The appropriateness of clinical microbiology laboratory investigations: a retrospective study of the cost and clinical relevance of specimen management and processing

By

Yasin Abdi BSc, MSc, CSci, FIBMS

A portfolio of research and development in a professional context

The thesis is submitted in partial fulfilment of the
Degree of Professional Doctorate in Biomedical Science

School of Pharmacy and Biomedical Sciences
Faculty of Science
University of Portsmouth
September 2011

ABSTRACT

Each year, NHS clinical laboratories carry out more than 700 million laboratory tests, of which 50 million are microbiology investigations. Several studies have shown that between 25% and 40% of all tests sent to the laboratory are unnecessary, and up to 46% of ordered microbiology tests are inappropriate. In light of these accounts, the present study was undertaken to evaluate the process of microbiology specimen management in order to assess microbiology test utilisation and the appropriateness of the test ordering processes. The study focussed on respiratory tract specimens using sputum microbiology as a model for the microbiology service inappropriate test utilisation.

The overall main aim of this study was to determine the appropriateness of clinical microbiology test utilisation, its clinical relevance and cost-effectiveness, hence recommend better utilisation strategies.

A total of 15,941 respiratory tract samples from Barts and The London NHS Trust were randomly selected from the years 2004/05 and analysed retrospectively. Seven hundred microbiology laboratory request forms from patients for whom respiratory tract cultures were requested over a three month period were examined in detail. These requests were derived from 511 sputum specimens, 100 throat swabs, 63 ear swabs and 76 samples from other respiratory tract sites. 641 (91%) of microbiology test requisition forms were completed, provided all requested details by the service users and were therefore considered as appropriate microbiology test requisitions. 660 (94%) of those examined stated the patient's clinical diagnosis and only in 65 (13%) of these patients was the stated diagnosis as respiratory tract infection.

Sixty percent of sputum specimens examined were considered as poor quality. Forty percent of respiratory specimens were reported as culture positive, based on the local hospital criteria of microbiology test reporting. In sputum culture, 39% was reported as culture positive; however, less than 18% were positive with recognised respiratory pathogens, whilst 27% of throat swabs were reported as culture positive, of which 67% had throat pathogens. From the beginning of this study and before, there were no microbiology test comments and interpretation of test results provided with the test result reporting.

The test turnaround time of respiratory microbiology results reported within three days in 2004/2005 was only 20%. The total inappropriate respiratory specimens processed locally were 9,575. Extrapolating from our results, this suggests that 2,153,977 nationally were inappropriate in NHS hospitals in 2004/2005. The total cost of inappropriate respiratory microbiology test use was approximately £152,000 in local NHS hospitals. Extrapolating from our results, this suggests that £23,900, 000 nationally was the total cost of inappropriate tests in the NHS hospitals.

Following implementation of this study, follow up studies in 2006 and onwards indicated that there has been an improvement in the quality of the microbiology service. The number of good quality sputum specimens was 69% compared to 40% in 2004/2005. While the total microbiology test turnaround time that was reported within three days in 2009/2010 was more than 94%. From mid 2006 onwards, test interpretation comments have been used in all microbiology test result reporting. The total workload of respiratory tract microbiology activity decreased from 18,915/year to 16,651/year over the years 2004/2005 to 2007/2008, which is down nearly 8%.

Analysis of the findings showed that the usefulness of culture results was limited by the collection of inappropriate specimens, and lack of clinical information on the microbiology request form. The crucial importance of the role of clinical and nursing staff is stressed if the clinical relevance of sputum culture is to be maximised. The increasing introduction of electronic pathology test requests gives new opportunities to restrict the collection of inappropriate specimens and make substantial savings in resources, both in the ward and the laboratory. This type of study and audit can give invaluable information about the rationale behind testing, and the appropriateness of sampling and transport time. Appropriate measures for corrective actions can be identified.

CONTENTS PAGE NUMBERS

List of tables

List of figures

ABBREVIATIONS

A&E	Accident and Emergency
AIDS	Acquired immune deficiency syndrome
ATS	American Thoracic Society
BAL	Bronchoalveolar lavage
BLT	Barts and the London NHS Trust
BMS	Biomedical scientists
BSc	Bachelor of Science
BTS	British Thoracic Society
C & S	Culture and Sensitivity
C.diff	*Clostridium difficile*
CAP	Community acquired pneumonia
CAP	College of American Pathologists
CFUs	Colony-forming units
CL	Clinic
COPD	Chronic obstructive pulmonary disease
CPA	Clinical Pathology Accreditation
CPOE	Computerised Physician Order Entry
CRS	Care record service
CSci	Chartered Scientist
CSF	Cerebrospinal fluid
CSU	Catheter Specimen of Urine
DBMS	Doctor of Biomedical Science
DoH	Department of Health
ECOPD	Empyema Chronic Obstructive Pulmonary Disease
ELISA	Enzyme linked immunosorbent assay
ES	Ear swab
ESR	European Respiratory Society
ETT	Endotracheal tube
GP	General Practitioner
h	Hour
HAP	Hospital acquired pneumonia
HIV	Human immunodeficiency virus
HRGs	Healthcare Resource Groups
IBMS	Institute of Biomedical Science

ID	Infectious diseases
IDSA	Infectious Diseases Society of America
IP	Inpatient
IT	Information Technology
LIMS	Laboratory information management system
LREC	Local Research Ethics Committee
LRTI	Lower respiratory tract infections
LRTS	Lower respiratory tract system
MALDI-TOF	Matrix Assisted Laser Desorption Ionisation - Time of Flight
MC & S	Microscopy, culture and sensitivity
MDR	Multi-drug resistant
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin Sensitive *Staphylococcus aureus*
MSc	Master of Science
NAA	Nucleic acid amplification
NBHS	No beta-haemolytic streptococci
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NPA	Nasopharyngeal aspirates
OP	Outpatient
OPD	Outpatient department
PCR	Polymerase chain reaction
PCT	Primary care trust
PhD	Doctorate of Philosophy
PRP	Potential respiratory pathogens
RTS	Respiratory tract specimen
SARS	Severe acute respiratory syndrome
SECs	Squamous epithelial cells
SHAS	Strategic Health Authorities
SOP	Standard operating procedures
TAT	Turnaround time
TB	Tuberculosis
TS	Throat swab
TTP	Total testing process
UK	United Kingdom
UNK	Unknown
URTI	Upper respiratory tract infection

WHO	World Health Organisation
www	World Wide Web

ACKNOWLEDGMENTS

There are a lot of people who helped me with their support during the years of my (mostly part time) DBMS studies in order to complete my thesis.

I would like to thank my supervisor and director of professional doctorate studies, Prof. Graham Mills, University of Portsmouth, for his advice, guidance, help, support, continuous encouragement, patience with me through the tough times, and his ability to keep me motivated during periods of self-doubt. I would like to thank my second supervisor, Mrs Myra Wilkinson, for her constant help and guidance.

I would like to thank Dr. Mark Wilks, QMW University of London, who accepted to be the second supervisor of the thesis and for being available for help and support throughout the period of completing this thesis. His advice, encouragement and discussions during the tenure of the work were invaluable.

I am grateful to Dr Mike Millar, Consultant Medical Microbiologist Barts and The London NHS Trust, for his advice and guidance in the areas of clinical microbiology service rationalisation.

I would like to thank Mr S. Uddin for his help in the data extraction and analysis of results.

I would like to thank also, all the academic staff of University of Portsmouth who taught me the taught components of the programme, particularly Dr Sally Kilburn and Ms Sue Crane for their help and guidance.

I wish to thank both the staff and management team of clinical microbiology department, particularly Melvyn Eydmann and David Ball for their support and encouragement during my studies.

Finally, I would like to thank my wife and children for their support, help and patience.

DEDICATION

It gives me great pleasure to dedicate this study to my wife and children, who never doubted the outcome.

DECLARATION

I declare that whilst studying for the Doctorate in Biomedical Science at the University of Portsmouth, I have not been registered for any other award at another university. The work undertaken for this degree has not been submitted elsewhere for any other award. The work contained within this submission is my own work and, to the best of my knowledge and belief, it contains no material previously published or written by another person, except where due acknowledgement has been made in the text.

Yasin Abdi
September 2011

Chapter 1 Introduction

The pathology service is a largely hidden science that saves numerous lives. Clinical Laboratory testing plays an essential role in the delivery of quality healthcare. Laboratory tests provide physicians, nurses, and other healthcare providers with objective information that is needed to prevent, diagnose, treat, and manage disease. It is estimated that more than 70% of clinical decisions involve pathology laboratory test results (Forsman 2002, Regan and Forsman 2006), and yet pathology accounts for less than 5% of the NHS budget (Lord Carter of Coles 2006).

Recognition of this central role that pathology provides in the delivery of medical care to patients has led to a previous Government initiated programme of modernisation of the pathology service (Department of Health 2005). One of the principal aims of this programme was to identify novel ways of delivering pathology services that are more responsive to patient needs. This may well include an expansion of point of care testing, that is the delivery of pathology services by non-laboratory staff at sites outside the laboratory (e.g. pharmacies, GP surgeries, outpatient departments and wards) with nurses and other non-laboratory healthcare professionals becoming more involved in patient testing.

NHS clinical laboratories carry out more than 700 million pathology investigations every year, including 50 million microbiology tests (Lord Carter of Coles 2006). A report by the Audit Commission in 1993 revealed that around 85 million pathology test requests were being processed annually by around 400 NHS clinical pathology departments in England and Wales (Audit Commission 1993). Over the intervening years, the workload has continued to rise by up to 10% per annum (Beastall 2004). There is currently an estimated year on year increase of 6% in the number of tests performed (Anon 2012).

In addition to the modernisation of pathology services, the last Government ordered Lord Carter to review NHS pathology services in England (Lord Carter of Coles 2006). Before this review had begun, the author of this thesis started the following study project to investigate the appropriateness of clinical microbiology laboratory investigations and carried out a retrospective study of the cost and clinical relevance of specimen management and processing. The concept of the project

was to provide valuable research information to establish an optimal clinical microbiology service based on sound principles that is to provide a clinically relevant microbiology (appropriate utilisation).

Healthcare reform and economics are driving dramatic changes in healthcare delivery and numerous strategic reviews have begun since this project started. Drivers for change in pathology services include:

1. Implementations of Carter recommendations: - commissioners, payment by results (PbR), pathology tariff, plurality of providers, consolidation networked laboratories, quality, end to end service and efficiency savings required of 20% (Lord Carter of Coles 2008).
2. Healthcare Commission's report 2007. Getting results: Pathology services in acute and specialist trusts (Healthcare Commission 2007).
3. Implementations of Lord Darzi recommendations: - high quality care for all, and healthcare for London (Lord Darzi 2008).
4. Modernising Scientific Careers (MSC):- which is an ambitious work programme which seeks to ensure that the healthcare science workforce is well equipped to meet the challenges and opportunities of the future delivery of care. Modernising Scientific Careers: The UK Way Forward (Department of Health 2010).
5. Changing Technology and Microbiology Total Automation; - Nowadays, MALDI TOF technology has been implemented as a valuable tool for the identification of micro-organisms (Giuseppe Cornaglia and René J. Courcol 2012). Chemistry and haematology services have long had the advantage of total laboratory automation. Automation will eventually become the norm in the microbiology laboratory and opening a new era (Matthews and Deutekom 2011).
6. The introduction of a National Laboratory Medicine Catalogue: - will bring greater standardisation and more appropriate use of tests and pathology knowledge. This catalogue is the first comprehensive standard for pathology test requests and result reporting, and will be available from July 2012.

In the following parts of this introductory chapter, it will briefly discuss the discipline of clinical microbiology, microbial infectious diseases, and microbiological investigation strategies, how they are applied and the role of clinical microbiology laboratories. The following part of the introduction will describe the background to

this study, illustrating the problems of inappropriate use of clinical microbiology tests and the importance of this current study using sputum specimen as a study model for appropriate or inappropriate utilisation of the microbiology laboratory service.

The second part of the introduction reviews the literature; the issues related to this study that are reviewed here include the common examples of pitfalls in routine microbiology laboratory investigations, the appropriate utilisation of clinical microbiology, such as the clinical relevance and cost-effectiveness, and turn around times in clinical microbiology tests. In addition to these, the impact of specimen management in clinical microbiology tests and total testing process will be described briefly.

