcal infection was caused by an erythromycin-resistant group III organism which had its main reservoir in the nurseries and paediatric units.

An outbreak of sepsis among medical patients demonstrated

the dangers of bacterial dispersal from a patient with a chest infection; indirect evidence of dispersal from the bowel and the skin was obtained in other instances.

If the present findings are representative, the importance of the staphylococcus in infection has been over-emphasised and insufficient attention has been paid to Gram-negative bacilli. Again, investigators have shown great interest in the problems of maternity and surgical units, but other departments appear to have received inadequate attention.

The third part of the thesis describes a long-term investigation in a dermatology department. Over a four-year period, dermatological wards were found to be ideal models for the planned study of hospital infection: patients remained in hospital for an average of 39.2 days; the extensive skin lesions of 45 per cent yielded significant cultures of pathogens on admission; and during their stay the lesions of 43 per cent of 'unprotected' patients were colonized by pathogenic bacteria - mainly subclinically. Sepsis was, however, uncommon at sites remote from the skin lesions.

Gram-negative bacilli were prominent in dermatological lesions and the environment although Staph. aureus usually predominated.

Whereas 15 per cent of the patients who were nasal carriers of Staph. aureus on admission developed endogenous infection of their skin lesions, exogenous staphylococcal infection was relatively infrequent in this group.

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The importance of skin lesions as the principal sources of hospital infection and contamination was shown indirectly by trials of anti-bacterial agents. Their use on skin lesions was accompanied by striking reductions in environmental contamination; and colonization of both the lesions and the anterior nares was virtually abolished. In contrast, nasal disinfection resulted only in the suppression and prevention of nasal carriage.

Direct studies on individuals showed that staphylococcal nasal carriage alone resulted in minimal environmental contamination, whereas profuse bacterial dispersal was commonly caused by patients with subclinically infected skin lesions. The main vehicle of infection was evidently the skin scale, but the particle size-distribution differed in the various skin diseases. Patients with clinically infected eczema usually shed fewer bacteria conveyed on smaller particles than patients with subclinically infected psoriasis. The latter group constitutes a hidden menace in hospital.

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I wish to thank Mr. T.C. Dodds and his staff for preparing the photographs. The illustrations used in figures 7 and 8 are reproduced by permission of the Wellcome Trustees. Figure 5 appears by permission of Routledge and Kegan Paul.

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