The final part of this review will illustrate the reasons for the selection of respiratory tract specimens for this study, the role of microbiology in the diagnosis of lower respiratory infections, and the latest guidelines that are available to clinical microbiology laboratories for the evaluation of respiratory tract microbiology specimens, potential limitations and clinical indications for their use will be taken into account. Finally, the importance of sputum specimen 'quality' and methods of its assessment will be reviewed, and at the end aims and objectives of the project will be stated.

1.1 Clinical microbiology

Clinical microbiology is a clinical service which supports the investigation and management of patients suspected of having infections and infectious diseases through all stages of their care, from diagnosis, to therapy, to prognosis. The clinical microbiology laboratory uses methods for detection, isolation, identification, characterisation, sero-diagnostic investigation, laboratory surveillance, and antimicrobial susceptibility testing of clinically significant microbial pathogens or their products of diagnostic significance, e.g., toxins, antigens and nucleic acids.

An infectious disease is a clinically evident disease resulting from the presence of pathogenic microbial agents. Therefore, clinical microbiology studies their biology, diagnosis, treatment, control and prevention. To clinicians caring for patients with infectious diseases, the clinical microbiology laboratory provides a wide range of

facilities to assist in the diagnosis and treatment of infectious diseases and other related health conditions susceptible with microbial infections. Samples from a wide range of body sites are analysed to determine whether pathogenic micro-organisms are present in clinical specimens collected from patients with suspected infections. If micro-organisms are found, these are identified and their susceptibility profiles, when indicated, are determined.

Approximately 25% of all deaths worldwide are due to infectious diseases, and in some countries this number approaches 50% (World Health Organisation 1997). New infectious diseases, such as HIV, SARS, Avian Flu and Swine Flu, are continually emerging, and old diseases, such as tuberculosis are re-emerging. Across the globe, infectious diseases account for greater than 60% of the deaths of children less than four years of age. Governments are spending billions to combat the threat of bioterrorism. Thus, all of the above areas represent topics of major concern in the field of clinical microbiology. Common topics of interest to clinical microbiology include the nature of the etiologic agents, their interactions with the immune system, and the diagnosis and epidemiology of the infectious disease.

For microbiological investigations, the collection of patient specimens is driven by symptomatology and clinical examination of the patient. The first step taken is the collection of specimens before antibiotic therapy has been started and quickly sent to the microbiology laboratory. Sampling may be performed for epidemiologic purposes; here the goal is to detect patient colonisation by potentially hazardous and multi-drug resistant bacteria. The major goal of microbiological investigation is to diagnose microbiological infection and treat the patient with appropriate antibiotics. The bacteria may be detected in one or more of the following ways: (1) analysis of bacteriological samples by microscopy (2) culture and identification of bacteria from samples (3) serological tests and nucleic acid tests.

Diagnosis and effective treatment of an infection depends not just on isolating an organism, but in establishing a plausible link between the patient's clinical conditions, results from non-microbiological tests, microbiological findings, and the recognised syndromes. One of the major problems encountered in a clinical microbiology laboratory is the separation and identification of infectious micro-organisms (pathogen) from those that are normal or normal flora (non-pathogen). The normal microbial flora of the human body is mainly located in the superficial

layers and gastrointestinal tract. Certain areas of the body, such as skin, upper respiratory tract, intestinal tract, female genital area and open wounds, develop an environment of normal microbial flora, or micro-organisms. These sites are called non-sterile body sites. These sites are open to the external environment and normally contain bacteria.

Lower respiratory and upper urogenital tracts are normally sterile, but they are susceptible to microbial invasion from adjacent sites. Sterile body sites are areas that normally do not contain any bacteria, so any bacteria found there are significant. Blood and cerebrospinal fluid (CSF) are good examples. However, microbial contamination during specimen collection, processing and culturing in the laboratory, plus the patient's microbial colonisation as a result of long term antimicrobial treatments and in hospital environments could also cause significant difficulties for the interpretation of microbiological results.

The validity of clinical microbiology laboratory results and reports is dependent upon the following factors:

1. Appropriateness of specimen
2. Proper collection and adequacy of specimen
3. Appropriate transport to the laboratory
4. Use of culture media of known quality
5. Culture and isolation by knowledgeable personnel using equipment known to be correctly functioning
6. Confirmation by tests of known quality
7. Results interpreted and reported by professional staff
8. No transcription or computer errors.

The clinical microbiology laboratory test results can have a positive impact on patient's healthcare and have positive outcomes, such as:

1. The reduced length of hospital stay
2. The reduced cost of hospital stay
3. The reduced turnaround time for diagnosis of infection
4. The change to appropriate antimicrobial therapy
5. The customer (physician/clinician or patients) satisfaction.

Thus, the clinical microbiology laboratory service is a cornerstone for infectious diseases diagnosis, and the philosophy behind the clinical microbiology laboratory is to place maximum emphasis on speed of processing number of tests on specimens often obtained from complicated infections and associated disease.

1.1.1 The role of clinical microbiology laboratories

The role of clinical microbiology laboratories evolves in response to clinical needs and flow of information between patients, clinical microbiologists and physicians and could change in the future, with some tests being carried out by patients and doctors, and redistribution of clinical microbiology services to large, centralised laboratories (Bartlett et al. 1994, Barenfanger 2001, Reller et al. 2001, Baron 2011). The role of the microbiology laboratory and microbiologist are especially important to the clinician caring for a patient with compromised host defences. The microbiologist can assist in establishing a differential diagnosis and selection of laboratory tests to make an infectious diagnosis. Complete understanding of microbiology test results not only improves patient management, but also reduces the cost of medical care. Therefore, one of the main goals of the clinical microbiology laboratory is to improve the usefulness of microbiological results and data to clinicians, and the multiple roles of the clinical microbiology laboratory can be summarised as following:

1. Diagnosis of a microbiological infection
2. Antibiotic therapy advice
3. Epidemiological surveillance: multi-drug resistant bacteria (MDR)
4. Introduction of new diagnostic tests
5. Identification of new bacterial species
6. Identification of new resistance mechanisms.

The delivery of microbiology services is an integrated service that requires a range of trained professionals (clinical microbiologists, clinical scientists, biomedical scientists, nurses, pharmacists and information technology specialists) working in an organisational framework for the delivery of clinical care (primary, secondary and tertiary care) and health protection, and also draws in expertise from academia and industry. As part of the pathology services, the clinical and health protection requirements of a microbiology service must also be balanced within the overall pathology modernisation programme that was announced by the Department of

Health (DOH) in 2004, and which aims to provide a networked responsive and quality assured pathology service (Department of Health 2004).

The science of clinical microbiology has, and is, undergoing radical transformation and modernisation to cope with an ever-increasing problem of new, emergent, and re-emergent infectious diseases, as stated earlier. Recently, the diagnostic microbiology laboratories at some UK hospitals has introduced a new method of rapid microbial identifications, MALDI-TOF (matrix-assisted laser desorption ionization-time of flight) which is a modified mass spectrometry method (Seng et al. 2009, Seng et al. 2010, Cherkaoui et al. 2010, Van Veen, Claas and Kuijper 2010). This makes diagnostic microbiology tests more clinically relevant in a shorter time frame, which is very important in modern healthcare, with its emphasis on shorter lengths of stay, ambulatory style care, and also in public health. MALDI-TOF technology has improved the test turnaround time (TAT) and the accuracy of organism identification, speed, minimal reagent and labour costs of the technology (Van Veen et al. 2010, Cherkaoui et al. 2010, Wolk and Dunne Jr 2011).

In addition to MALDI-TOF technology, the diagnostic clinical microbiology laboratory has seen rapid developments in the area of laboratory automation over the last few years, some as a result of new and affordable technology allowing automation of routine processes. Meanwhile, laboratories have also faced increasing workload demands, and an increasing need for cost-effectiveness. In the bacteriology laboratory, two thirds of a medical laboratory scientist's time may be spent on non-core activities, with one-quarter being spent on inoculation of plates and broths. The development of systems combining biology, informatics, imaging and engineering can allow automation of repetitive tasks, enabling the medical laboratory scientist's and microbiologists to focus on 'high value added' activities. In microbiology, successful automation means 'fast microbiology'. Fast microbiology is based on the premise of faster results; reducing the time needed for results, to allow earlier and optimised patient management (Dumitrescu, Dauwalder and Lina 2011, Matthews and Deutekom 2011, Greub and Prod'hom 2011, Mulatero, Bonnardel and Micolaud 2011).

In the past four years, several automated specimen processing instruments have been placed on the European market and in the United States (Paxton 2011). The WASP (Walk Away Specimen Processor), manufactured by Copan in Italy, was

introduced in 2008 as a new system for automated plating and streaking of all microbiology samples, and in 2010 the next-generation of WASP was introduced. The second preanalytical device is the PREVI Isola, made by the French firm BioMérieux. The PREVI Isola employs advanced robotics to inoculate, streak, and label specimens, managing 90% of the steps required to process liquid microbiology specimen samples. Another instrument, the Innova Preanalytical Automated Microbiology Specimen Processor, formerly made by Canadian company Dynacon, is now owned by Becton Dickinson and marketed in Europe. One other similar instrumentation in Europe is Kiestra Laboratory Automation, which is now owned by Becton Dickinson and specialises in total laboratory automation for the bacteriology laboratory. Kiestra is a laboratory automation system from end to end for specimen processing and culture reading using image analysis of bacterial growth. Kiestra stresses the modular, open architecture of its system components, which can be adjusted to fit the space available. The goal of microbiology laboratory automation is to benefit healthcare systems by speeding up laboratory test turnaround times, while also eliminating the cost of laboratory services.

Clinical microbiology may direct decisions regarding hospitalisation, isolation and anti-infective therapy, but it is not effective at the time of initial presentation for example at A&E (Cohen-Bacrie et al. 2011). To resolve the time lag between test results and patient care, effective microbiology test is needed in the form of point of care testing (POCT). These tests address the need to hospitalise patients, to isolate contagious individuals and to initiate and focus anti-infective therapy. For example, the rapid testing of Group B *Streptococcus* colonisation in pregnant women at delivery enables timely, focused prophylaxis of materno-fetal infections (El Helali et al. 2009, Cohen-Bacrie et al. 2011). This strategy might represent a major evolution of decision-making regarding the management of infectious diseases and patient care. We assume that clinical microbiology in the 21st century will focus on concerns regarding the real-time management of patients by delivering results at the time of care.

Clinical microbiology staff are at the forefront of responses to high profile healthcare problems (e.g., MRSA, antibiotic resistance, *Clostridium difficile* infection, HIV, syphilis, chlamydia, and respiratory diseases such as influenza). Thus, the clinical microbiology laboratory is organised to provide rapid, relevant and clinically useful services. Good two-way communication between clinicians and medical

microbiology laboratory staff is of utmost importance. Clinicians should identify and mention factors and conditions which will direct the management of microbiological investigations, while the medical microbiology laboratory should inform clinicians about changes in nomenclature, interpretation criteria, and the introduction of new or modified tests, and assist in the interpretation of the results they generate.

As far as the clinicians are concerned, the aim of laboratory medicine is generating information from clinical specimens. As “information brokers”, clinical microbiologists play an important role in how that information is generated and used. This role starts with the specimen and accompanying information received in the laboratory (in the form of test orders from the physician) and is completed when the final product is presented and distributed (in the form of test reports to the physician).

The design and utilisation of both test order forms and reports, whether written or electronic, provide an opportunity for clinical microbiologists to educate those involved in these processes and improve the quality of patient care. As the test report is directly viewed by the clinician managing the patients, presentation of additional information in the form of textual comments provides an important direct and continuing opportunity to educate about appropriate test utilisation and interpretation.

The importance and demand for microbiological tests is increasing due to healthcare drivers, including the aging population, increasing infections in the modern society, such as those related to immunocompromised patients (splenectomised patients, renal haemodialysis patients, chronic ambulatory peritoneal dialysis (CAPD) patients, solid organ transplant patients, AIDS patients, haematology and oncology patients), intravenous drug users, and intensive care patients. There is an unknown threat from biological warfare or bio-terrorism and pandemic flu. As a result of these increases, it has been estimated that workloads in microbiology are likely to increase in the future, particularly as a result of:

1. The growing burden of microbial disease, for example new and emerging microbial infections and the development of antimicrobial resistance e.g. MRSA.
2. Initiatives requiring microbiological support, for example cancer networks, HIV and the sexual health strategy, tuberculosis.

3. Initiatives on healthcare associated infections.
4. Initiatives on the use of antimicrobial drugs, including antiviral drugs, and effort to control the emergence of drug-resistant infections.
5. Increased requirements for clinical microbiology advice as a result of patients with more complex conditions, with a delegated service delivery to multidisciplinary teams and increasing specialised care in the community.

From this introductory account it is clear that, as stated in the beginning, approximately 70% or more of medical decisions made by clinicians are based upon laboratory tests, and microbiology laboratory results have an impact on patient care. It also shows that all laboratory results need to be accurate, precise, timely, and relevant, and must reflect true patient state. In addition to this, the goal of a microbiology testing is to detect and identify the causative infectious agent(s), guide effective treatment and eliminate infection as a cause of clinical presentation. On the other hand, there are risks of poor microbiology test results, such as not detecting the infectious agent causing disease and attributing infection to non-causing micro-organisms. Either case is an injustice to the patient, and the healthcare system. These will cause inappropriate therapy e.g. no treatment when needed, over treatment when not necessary and poorly directed therapy. Similarly, it will cause additional work up and testing of patients, as well as confounding information and unnecessary cost. The present study will investigate the inappropriate utilisation of microbiology tests.

1.1.2 Background and rationale for the study

To be appropriate, a test should have the potential to affect a patient management decision. In clinical microbiology, this primarily occurs through demonstration and identification of micro-organisms and determination of their antibiotic susceptibilities. This generates several test results, each of which may influence clinical decision making and reduce the length of patient stay in the hospital.

Appropriate use of clinical microbiology tests depends largely on one's perspective. For the clinician or physician, appropriate laboratory use is defined by what is believed to be necessary to care for a specific patient at a specific point in time. For a laboratory providing services to that clinician or physician, appropriate use might be defined by test performance parameters, test cost, or the availability of alternative test methods.

For third-party payers (e.g., financial departments and insurance companies), appropriate use is likely to be defined as that which limits testing to minimise healthcare costs. For public health officials, appropriate use may be defined as that required to screen patient populations for diseases or infections of public health interest. For regulatory bodies, appropriate laboratory use is defined by the principle of medical necessity.

Above all other considerations, defining appropriate test use must be based on the clinical relevance of tests. The term ‘clinical relevance’ is roughly synonymous with ‘clinical significance’ and ‘clinical importance’, as described in the review of literature in section 1.2.3. Tests that are not clinically relevant have no appropriate use. It is unlikely that tests that are not cost effective, have poor performance parameters, or have an unacceptable TAT can be used appropriately.

Most of the published literature regarding inappropriate test use deals with the issues of overuse and strategies to decrease it. Relatively few controlled studies have been conducted on the issue of under use. Yet, as Van Walraven and Naylor (1998) and Lundberg (1998) have pointed out, inappropriate use has yet to be defined. Nonetheless, it is easy to recognise that the use of some tests is inappropriate. These include tests that:

1. Are requested or performed on specimens that were collected improperly or from an inappropriate site.
2. Are performed on specimens for which the performance parameters are unknown, or for which the test has not been approved or cleared for testing by the regulatory bodies.
3. Result in increased healthcare costs without benefit to the patient or to the healthcare system, one example being duplicate tests, particularly when the same test is ordered by different clinicians or physicians caring for the same patient (Valenstein, Leiken and Lehmann 1988, Branger et al. 1995).
4. Result in harm to the patient (e.g., unnecessary procedures, tests, or therapies, wrong therapy, or prolonged hospitalization).

The challenge for tests in this category is not in recognising them, but rather to decrease or eliminate their use by physicians/clinicians. In the same way, it is easy to recognise that the use of some tests is appropriate. A test that is:

1. Performed on a properly collected and appropriate specimen.
2. Performed using a method with known performance parameters.
3. Done in an accredited laboratory.
4. Completed in a clinically relevant time frame.
5. Easily interpreted by physicians or clinicians.
6. Is used to initiate, modify, or stop therapy that is less likely to be used inappropriately.

Little has been written about the significance and impact of the inappropriate ordering of laboratory tests for infectious diseases (Baron and Peterson 2001, Wilson 2002). Inappropriate and redundant laboratory testing is not only wasteful, but more importantly it may lead to unwarranted and potentially toxic drug treatment (Wilson 1997). Inappropriate laboratory utilisation harms the patients, is expensive, unnecessary and may be clinically misleading. The utilisation of the laboratory service, and the running cost, has increased recently. It may be due to inappropriate test orders, staff salaries, and/or costs of supplies and services.

Conversely, we should consider not only factors responsible for inappropriate or excessive use, but also those that foster under use. The latter includes failure to review test results and an inability to interpret them. Optimising clinical microbiology laboratory utilisation requires explicit criteria regarding when laboratory tests should be used, and development of methods to insure that the resulting data are utilised properly. In the review of literature section, some examples of the common problems of inappropriate use of clinical microbiology services in the field of infectious disease that clinicians should be aware of while ordering clinical microbiology tests will be illustrated.

A report on a systematic review of laboratory audits performed by Naylor and Carl van Walraven in 1998 demonstrated that inappropriate testing is very common, and they pointed out that this is not only causing unnecessary patient discomfort, but it also increases the likelihood of increasing the number of false positive results, causing unnecessary worry and the need for further investigations (van Walraven and Naylor 1998).

This systematic review report of laboratory test use showed up to 46% of ordered microbiology tests were inappropriate and unnecessary, as shown in Table 1.1 (van

Walraven and Naylor 1998). The question left unanswered was that of how to change behaviour to prevent inappropriate requesting and perhaps save considerable sums of money, improve value for money, and reduce the huge workloads placed on our laboratories.

Table 1.1 Summary of inappropriate test use

Study	Number of reports	Number of tests	Percentage inappropriate	Range (%)
Studies with implicit criteria	11	5360	56	11-95
General biochemistry & haematology	5	63030	15	11-70
Microbiology	7	4979	46	5-95
Cardiac enzymes	2	843	39	38-96
Thyroid function	4	2490	30	17-55
Drug monitoring	16	2787	46	5-83

The data in this table is compiled from reference (van Walraven and Naylor 1998).

The studies of the common pitfalls of routine microbiology laboratory investigations have been described in the review of literature in section 1.2.1, these clearly demonstrate how such testing may lead to inappropriate use of tests and unnecessary antimicrobial treatment, which can be expensive and associated with potential adverse effects. In this era of increasing antibiotic resistance, it is crucial to educate medical students, clinicians, and staff physicians about the deleterious consequences of misusing both antimicrobial agents and laboratory tests (Hayden and Frenkel 2000). The use of computerised reminders for test requesting physicians is an educational tool that holds promise for decreasing unnecessary laboratory testing (Bates, Boyle and Rittenberg 1998). Furthermore, microbiology laboratories should develop and implement specific guidelines that allow them to reject inappropriate specimens.

In addition to unnecessary laboratory tests, specimens submitted for microbiological testing require proper handling, from the time of collection through

all stages of transport, storage and processing. Issues common to all clinical specimens submitted for microbiological testing include, not only proper identification, but also collection techniques that maximise recovery of microbiological pathogens and minimise contamination. For specimens like sputum and urine, the relative proportions of micro-organisms present *in vivo*, must be preserved, or culture results can be misleading. If specimens are handled properly, culture results are easier to interpret, patient care is improved and costs are potentially decreased.

As the above stated reviews of inappropriate use of clinical microbiology tests and associated problems indicate, there is a need to address this issue both locally and nationally. Hence, this study was carried out to investigate and provide information about the appropriate use of clinical microbiology tests with reference to specimen management, particularly respiratory tract specimens.

1.1.3 Purpose of the study

Given the crucial role that microbiology laboratory results play in healthcare decision making, it is important that they are accurate and specific. Compared to other types of laboratory results, such as chemistry or haematology, microbiology results have greater potential for misunderstanding and misinterpretation, because there are no normal values in microbiology test results. It is therefore the responsibility of the microbiologist to provide clinicians with reports with clear-cut conclusions that include only clinically relevant results. The microbiologist should not assume that the physician is aware of current laboratory best practices or organism names, and should provide interpretive information whenever necessary, as in the case of organisms that represent contamination.

Further to this, clinical microbiology is distinct from other disciplines in laboratory medicine. The diversity of specimens and analyses in microbiology is much greater than in other disciplines, and materials are often highly variable in nature. Microbiology laboratories work with live pathogenic micro-organisms that need to be propagated for detection, and there may be the presence of contaminating indigenous or environmental flora. Organisms can be pathogenic at one time but play a commensal role at another. Microbiology results are, therefore, often interpretative with no “normal levels” as previously stated. The majority of

specimens submitted to the clinical microbiology laboratory do not yield a clinically relevant pathogen.

The outcome of microbiology tests is directly influenced by the quality of the initial specimen; an improperly collected specimen means uninterpretable results. Proper specimen management, therefore, has a significant impact on the final outcomes, measured in post-analytical benefits to the patient. Simply put, time spent developing results for which there is no clinical benefit, on specimens that were poorly collected, is wrong. Specimens are the key to accurate microbiological diagnosis, in particular, they:

1. Directly affect patient care and patient outcomes.
2. Influence therapeutic decision-making.
3. Impact on hospital infection control.
4. Impact on patient length of stay, hospital costs and laboratory costs.
5. Influence laboratory efficiency.

However, with the growing pressure for laboratories to decrease costs and increase efficiency, it is important to critically evaluate the clinical utility of diagnostic tests. One of the ways we can improve patient care while lowering costs is to establish rules “up front” on when to culture and when not to culture. The service users and microbiologists must work together and develop laboratory guidelines.

The current research project investigates the ways in which existing microbiology laboratory services could be used appropriately, investigates the use and misuse/abuse of routine microbiology investigations and examines the efficiency with which services users use routine microbiology tests.

The focus of this study is on respiratory tract specimens using sputum samples as quality indicators for the examination of the total testing process in the microbiology service, as there are some common denominators for specimen quality. Respiratory specimens represent the most perplexing problem for clinical laboratories. Specimens which are representative of infection in the lower respiratory tract alveoli (lungs) cannot be easily obtained without contamination by upper respiratory tract secretions. The normal flora of the respiratory tract contains many organisms which can, under certain circumstances, act as pathogens.

Recovering organisms is not the main challenge; rather, it is determining their significance.

In addressing the appropriateness of specimens and interpretation of test results, it is important to evaluate the quality of specimens submitted to the laboratory. A model for the assessment of the quality of sputum specimens for routine microbiology is described. Using similar methods, the other clinical specimen types from respiratory tract systems were examined briefly for their appropriateness, including the following: throat swab, ear swab, nose swab, mouth swab, bronchial washing (BAL), nasopharyngeal aspirate (NPA), tongue swab and tracheal secretion.

The cost implication of inappropriate test utilisation (cost-effectiveness) was assessed during the study. The data from this project was used for the introduction of cost effective and clinically relevant strategies for the work up of microbiology services and other similar pathology sub-specialities in the modern NHS.

1.2 Review of literature

For the literature search strategy, databases were searched by crossing several subject headings (laboratories, diagnostic services, and diagnostic service-routine, quality assurance-healthcare) with several topic headings (guidelines, utilisation review) or text words (unnecessary, duplication, efficiency, inappropriate, over utilisation, underutilisation, quality control, quality assurance, guidelines, utilisation, utilisation review). Databases were also searched for the following terms: clinical microbiology service, pathology services, NHS, medical laboratory service, service utilisation, cost effective.

The data bases used included: PubMed, PubMed and Medline, Embase and PubMed and Cochrane Library. The relevant health circulars and publications were searched for the Department of Health internet site (www.doh.gov.uk). Additional resources and other databases used included the National electronic Library for Health (www.nelh.uk) and the British Library (www.bl.uk). Endnote was used for bibliographies formatting and simplifying reference.

Online search for information and articles, the following **Key words** were used separately on different occasions: sputum, poor quality, lower respiratory tract

infections, community acquired pneumonia, pneumonia, Gram stain, sputum culture, test utilisation, clinical relevance, cost effective, specimen management, sputum macroscopic examination, sputum quality, microbiology laboratory test utilisation service, pathology service, NHS pathology, cost of pathology services.

Pathology tests, including clinical microbiology, are not optimally used. Referring back to an editorial he had written in the Journal of the American Medical Association (JAMA) in 1984, Professor George Lundberg asked the question in a further 1998 JAMA editorial: have we had advances in the field of best practice (in Pathology)? “Sadly, the answer in 1998 is that we still do not know, not even in a research mode. We not only haven’t gotten to first base, we haven’t even picked up our bat” (Lundberg 1998).

Laboratory medicine testing is increasing at around 6-10% annually (Smellie 2003). In the UK, changes in National Health Service contracting will mean that increased pathology expenditure must ultimately be paid for by reducing clinical activity. Regardless of country, unnecessary testing carries a large financial burden. Large inequalities exist in testing activity between different general practices and hospital laboratories. These are not explained by patient or practice factors (number of practitioners, age, sex distribution of patient list, deprivation index etc.) (Smellie et al. 2002).

Inappropriate use of tests leads to unnecessary expenditure, avoidable further investigation and referrals, and conversely, under use of certain tests leaves patients with sub-optimal management and potentially missed diagnoses (Barth and Jones 2003). Failure to act appropriately on the result of a test also has serious potential repercussions on patient management. The need for a better evidence base and for improvement in the use of pathology tests was recognised twenty eight years ago (Rinsler 1984), although little progress has been made. This has been the subject of several recent reviews. There is good evidence that practice behaviour can be changed by a combination of educational and facilitating mechanisms (Solomon et al. 1998), although these must begin with knowledge of what is best practice, followed by interventions to introduce this knowledge into practice. There is good evidence, for example, that outreach visits can help in this area.

There has to date been no concerted attempt to collate all of the available evidence and guidance for pathology tests in a form supported by all of the relevant professional associations. The mismatch between resources used to develop and study new tests, and everyday guidance for users, has left many users uncertain as to the best use of tests. Although there is abundant scientific literature dealing with increased laboratory quality (mainly analytical), the literature on appropriate use of clinical microbiology tests is scarce. The task facing us now is how to introduce the knowledge we have into clinical care to reduce the adverse effects of inappropriate testing and the actions following on, and optimise the care that good use of tests can bring.

This review section will focus on this issue in the field of the clinical microbiology laboratory reviewing inappropriate utilisation of the service and comparing it, where possible, with appropriate use.

1.2.1 Common pitfalls of microbiology laboratory investigations

The following common routine microbiological specimen examples illustrate some of the common pitfalls of the microbiology laboratory in the investigation of infectious diseases and infections that need to be investigated.

Daily sputum cultures and poor quality of sputum specimens: One example of inappropriate use of clinical microbiology tests is daily requests for sputum cultures. In order to reduce this unnecessary practice, the laboratory must work with clinicians to help them collect the correct specimen for the test desired, organism suspected, or clinical condition of the patient (Sharp et al. 2004). For example, multiple specimens within 48 hours should not be processed. Also, a test of cure is not necessary if the patient has responded to therapy.

Sputum quality screening is important, since sputum is among the least clinically relevant specimens, with no agent isolated in 40 to 60% of cases (Forbes, Sahm and Weissfeld 1998, Isenberg 2004). Respiratory specimens are frequently contaminated with resident flora; therefore, it is difficult to determine what is a respiratory tract pathogen. Direct Gram stain results should be used to aid in the selection of organisms to work up in the culture (Heineman, Chawla and Lopton 1977, Skerrett 1997). Most of the literature supports the usefulness of the Gram stain in screening sputum specimens (Geckler et al. 1977, Heineman et al. 1977,

Kalin, Lindberg and Tunevall 1983, Joyce 1986, Skerrett 1997). However, the Gram stain has varying sensitivity and specificity, depending on the specimen and the reader's level of skill (Isenberg 2004).

However, for the diagnosis of lower respiratory tract bacterial infections, sputum is the gold standard specimen, but the quality of the specimen is the key, because oral and gastrointestinal secretions may contaminate it. Ideally, there should be "good quality" sputum for microbiological processing, and samples must be properly collected in order to be clinically relevant and provide a quality culture and susceptibility result for the patients. As stated by Bartlett, a culture of lower respiratory secretions may result in more unnecessary microbiologic effort than any other type of specimen (Bartlett 1974). More details of what is meant by good quality sputum specimens will be described in the review section of microbiological investigations of respiratory specimens (sections 1.2.8 and 1.2.9).

Routine stool culture of patients more than three days in hospital: Several studies have shown that microbiology laboratories need to perform only a very limited range of tests on in-patients with hospital acquired diarrhoea (Hobbs et al. 1997, Ozerek and Rao 1999, Gopal Rao, Ozerek and Jeanes 2001, Bauer et al. 2001, Guerrant et al. 2001). If the diarrhoea is community acquired or acquired from travelling, the minimal testing recommended is: (a) perform cultures (which detect Salmonella, Shigella, and Campylobacter spp.) and suspected patients with bloody diarrhoea are tested for *Escherichia coli* 0157. (b) if the patient has taken antibiotics or chemotherapy in recent weeks, then additional testing for *Clostridium difficile* toxin is recommended.

If the diarrhoea is nosocomial (hospital acquired, has onset after >3 days of hospitalization), then only *C difficile* toxin should be requested. *C difficile* is the most common enteric pathogen causing diarrhoea in hospitalised patients, and pseudomembranous colitis can occur in patients who have not been recently exposed to antibiotics (McFarland, Surawicz and Stamm 1990). The detection rate for bacterial pathogens such as Salmonella*,* Shigella*,* Campylobacter, and Yersinia, and for enteric parasites is less than 0.5% for persons who have been in hospital for greater than 72 hours (Siegel, Edelstein and Nachamkin 1990, Chitkara, McCasland and Kenefic 1996). Therefore, there should not be routine stool culture from hospitalised patients and the "three day rule" should be applied when ordering stool investigation in a hospitalised patient who develops loose stools.

The "three day rule" advises clinicians to avoid ordering tests for enteric bacteria and stool parasites for patients who have been hospitalised for more than three days, unless there is an ongoing nosocomial outbreak of food poisoning, or unless investigation determines that patients have access to food which may have been prepared under unhygienic conditions. Patients seropositive for HIV, neutropenic patients, and patients more than 65 years of age with immunosuppressive co-morbid illnesses can be considered exceptions to the "three day rule" (Bauer et al. 2001). Indiscriminate requests for routine bacteriology and for the examination of faeces for ova, cysts and parasites are a great nuisance to microbiology laboratories; the microbiological examination of faeces specimens is highly labour intensive.

Repetitive daily cultures from a suspected site of infection (catheter tips): One of the repetitive daily cultures from a suspected site of infection is the catheter tip. It has been shown that qualitative intravenous catheter cultures have minimal value as predictors of catheter related bacteraemia and such culturing of catheter tips should be discouraged (Nahass and Weinstein 1990, Widmer et al. 1992). Some laboratories will not process a catheter tip sent for culture if a concurrent blood culture has not been submitted within a 24 hour period, either before or after the catheter removal, or if a recent (≤24 hour) blood culture is negative (Schreckenberger 2001). Bacterial growth from catheter tips generally represents clinically insignificant catheter colonisation or contamination (Maki, Weise and Sarafin 1977). Patients collected from such repetitive qualitative catheter tips could lead to an incorrect conclusion that the patients were infected and treated with antibiotic therapy and unnecessary exposure to potentially toxic drugs.

Swab sampling of superficial patient material (surface of an open ulcer): While swab culture from the surface of an open ulcer can identify wound colonisation that may help determine appropriate isolation precautions (for example, as in the case of MRSA, vancomycin resistant enterococcus, or other multi-drug resistant bacteria), it frequently leads to an uninterpretable result that does not accurately reflect the true underlying pathogen (Mackowiak, Jones and Smith 1978, Cierny and Mader 1984, Wheat et al. 1986, Perry, Pearson and Miller 1991). Micro-organisms recovered from the surface of a wound do not reliably predict the causative pathogens to be found deep within underlying soft tissue or bone. Cultures of material obtained from curettage of the ulcer, or from deep tissue

biopsy, will be less contaminated and provide cultural information more useful in guiding antimicrobial therapy.

Daily culture of urine specimens: Urinary tract infection is one of the most commonly encountered acute infectious diseases and accounts for the majority of the workload in clinical microbiology laboratories. Due to the large workload, identification of what are often insignificant organisms can waste laboratory resources, confuse the physician, and ultimately result in unnecessary antimicrobial therapy, which leads to resistance. It is now widely accepted that currently available urine “dip sticks”, which detect nitrites and leukocyte esterase, have high negative predictive values (90-95%) and can be used to exclude urinary tract infection in most patients (Hobbs et al. 1997)**.** Similarly, catheter specimens of urine (CSU) should be tested only in the presence of symptoms. Routine testing of CSUs is wasteful and may lead to unnecessary antibiotic treatment.

Other microbiological specimens that have similar pitfalls include the daily collection of CSF (lumbar puncture) for cultures from patients without suspected meningitis infection performed routinely (Campos 1994) and excessive numbers of contaminated blood cultures collected from patients in A&E departments (Kelly 1998).

In addition to these examples of common microbiological pitfalls, these studies also highlight the lack of communication between the microbiology laboratory, clinical and medical staff. Communication between the laboratory and clinical staff is perhaps the most important ingredient of a quality service from a microbiology laboratory. Good advice on specimen collection can be priceless, while the relevance of microbiological results often only become clear in a discussion between a clinical microbiologist and a treating physician. Antimicrobial sensitivity testing may guide therapy, but optimal therapy cannot be advised without considering certain patient-related factors, such as the site of infection, which may have a profound effect on the ability of a specific agent to act effectively.

The conclusions from the above examples and studies illustrate the frequency and importance of minimising unnecessary laboratory tests, or tests that have no clinical relevance. In this context, the current study will investigate the factors affecting the quality of sputum specimens.

1.2.2 Appropriate utilisation of clinical microbiology tests

As stated previously, clinical microbiology laboratories perform tests to aid in the diagnosis of infectious diseases, to help guide therapy for those diseases, to help control and prevent infection in healthcare settings, and to educate and train healthcare professionals. This is a broad and challenging mission. To accomplish this mission, a clinical microbiology laboratory must provide a wide variety of tests that span a number of different disciplines, from bacteriology to virology to parasitology to antimicrobial susceptibility testing. This mission has become even more challenging in recent years because of the emphasis on cost control in healthcare, the introduction of new (and often more expensive) diagnostic technologies, and increasing regulations. Thus, to meet their mission, laboratories must maintain or expand their services with fewer resources. One of many approaches to this dilemma is for laboratories to focus and limit testing to those tests that are both clinically relevant and cost-effective.

The issues of utilisation and appropriateness are related. While utilisation is primarily concerned with the frequency of testing, appropriateness is concerned with the use in the right patient in the correct setting for the proper diagnostic, monitoring, or therapeutic reasons. Improving utilisation has the ability to reduce laboratory costs, while precluding several less pleasant alternatives, such as rationing laboratory tests or eliminating some altogether.

It has long been evident that laboratory tests are over requested. Until recently, however, efforts to curb unnecessary laboratory testing were undermined by lack of incentives for change, and because of inability to predictably modify physician test ordering patterns. As with any type of laboratory testing, the cost-effectiveness and clinical relevance of microbiology tests are affected by pre-analytical, analytical and post-analytical variables, as discussed in the following section.

The published data regarding appropriate laboratory utilisation has, until recently, focused on the issues of the relative accuracy of diagnostic methods, clinical relevance of tests, or the cost-effectiveness of different diagnostic methods. These issues first received emphasis in the early 1970s, when controlled clinical comparisons of diagnostic laboratory methods became more common, investigators began looking at the clinical relevance of diagnostic tests, and the

issue of cost control became increasingly important. As noted by van Walraven and Naylor (1998) and commented on by Lundberg (1999), much of the published literature about clinical relevance and cost-effectiveness lacks the scientific rigor that characterises evaluations of other diagnostic modalities and therapies.

These criticisms are almost certainly valid, but holding laboratory tests to the same standards as other diagnostic procedures or methods may be unrealistic. There are two reasons for this. First, laboratory methods are usually used to confirm clinical impressions or to supplement clinical, radiographic, or other laboratory data. This is different from, for example, histological examination of a biopsy that, by itself, may provide definitive diagnostic information. In other words, many microbiology laboratory tests do not stand alone for the purposes of making diagnoses, whereas many other types of diagnostic methods or therapies do.

Second, the clinical impression of the provider has an important effect on the interpretation of the test result. This is because the pre-test probability of a disease affects the post-test probability of a laboratory test result (Irwig et al. 2002). Thus, while it is often possible to design controlled clinical trails of novel diagnostic methods or therapies, evaluating laboratory methods is not as straightforward because other factors affect the interpretation of the laboratory test. This is not true of many other types of clinical evaluations, in which the process of blinding the study can remove clinical impressions as a factor in test interpretation.

Despite these limitations, some issues regarding laboratory tests can be studied adequately via controlled clinical trails, including product comparisons, comparison of new diagnostic tests with older methods, evaluations of the relative cost effectiveness of different tests, and even some evaluations of clinical relevance. Some aspects of the clinical effects of laboratory testing can also be studied adequately, such as the impact of the timeliness of result reporting.

One can approach the issue of laboratory appropriate utilisation from a number of perspectives, including those that are based on financial models, staffing ratios, productivity or other benchmarks, treatment and evaluation guidelines, and so on. Regardless of the approach that is taken, the one principle that must play a role in any assessment of laboratory utilisation, is that of clinical relevancy; no test can be cost-effective, no laboratory can be efficient and productive, and no organisation

can provide good patient care unless laboratory testing is clinically relevant. The other approaches that affect the patients care, include the cost-effectiveness of the tests and TAT of the test results.

1.2.3 Clinical relevance in clinical microbiology tests

An important criterion of quality for a microbiological test is how much it contributes to the prevention or cure of infectious diseases; this is called its clinical relevance. The term ‘clinical relevance’ is roughly synonymous with ‘clinical significance’ and ‘clinical importance’. The term is not used consistently, however, because there is no standard definition, nor is there yet a quantifiable way to measure clinical relevance. This lack of objectivity should not impede assessments of clinical relevance, or lead to inaction. Clinically relevant tests share certain characteristics that can be used in assessment and, to be clinically relevant and cost-effective, diagnostic laboratory tests must have certain characteristics, as shown in Table 1.2.

Table 1.2 Characteristics of clinically relevant microbiology tests

1. Therapy can be altered based on test results.
2. Test results can be used to alter therapy.
3. Test results are available in a clinically relevant time frame.
4. Tests are sufficiently sensitive and specific to provide false-positive and false-negative results with a frequency and consequences acceptable to users.
5. Test positive and negative predictive values are appropriate for the type of test and clinical setting.
6. Users can easily interpret test results.

Therefore, the guiding principle for all microbiologic testing should be that of clinical relevance (Wilson 1997). No microbiology test should be ordered or performed unless it is of immediate relevance to a physician caring for a patient, or it is needed by public health authorities or hospital epidemiology and infection control personnel. For the physician, clinically useful tests yield results that allow the physician to initiate, stop or modify therapy based on the test result. For public health authorities, clinically useful tests allow for treatment of patients, follow up of case contacts, and collection of epidemiologic information. For hospital

epidemiology and infection control personnel, clinically useful tests allow patients to be placed in or removed from isolation, case contact follow up to occur, patients to be cohorted, and epidemiologic information to be collected and collated.

Determining the clinical relevance of tests is challenging, however, because (1) physicians order laboratory tests for many reasons, and a given test has varying clinical relevance when used in different settings or for different reasons (Kassirer 1989, Pannall et al. 1996); (2) laboratory tests are interpreted in the light of complex clinical scenarios, not as isolated or independent results; (3) clinical diagnoses are based on both objective and subjective information and (4) physicians presented with the same information may have differing interpretations of the importance or relevance of a test result. Both clinicians and laboratory scientists recognise that clinical medicine is not a simple matter of matching signs and symptoms with the results of laboratory or radiologic tests to generate a diagnosis and treatment plan. Most tests may be of more or less relevance to the physician depending on the clinical history, review of systems, family history, signs and symptoms, physical examination, and the results of other tests or studies. As a result, the pre-test probability of a disease (infectious disease) or condition substantially influences the physician's interpretation and the clinical relevance of the test result (Aronson and Bor 1987). Moreover, the results of many laboratory tests cannot be interpreted accurately outside the context of clinical information.

Use of algorithms is also a potential mechanism for limiting a physician's pursuit of diagnostic certainty. Clinical relevance should inform laboratory practice at every stage in the process. The father of the drive for clinical relevance in diagnostic microbiology laboratories is Raymond Bartlett, a distinguished microbiologist from the United States (Bartlett 1974). Clinical relevance can only be ensured when there is good communication between the clinician and the laboratory.

1.2.4 Cost effectiveness in clinical microbiology tests

The term cost effective is poorly defined. It is often used as a euphemism for inexpensive, least expensive, or expensive but still worth doing (Wilson 2000). It was considered anti-academic, impure, or even dangerous by traditional microbiologists. Another way to view the issue, however, is the application of clinical relevance to diagnostic microbiology. The point is not to identify every organism that might be recovered, or to perform susceptibility tests on every

organism that will grow in the laboratory. The point is to provide clinicians with information that will allow them to provide the best care for their patients. In the process, the work can usually be done more economically than if everything possible is done. Thus, clinical relevance usually equals cost-effectiveness. Cost-effectiveness does not mean cheap: it means the best value for money, as indicated in Table 1.3.

Table 1.3: Characteristics of cost-effectiveness in microbiology tests

1. Test methodology is technically feasible, reproducible, reliable and economical.
2. Test volume is sufficient to maintain performer competence.
3. Test results are readily interpretable by laboratory staff.
4. Test results are easily communicated.
5. Tests are sufficiently sensitive and specific to provide false-positive and false-negative results with frequencies and consequences acceptable to users.

Therefore, appropriate test use depends on the use of the most cost-effective test for a given purpose. Unfortunately, for obvious reasons, these definitions are inadequate. Using expensive microbiology tests when cheaper but acceptable alternatives are available, or using inexpensive tests that do not provide accurate test results, both increase costs without benefiting either the physician or the patent. A better, albeit descriptive, definition is “the least expensive method that yields clinically relevant test results in a timely manner and that does not increase costs elsewhere in the healthcare system” (Wilson 2000). What is needed beyond a descriptive definition, are definitions, particularly mathematical descriptions that can be used in controlled clinical evaluations to quantify and compare the cost effectiveness of alternative tests or methods.

When alternative test methods are well characterised and have similar performance parameters and test TAT, then the most cost-effective method may be defined simply by its cost. In this case, the least expensive method is likely to be the most cost-effective method. On the other hand, for many clinical microbiology tests, alternative methods differ not only by cost, but also by their performance parameters and test TAT. In this case, the least expensive test may still be the most cost effective, but if a more expensive test has better performance parameters or test TAT then it may be the most cost effective method. This is one of the

problems with defining cost effectiveness: the cost of performing a test may or may not be the most important factor (or even a relevant factor) in determining whether the method is cost effective or not. A related issue is determining the point at which the costs required to achieve incremental gains in test performance parameters or test TAT make the method no longer cost effective.

For example, nucleic acid amplification (NAA) tests are the most analytical sensitive tests for detecting and identifying pathogenic microorganisms, but increased analytic sensitivity may or may not result in increased diagnostic sensitivity. If a test method does not increase diagnostic sensitivity, or increases it only marginally, then the higher cost of using the method makes it less cost effective compared with one that has lower analytic but higher diagnostic sensitivity. Defining cost effectiveness is perhaps even more challenging than defining clinical relevance, partly because the cost effectiveness of a test depends on its clinical relevance, but also because many other variables must be considered. As another example, use of rapid automated methods for bacterial identification and antimicrobial susceptibility testing may result in improved clinical outcomes, decreased use of other laboratory tests, shorter hospitalisation, and decreased hospital costs (Granato 1993, Doern et al. 1994).

Even in the absence of rigorous definitions and analytic methods, there is much that clinical microbiology laboratories can do to increase the cost effectiveness of microbiology tests. One of the ways to increase cost effectiveness of the tests is to follow the principles of cost effectiveness and clinical relevant microbiology testing, as previously described and stated in Table 1.4.

Table 1.4: Principles of cost effective and clinically relevant microbiology testing[a]

1.	Test only properly collected, transported, and labelled specimens.
2.	Test only appropriate specimens; reject inappropriate specimens.
3.	Perform and interpret tests according to their Food and Drug Administration approval or clearance.
4.	Perform and interpret tests according to manufacturer's recommendations.
5.	Perform and interpret tests using standard microbiologic methods.
6.	Use adequately trained and competent staff to perform tests.
7.	Perform tests only if there is sufficient test volume to ensure competency and proficiency.
8.	Refer esoteric tests to the most appropriate reference laboratories.
9.	Minimise test result turnaround time.
10.	Report test results using the most appropriate mechanism for the importance of the test.
11.	Develop and implement effective laboratory consultation and education programmes.

[a)] adapted from: Clinically relevant, cost-effective clinical microbiology: strategies for decreasing unnecessary testing. Am J Clin Path 1997; 107:154-67 (Wilson 1997).

1.2.5 Test turn around times in clinical microbiology

TAT is the interval between the beginnings of one event to the end of another in the total testing process. Typically measured as the collection to reporting time, or as the receipt of specimen in clinical laboratory to reporting time. Inadequate clinical laboratory test TAT is one of the most common complaints that come to the laboratory manager. Since clinical evaluations typically require support from laboratory testing, until results are available, diagnoses are less certain and management decisions are delayed. From an outcome perspective, slow test TAT leads to longer waiting times for the patient, or incomplete information at the time of a clinical encounter. As a general rule, faster service is associated with higher costs and sometimes lower quality of test results. Therefore, it is the laboratory manager's responsibility to determine the most effective overall testing processing and schedules that will provide the most cost effective and reliable results within a time frame that is clinically appropriate.

Microbiology test results that are not available within a reasonable period of time are unlikely to be clinically relevant or to be used appropriately. The first challenge is to define a reasonable test TAT for each method, for each type of healthcare professional who uses the results, and for different healthcare organisations (Howanitz et al. 1993). A second challenge is to determine which measure of test TAT should be used (Valenstein and Emancipator 1989), and to develop a system to monitor and improve test TAT. A third challenge is to determine what can be done to decrease test TAT to acceptable levels, and how much it will cost to achieve the shorter TAT. The final challenge is the question of whether one can satisfy clinician's demands for shorter TAT, or if the laboratory should even try to do so (Valenstein 1989, Valenstein 1996). Satisfying physician's expectations for improved test TAT is a complex process for which there is no single solution (Steindel and Howanitz 2001).

No one argues that the results of some microbiology tests must be available quickly. At the same time, no one argues that physicians do not need the results of some laboratory tests for days or weeks (or it is not possible to obtain the results more quickly than that). It is easy to manage the TAT for those tests that fall into these two categories, which lie at either end of a continuum. It is much more difficult to manage the test TAT for those tests that fall between these categories; for most laboratory tests the acceptable test TAT is defined by the clinical status of the patient. For many tests, the acceptable test TAT may be minutes for one patient or days for another.

The issue of test TAT is especially problematic in a clinical microbiology laboratory. Most clinical microbiology testing still relies on a culture-based isolation of microorganisms, biochemical identification, and traditional methods for antimicrobial susceptibility testing. Test TAT has been decreased significantly in some areas of clinical microbiology, such as mycobacteriology (if used rapid techniques e.g. PCR and microscopy examination), but for much routine microbiologic testing there has been little or no change in TAT. Some manufacturers have introduced more rapid methods, but there are only limited data to indicate whether the shortened test TAT improves the outcome of patient care (Granato 1993, Doern et al. 1994, Schifman, Pindur and Bryan 1997). In addition, where such data do exist, it should be emphasised that improvement in the outcome demonstrated for shortened test TAT

for a given test may not occur with other but similar tests, in different healthcare settings, or for patients with different clinical scenarios.

The turnaround times for tests in microbiology are quite varied. Ranging from 24 hours to a few weeks and an average microbiology tests TAT is as following: bacteriology culture and sensitivity – 2 to 4 days, serology tests – 1 to 24 hours onwards, TB culture – up to 6 weeks, mycology tests – up to 4 weeks, parasitological microscopic examination- few minutes to hours and tests sent to reference laboratories – 2 to 3 weeks.

Electronic reporting of culture results instead of reporting on paper may shorten the turnaround time and may ensure correct communication of results (Bruins et al. 2011). Clinician's value electronic reporting of clinical microbiology results, because it increases the efficiency in their medical practice and saves valuable time. Final culture results may be available sooner compared to the former practice of reports by paper, but, in contrast to current opinions, this shorter turnaround time does not automatically influence medical decision making. Where the fast reporting of first results is of importance, telephone reporting is still the communication method of choice.

1.2.6 Total testing process and test ordering

The total testing process (TTP) is a multistep process that begins and ends with the needs of the patient. The total testing process consists of three key components or phases as shown in Figure 1.1 and is presented here in briefly with reference to appropriate utilisation of clinical microbiology tests. These phases are pre-analytical, analytical and post-analytical phase.

Identifying the many steps in the TTP and planning and using an interdisciplinary team to begin a coordinated effort will improve the process and offer optimal patient care. The TTP is one of the systems used in applying quality management approaches to the clinical laboratory (Barr and Silver 1994, Schumacher and Barr 1998). The TTP refers to the sequence of eleven steps of laboratory testing, outlined in Figure 1.1, beginning with a clinical question prompted by the patient-clinical encounter and concluding with the impact of the test result on patient care.

Clinical microbiology testing, like other clinical laboratory testing, is a highly complex process. Therefore, TTP describes the full sequence of laboratory testing activities, which, when applied to the analysis and interpretation of clinical microbiology specimens, leads to decision that influence patient outcome resulting from test results.

The testing cycle, commonly called the TTP was well described several years ago by George D. Lundberg, who pictured it as a “brain-to-brain” (Lundberg 1999). The starting point for a microbiology test, a question made by the physician to the laboratory, can concern diagnostic, prognostic and monitoring processes, and/or health maintenance and promotion. The end result of the testing cycle is patient outcome and the effectiveness of laboratory information in improving medical and economical outcomes. In this cyclical process, the laboratory test is ordered, the patient identified, and the specimen collected, transported and prepared for analysis and process. After the specimen has been analysed, the results are interpreted and reported to the physician or whoever ordered the tests. The action finally taken is based on the interpretation of the test results.

Traditionally, microbiology laboratories have focused their attention on quality control methods and quality assessment programmes dealing with analytical aspects. However, a growing body of evidence accumulated in recent decades demonstrates that quality in clinical laboratories cannot be assured by simply focussing on purely analytical aspects (Plebani and Carraro 1997). A study review of errors in laboratory medicine concluded that in the delivery of laboratory testing, mistakes occur more frequently (pre-analytical phase) and after, the test has been performed (Bonini et al. 2002).

Many of the mistakes in TTP are referred to as “laboratory errors”, but are actually due to poor communication, actions taken by others involved in the testing process (physicians/clinicians, nurses and phlebotomists) or poorly designed processes which are outside the laboratory’s control (Plebani and Bonini 2002). Likewise, there is evidence that laboratory information is only partially utilised: a recent report demonstrates that 45% of the results for urgent laboratory tests requested by A & E department of one hospital were never accessed, or were accessed far too late (Kilpatrick and Holding 2001). In the modern approach to total quality management in clinical laboratory, which is centred on patient’s needs and satisfaction, the risk of

errors and mistakes in pre-and post-examination steps must be minimised in order to guarantee total quality of laboratory services.

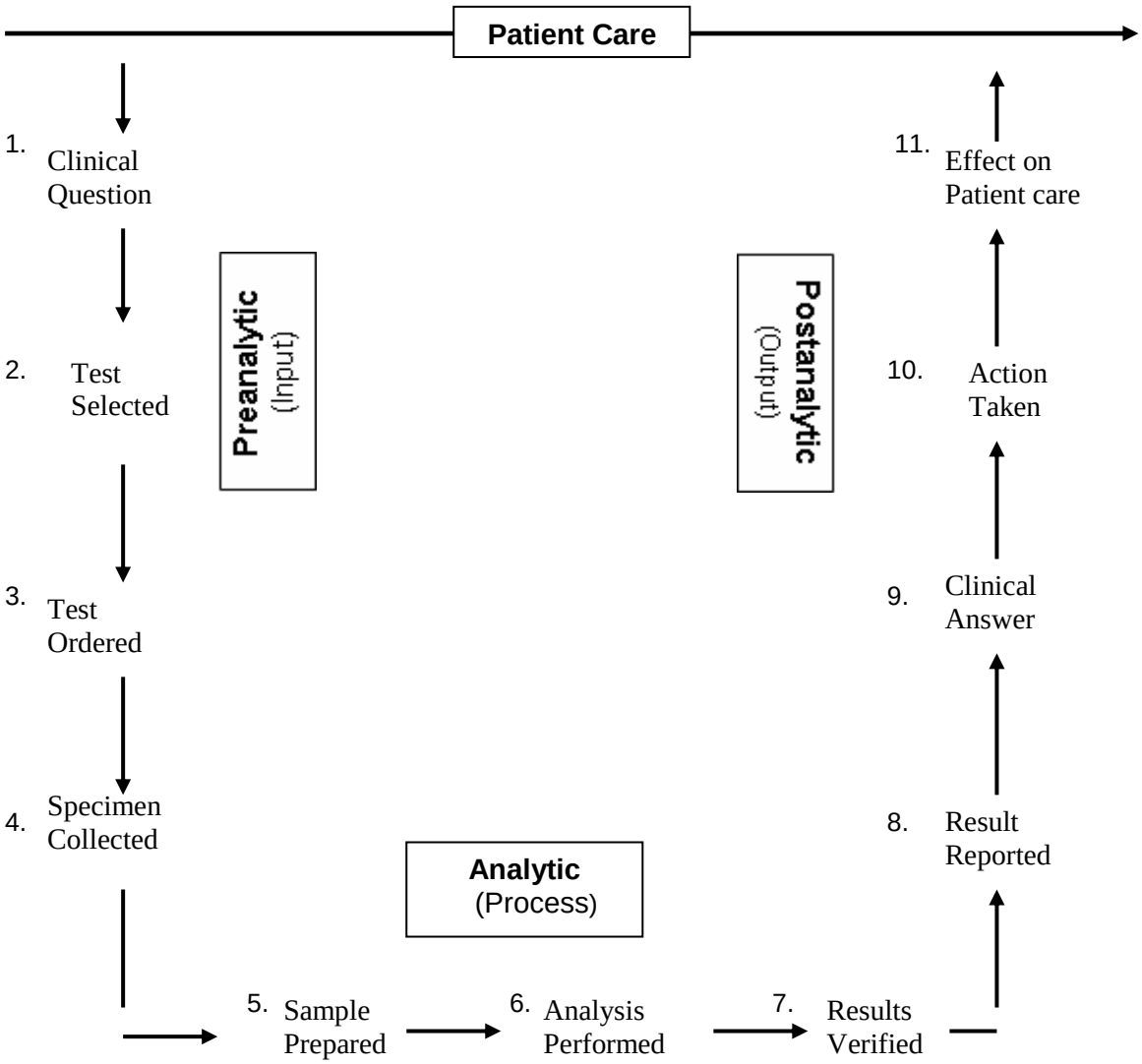

Figure 1.1: The total testing process[a]

[a)] adapted From: The total testing process applied to therapeutic drug monitoring. *Therapeutic Drug Monitoring*, 47-82 (Barr and Schumacher 1995).

Today, many clinical laboratories still operate according to the traditional laboratory model, the old laboratory model (Figure 1.2), which is a linear, unidirectional flow process of one activity preceding the next activity. The traditional (current) clinical microbiology laboratory is isolated from what tests are ordered (input) and how their results are interpreted (output). The traditional laboratory cycle operates in one direction. The major concern in this model is the quality of test performance and the

production features and internal organisation of the laboratory (analytical phase). In the traditional model, the focus is on the science and technology and quality of test performance, and communication is almost non existent prior to the test request, or after the result is released. In this model, the clinical laboratory is not concerned with clinical appropriateness or interpretation of test results (Barr 1999).

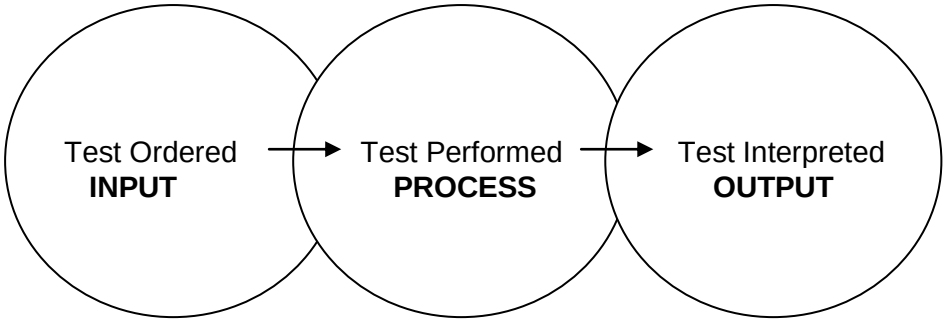

Figure 1.2: The traditional laboratory cycle

The new laboratory model (Figure 1.3) is an interactive process, and the scope of laboratory services is broader. In the interactive clinical microbiology laboratory cycle, laboratory scientists and clinicians interact to improve how tests are ordered, how tests are performed, and how results are interpreted. The interactive laboratory cycle operates both directions. In this model, the focus is not only on the quality of test data generated (process/analytical), but also on the clinical appropriateness of test requests (input/preanlytical) and the correct interpretation of and response to laboratory information (output/postanalytical). The laboratory's involvement in the entire total testing process will have a positive impact on patient outcomes, improve the clinical relevance and value of the laboratory's service, and greatly enhance the cost-effectiveness of the laboratory operation (Barr 1999).

To demonstrate how appropriate test utilisation will promote a better integration of laboratory services into the patient care process. This was described by Barr, and is known as Barr's model of laboratory utilisation (Barr 1999). This model identifies the factors that affect the clinician's decisions or actions at each step of the laboratory utilisation process.

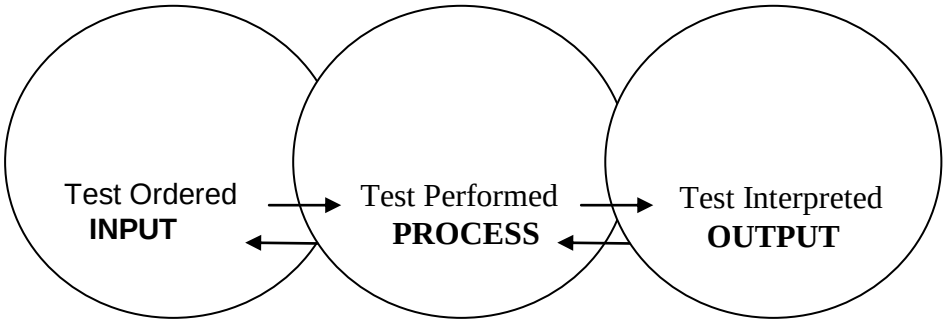

Figure 1.3: The New Interactive Laboratory Cycle

According to Barr's model, in the input phase (pre-analytical), one must question if the test is appropriate for the stage of the clinical condition and if the time of specimen collection is correct. During the process phase (analytical), one must determine if, within clinically relevant guidelines, the test result is accurate and precise and timely with respect to the TAT needs of physicians. Finally, in the output phase (post-analytical), one must evaluate if the results are properly interpreted and integrated into patient care or if data overload is confusing or misleading physicians (Barr 1999).

Barr's model also demonstrated any appropriate roles for the laboratory scientist at each step of this process. Starting with the clinician's assessment of the patient's condition, the laboratory utilisation process moves to laboratory testing phases**,** which result in the application and integration of the test results into patient care. All three phases are critical. If a test is clinically indicated, or the laboratory's precision is beyond that needed for clinical judgements, or if the result is misinterpreted, then an accurate and precise laboratory result is of no value.

1.2.7 Impact of specimen management in microbiology tests

Recent years have seen significant advances in the technology available within the clinical microbiology laboratory. Traditional methods have been improved with the availability of chromogenic media and spiral platers, while automated systems are used for blood culture, urine handling and analysis, immunoassay, bacterial identification and antibiotic susceptibility testing. Difficult cases will yield their answers to advanced molecular techniques, such as ELISA and PCR. These

methods, combined with the technical expertise of dedicated clinical microbiologists, enable laboratories to provide accurate results quickly, often on-line, so that patients can be treated appropriately and effectively.

The one area that is often overlooked is that of specimen management particularly specimen collection and transport. Centralised laboratory services often mean microbiology specimens being sent to laboratories many miles away. Although some laboratories may provide 24 hour service, this is not universal and specimens often have to wait until the next day for processing.

In addition to this, specimen's method of collection, time of sampling, the source of the specimen and sample transport are often outside the direct control of the microbiology laboratory, but have a direct bearing on the ability of the laboratory to achieve reliable results. The other factors that the laboratory can control and that affect quality are the specimen quality assessment, identification, storage, and preparation (processing) of specimens. The laboratory therefore has a role in educating those taking and transporting specimens. Written instructions should be made available and regularly reviewed with the clinical and nursing staff.

The clinical utility of clinical microbiology culture results is directly related to the types of specimens submitted for culture and their quality. If this initial requirement for specimen quality fails to be met, subsequent processing and culture work-up becomes irrelevant for meaningful patient management. The adage "garbage in results in garbage out" can be used to descriptively refer to the issue of specimen quality in the clinical microbiology laboratory.

Specimen management in microbiology includes all the steps involving the specimen submitted for analysis of meaning selection, collection, transport, storage, analysis, and reporting. When errors occur at any point in this specimen management process, regardless of who might be responsible for error, the outcome of laboratory analysis can be affected and could lead to a negative outcome, such as misdiagnosis, extended length of stay, or inappropriate therapy.

Specimens submitted for microbiological testing require proper handling from the time of collection through all stages of transport, storage, and processing. Issues common to all clinical specimens submitted for microbiological testing include not only proper identification but also collection techniques that maximise recovery of

microbial pathogens and minimise contamination. For specimens such as sputum, and urine, the relative proportions of different micro-organisms present *in vivo* must be preserved, or culture results may be misleading. If specimens are handled properly, culture results are easier to interpret, patient care is improved, and costs are potentially decreased. Although most guidelines for specimen handling remain unchanged, recent emphasis has been placed on modifying traditional practices to decrease or eliminate unnecessary work, increase laboratory efficiency, and make microbiological testing more cost effective (Miller 1999).

Proper collection of microbiology specimens requires complex procedures that frequently have to be done by personnel outside the microbiology laboratory. Physicians, clinicians, nurses, and other healthcare personnel, as well as the patients or a parent, must perform the collection(s) of different types of microbiological samples from various sites. Although the microbiology laboratory provides collection instructions for different specimen types in the guide to microbiology services, specimen collection problems are the most common sources of laboratory error in microbiology operation.

The basic principle of microbiological specimen collection states that the material must be from the actual site of infection, collected with a minimum of contamination from adjacent tissues, organs, or secretions. For example, throat swabs for streptococcal screening should be taken from the peritonsillar fossae and posterior pharyngeal wall, avoiding contact of the swab with other areas in the mouth. Contamination of sputum or lower respiratory specimens with oropharyngeal secretions must also be minimised. Respiratory culture the source of contamination is from improper mouth care prior to collection of specimen and lack of deep cough to obtain lower respiratory material.

Microbiology specimens should be transported to the microbiology laboratory as quickly as possible. For instance, in a hospital setting, a maximum two hour time limit between collection and delivery of specimens to the laboratory is recommended (Wilson 1996, Wilson 1997, Miller 1999, Sharp et al. 2004). This time limit poses a problem for specimens collected in general practices and healthcare centres. Delays in transportation of microbiology specimens to the microbiology laboratory may result in a falsely negative result because the over growth of the normal flora over the pathogen(s) or pathogens may not survive in the delayed specimen transport.

Specimen acceptability should be based on various factors that apply to a particular source/site of sampling. The quality and/or volume of the specimen as well as its condition upon arrival at the microbiology laboratory are all important considerations. Microbiology specimen acceptance criteria for testing and the lists of microbiology specimens suitable for culture provided the specimens have met with the appropriate collection and transportation guidelines is in Appendix 1.1. and Table 1.5.

Similarly, the criteria for rejection of unsuitable specimens for culture must be established in microbiology laboratories (Wilson 1997). Although general guidelines exist and accrediting agencies have established standards, each microbiology laboratory must decide which parameters to utilise, depending on local conditions. Microbiology request forms and specimen labels must be checked to see that all essential information is included and is internally consistent. Should there be a problem; collection of a fresh sample is the best course of action. If the specimen cannot be re-collected, a responsible person should be contacted to make corrections. A comment should be entered on the final report that the specimen was received with a (specified) problem, and the name of the person who corrected the problem should be appended. Criteria for rejection must be readily available and microbiology laboratory specific. A list of specimen types or culture requests that should not be processed and rejected is shown in Table 1.5.

Table 1.5: Microbiology specimen rejection criteria

1. Unlabelled or improperly labelled specimens (should not be processed from non-invasive sites and those from invasive procedures discuss with sender).
2. Specimens received in leaking, cracked, or broken containers or improper container or use of improper transport medium.
3. Improper temperature during transport or storage.
4. Excessive transport time.
5. Specimen received in fixatives.
6. Oropharyngeal contaminated sputum.
7. Duplicate specimen's stools, sputum within a 24 hour period for the same test. (There may be exceptions in some patient cleared by the microbiology laboratory).
8. Specimens not appropriate for a particular test (specimens unsuitable for request e.g. anaerobic request from aerobic transport or tests of little or no diagnostic value) or improper collection site for test request.
9. Dry swab.
10. Unpreserved specimens received more than agreed time after collection (should not be processed specimens with prolonged transportation).
11. Twenty-four hour collection of urine or sputum for AFB or fungal culture.
12. Other criteria specific to the microbiology laboratory.

The most common causes of specimen rejection by clinical microbiology laboratories include the following:

1. Unacceptable specimens due to inappropriate collection.
2. Specimens with labelling errors.
3. Specimens received without date of collection.
4. No specimen received, only request form received.
5. Specimens with insufficient quantity.
6. Specimens received with no form or no name on the form.

As reported in the previous sections, the TTP begins with the patient–physician interaction. At some point, the physician should formulate a potential diagnosis to be ruled in or ruled out by microbiology data. Microbiology tests are ordered and

the necessary specimens are selected, collected, and transported to the microbiology laboratory, often by someone other than the physician or the microbiologists. In fact, the early steps that occur before the specimen arrives in the microbiology laboratory are perhaps the most critical in the entire testing process, yet they are often conducted by those who may know the least about what the physician or microbiologists needs.

Obtaining accurate and cost-effective microbiological test results is possible only when specimens are collected, transported, and stored properly. When proper procedures are followed, cultures of specimens are less likely to be contaminated and more likely to yield pathogens. Not only does this make interpretation of tests results easier, but it also reduces unnecessary work and, as documented for some specimens, reduces healthcare costs. Proper collection include submitting the appropriate number of specimens, submission of more that the recommended number of specimens does not improve the physician's ability to interpret test results. The result of any laboratory result is only as good as the sample received in the laboratory. "Most laboratory work and the greatest cost will be associated with specimens of the least clinical value" according to Bartlett (Bartlett 1974).

From these accounts describing the impact of specimen management in microbiology investigation, it is clear that microbiological confirmation of clinical diagnosis of infection depends upon the collection of high quality specimens and their rapid despatch to the microbiology laboratory with all the necessary supporting information, as stated previously. Laboratory tests detect micro organism or their products, or evidence of a patient's immune response to infection. While coming from different perspectives, culture and serologic methods are important, cooperative, approaches to the identification of clinically important pathogens. Interpretation of culture results depends upon the source of the specimen. From sites that are normally sterile, any isolated organism is significant. From sites colonised by commensal flora, isolating and identifying the pathogen can be more difficult. Good communication between the clinician and the microbiologists is extremely important.

1.2.8 Microbiological investigations of respiratory tract specimens

Lower respiratory tract infections (LRTI) are a very common cause of illness, representing a high proportion of consultations with GPs and also hospital admissions (NICE 2008). The following illnesses are different types of LRTI: pneumonia, including community acquired pneumonia (CAP), hospital acquired pneumonia (HAP), bronchitis and exacerbation of chronic obstructive pulmonary disease (ECOPD).

Pneumonia remains a major cause of death worldwide and the sixth most common in the United Stated of America. The one year mortality rates may be as high as 40% in patients who have been admitted to the hospital with CAP (Niederman 2009, Johansson et al. 2010). The median overall mortality is approximately 14%. In hospitalised patients mortality is as high as 30% (Fine et al. 1996). The population of patients above 65 years of age is increasing in the developed countries and CAP in this population, requiring hospitalisation, has an incidence of 1012 cases per 100,000 persons (Marston et al. 1997).

The facts about the burden of respiratory diseases, including respiratory tract infections in the UK are stark. A report from the British Thoracic Society in 2006 stated that the respiratory disease now kills one in five people in the UK as indicated in Figure 1.4 (British Thoracic Society 2006). CAP is a common cause of morbidity and mortality in the United Kingdom (British Thoracic Society 2006). Admissions relating to CAP accounted for 1.2 million bed days in 2004-2005 and CAP was identified as the cause of death in 34,000 people in 2004 (29% of all respiratory deaths) (British Thoracic Society 2006).

The report also shows that the treatment and investigations of respiratory disease costs the NHS £6.6 billion in 2004: 49% (£3.0 billion) inpatient care costs, 33% (£1.9 billion) in medication costs, 17% (£1.7 billion) in primary care costs and 1% in day cases costs. The cost of respiratory diseases is more than the running cost of the whole NHS pathology services, including clinical microbiology, which was £5.2 billion as reported by Lord Carter in 2006 (Lord Carter of Coles 2006.).

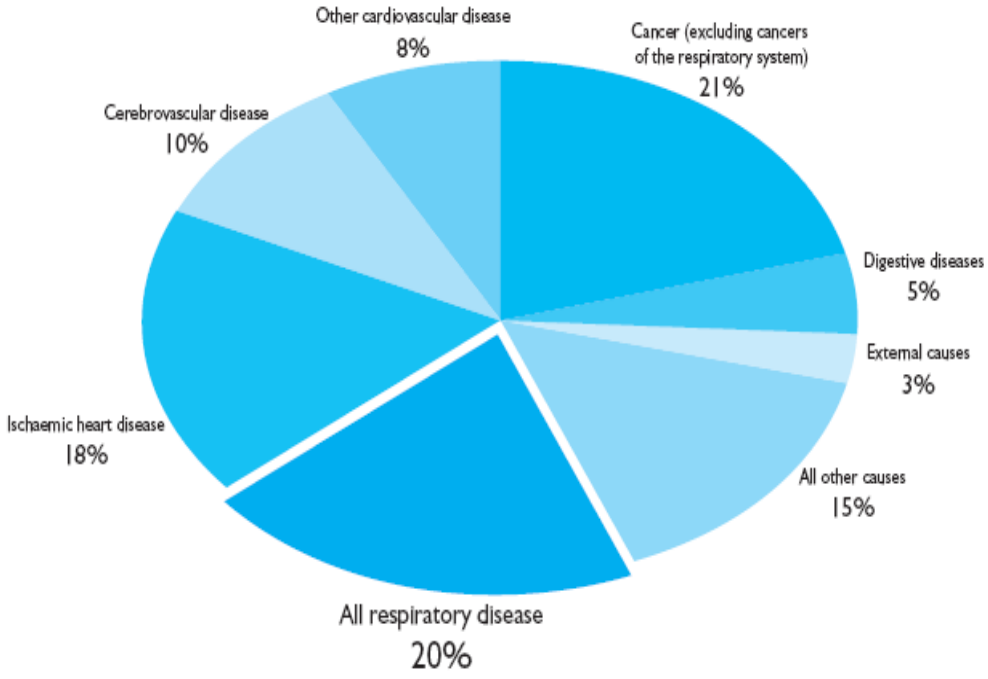

Figure 1.4: Deaths by cause in the United Kingdom

Both in primary care and in hospitals, doctors frequently use antibiotics to treat LRTI. Antibiotics are the appropriate therapy when the cause of LRTI is pathogenic bacteria, but are unhelpful when the LRTI has a viral or fungal origin (Bartlett 2010). It is estimated that most LRTIs do not have a bacterial origin and that antibiotics are over used (Bartlett 2010). Antibiotics frequently cause side effects including nausea, vomiting, diarrhoea and skin rashes. Also, the over use of antibiotics has been linked to the emergence of bacterial strains that are resistant to standard antibiotic therapy, and which cause infections that are difficulty to treat.

Patients admitted to hospitals with suspected LRTI undergo clinical examination and a series of investigations which may include:

- Sputum culture – to detect bacteria.
- Blood culture – to detect bacteria.
- Chest X-Ray.
- Standard blood tests, including arterial blood gases.
- Blood tests for biomarkers of inflammation or infection e.g. C-reactive protein.
- Urine test for legionella antigen.
- Nose/throat swabs to detect viral infection.

The aims of the medical investigations are to differentiate LRTI from other chest illness (e.g. pulmonary embolism), identify the LRTI subtype (bronchitis, ECOPD or pneumonia), to guide the correct therapy and possible pathogens (Table 1.6).

Table 1.6: Most common pathogens implicated in LRTI [a]

Disease and pathogen	Percentage of cases (%)
Acute bronchitis	
Respiratory viruses[b]	90
Bordetella pertussis & Bordetella parapertussis	5–10[c]
Mycoplasma pneumoniae	5–10[c]
Chlamydia pneumoniae	5–10[c]
Community-acquired pneumonia	
Streptococcus pneumoniae	66
Haemophilus influenzae	1–12
Legionella species	2–15
Mycoplasma pneumoniae	2–14
Klebsiella species	3–14
Enteric gram-negative bacilli	6–9
Staphylococcus aureus	3–14
Chlamydia species	5–15
Influenza virus	5–12
Hantaviruses	1–2
Other viruses	1–12
Mycobacterium tuberculosis	1–10
Moraxella catarrhalis	1–2
Unknown	23–49
Hospital-acquired pneumonia	
Gram-negative bacilli	
Pseudomonas aeruginosa	16
Enterobacter species	11
Klebsiella pneumoniae	7
Other enteric gram-negative bacilli	9
Acinetobacter	3
Legionella species	0–2
Haemophilus influenzae	0–2
Other	0–10
Gram-positive cocci	
Staphylococcus aureus	17
Streptococcus pneumoniae	2–20
Other	2–5
Anaerobes	10–20
Fungi	0–10
Mixed	13–54

a The information in this table is compiled from reference (Carroll 2002).

b Influenza A virus, Influenza B virus, parainfluenza virus type 3, respiratory syncytial virus, coronavirus, adenovirus, and rhinovirus.

c The values represent the collective contribution of all four pathogens listed.

For the above stated reasons, early diagnosis of the organism causing CAP should ensure that appropriate and specific antibiotic treatment is instituted, potentially reducing cost and antibiotic related events such as *Clostridium difficile* enteritis, and for Legionella infection, allowing relevant public health measures to be taken.

Diagnosis of LRTIs is frequently complicated by the contamination of specimens with upper respiratory secretions during specimen collection. As the upper respiratory tract may be colonised with potential pathogens (potential respiratory pathogens) not involved in the infection of the lower tract, and may yeild organisms capable of inhibiting the bacteria involved in lower tract pathology, this is the main challenge for the microbiology laboratory to ensure that an appropriate specimen is processed.

Sputum is the most common lower respiratory tract specimen received by the microbiology laboratory. It is also often the most problematic to assess due to contamination by oropharyngeal flora (Sharp et al. 2004, Loens et al. 2009). Other problems include difficulty in interpretation due to contamination of the sample by upper respiratory tract flora, which may include potential pathogens such as *Streptococcus pneumoniae* and coliforms (especially in patients already given antibiotics).

From the above stated short accounts and figures, it is clear that infections of the respiratory tract represent a significant proportion of all healthcare associated infections and a firm diagnosis of pneumonia and other LRTIs is not easy to make and it is even more difficult to establish its microbial aetiology. This is the reason it has been selected as a respiratory tract specimen for this study.

The role of diagnostic microbiology tests is based on the level of evidence and degree of the grading guideline recommendations based on the strength of the evidence gathered, using a three-tier scale (Table 1.7). The grading used in this review is from the updated guidelines of the Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) consensus guidelines on the management of CAP in adults released in 2007 (Mandell et al. 2007). The British Thoracic Society (BTS) guidelines in 2001(Macfarlane et al. 2001)and BTS updated version in 2004 (Macfarlane and Boldy 2004) also used a similar grading system in the last BTS update in 2009 (Lim et al. 2009).

These guidelines suggest that patients with LRTI should be investigated for specific pathogens that would significantly alter standard (empirical) management decisions, when the presence of such pathogens is suspected based on clinical and epidemiologic clues (strong recommendation; level II evidence).

Table 1.7: Levels of evidence [a]

Evidence level	Definition
Level I (high)	Evidence from well-conducted, randomized controlled trials.
Level II (moderate)	Evidence from well-designed, controlled trials without randomization (including cohort, patient series, and case-control studies). Level II studies also include any large case series in which systematic analysis of disease patterns and/or microbial aetiology was conducted, as well as reports of data on new therapies that were not collected in a randomized fashion.
Level III (low)	Evidence from case studies and expert opinion. In some instances, therapy recommendations come from antibiotic susceptibility data without clinical observations.

[a] Level of evidence simplified from IDSA/ATS guidelines in 2007 (Mandell et al. 2007)

The British Thoracic Society (BTS) Guidelines for the Management of Community Acquired Pneumonia in adults-2004 update and new guidelines in 2009 specifies a rationale for microbiological investigation in CAP as well as more specific guidance about particular investigations (Macfarlane and Boldy 2004, Lim et al. 2009), based on published evidence since the previous guidelines in 2001 (Macfarlane et al. 2001). The microbiological investigations that are recommended for patients with CAP are summarised in Table 1.8.

Table 1.8: Recommendations for microbiological investigation of CAP [a]

Pneumonia severity	Treatment site	Preferred microbiological tests
Low severity	Home	None routinely
Low severity	Hospital	None routinely
Moderate severity	Hospital	• Blood cultures • Sputum for routine culture and sensitivity tests for those who have *not* received prior antibiotics (± Gram stain) • Pneumococcal urine antigen test • Pleural fluid, if present, for MC & S and PAT • PCR or serological investigations For mycoplasma and respiratory virus • Where legionella is suspected: (a) Urine for legionella antigen (b) Sputum or other respiratory sample for legionella culture and direct immunofluorescence (if available).
High severity	Hospital	• Blood cultures (minimum 20 ml) • Sputum or other respiratory sample for routine culture and sensitivity tests (± Gram stain) • Pleural fluid, if present, for MC & S and PAT • Pneumococcal urine antigen test • Investigations for legionella pneumonia: (a) Urine for legionella antigen (b) Sputum or other respiratory sample for legionella culture and direct immunofluorescence (if available) • Investigations for atypical and viral pathogens:

[a] This table simplified from BTS guidelines update in 2009 (Lim et al. 2009)

In summary, it suggests that for patients with non-severe CAP routine microbiological tests may not always be needed, particularly for patients with no co-morbid illness. It suggests collection of a sputum sample in patients with moderate severity CAP who are freely expectorating and in patients with severe or high

severity CAP, it suggests that a “full range of microbiological investigations should be performed”, including sputum Gram stain, culture and blood culture as explained in Table 1.8.

However, the microbiological diagnosis of pneumonia is hampered by sputum cultures, which may yield unreliable microbial aetiologies of pneumonia (Broughton et al. 1991, Reed et al. 1996). In addition culture results are available after 48 hours and techniques of rapid diagnosis, such as PCR, are not sufficiently accurate and not available in every place (Ieven and Goossens 1997). Furthermore, reliable methods as bronchoscopic protected specimen brush and bronchoalveolar lavage cannot be used in everyday practice, and are not available in every hospital (Broughton et al. 1991).

For the microbiological investigation of lower respiratory tract infections there are a number of specimen types, corresponding to the various inflamed areas of the lower respiratory tract that may be submitted for microbiological analysis. These samples may be obtained non-invasively or by an invasive bronchoscopic or transthoracic procedure. The most common respiratory specimen received in the microbiology laboratory is sputum, expectorated or induced and blood culture samples from mainly hospitalised patients. Other types of specimens included in this category are tracheal aspirates, transtracheal aspirates, bronchial washes, bronchial brushings, and bronchoalveolar lavage fluids.

In addition, for specific bronchial pathogens, it may be appropriate to submit upper respiratory samples (e.g., throat or nasopharyngeal) for detection of the suspect agent. For a select group of infectious agents, urine may be submitted for the diagnosis of *Legionella pneumophila* infections and pneumococcal antigen testing, and in a few situations, serum may be collected to establish a retrospective diagnosis using serologic testing.

Sputum microbiological investigation is requested to establish the microbial cause of lower respiratory tract infections, particularly pneumonia and, as mentioned before, therefore is useful for several reasons:

(1) Identification of respiratory pathogens and antibiotic sensitivity patterns to select of optimal antibiotic regiments to treat patients with pneumonia.

(2) Targeted and narrow spectrum antibiotic therapy limits drug costs and the threat of antibiotic resistance and adverse drug reactions such as *C difficile* associated diarrhoea.
(3) Isolation of specific pathogens has public health or infection control significance, including legionella and penicillin resistant *Streptococcus pneumoniae* etc.
(4) Microbiological investigations allow monitoring of the spectrum of pathogens causing community acquired pneumonia and other lower respiratory tract infections over time. This allows trends regarding aetiology and antibiotic sensitivity to be tracked for public health needs.

However, the yield of sputum bacterial cultures is variable and strongly influenced by the quality of the entire process, including specimen collection, transport, rapid processing, satisfactory use of cytological criteria, absence of prior antibiotic therapy, and skill in interpretation. The yield of *S. pneumoniae,* for example, was only 40%–50% from sputum cultures from patients with bacteraemic pneumococcal pneumonia in studies performed a few decades ago (Barrett-Connor 1971, Lentino and Lucks 1987). A study of 100 cases of bacteraemic pneumococcal pneumonia found that sputum specimens were not submitted in 31% of cases and were judged as inadequate in another 16% of cases (Musher, Montoya and Wanahita 2004). When patients receiving antibiotics for > 24 hours were excluded, the Gram stain showed pneumococci in 63% of sputum specimens, and culture results were positive in 86%. For patients who had received no antibiotics, the Gram stain was read as being consistent with pneumococci in 80% of cases, and sputum culture results were positive in 93%.

Collecting good quality sputum samples is always a challenge. Given the number of variables involved, samples often arrive inadequately labelled, leaking or overgrown with contaminating bacteria.

1.2.9 Assessment of sputum quality as diagnostic tool

Sputum quality is important for the microbiological diagnosis and treatment of the LRTI and the reliability of sputum culture results depend on the quality of the specimens (Sharp et al. 2004, Loens et al. 2009, Campbell and Forbes 2011). Sputum examination is a simple and rapid diagnostic tool for the presumptive identification of pathogens and may be the oldest and most entrenched techniques

still in use in the microbiology laboratory. However, the usefulness of sputum examination such as Gram stain and culture in the initial approach to a patient with CAP is still controversial. While several authors have outlined important limitations of this tool in terms sensitivity, reliability, and impact on treatment decisions (Woodhead et al. 1991, Bates et al. 1992, Theerthakarai et al. 2001, Ewig et al. 2002, García-Vázquez et al. 2004), others consider sputum examination useful in the initial evaluation of patients with CAP (Boerner and Zwadyk 1982, Gleckman et al. 1988, Rosón et al. 2000, Kuijper et al. 2003, Musher et al. 2004).

Recent trends that favour a diminishing role for diagnostic testing in management algorithms and all the attendant controversies are well reflected in two major consensus guidelines. The infectious Disease Society of America (IDSA)/American Thoracic Society (ATS) consensus guidelines encourage that an expectorated sputum sample for Gram stain and culture should be obtained from hospitalised patients with clinical indications such as intensive care unit admissions, failure of outpatient antibiotic therapy, cavitary infiltrates, etc, but are optional for patients without these conditions (Mandell et al. 2007).

Sputum culture may identify the causative agent in CAP including unexpected or antibiotic resistant pathogens such as Staphylococcus aureus or antimicrobial resistant *Streptococcus pneumococci*. Routine sputum cultures are, however, neither very sensitive nor specific (Bartlett et al. 2000) and often do not contribute to initial patient management (Taylor et al. 1999). Problems include:

- The inability of patients to produce good specimens.
- Prior exposure to antibiotics.
- Delays in transport and processing.
- Difficulty in interpretation due to contamination of the sample by upper respiratory tract flora, which may include potential pathogens such as *S. pneumoniae* and “coliforms” (especially in patients already given antibiotics) as stated previously.

Traditionally, a Gram stain done on a valid expectorated sputum specimen has served as a guide for initial selection of antimicrobial therapy for patients with bacterial pneumonia (Boerner and Zwadyk 1982). There are a number of reasons why Gram stain testing is widely accepted, such as:

- Readily available, inexpensive and entails no risk to the patient.
- Does not require sophisticated equipment.
- Evaluation is completed within a few minutes.
- Provides valuable diagnostic and prognostic information (Ieven and Goossens 1997).

Controversy exists in the medical literature regarding the reliability of sputum Gram stain to guide initial antimicrobial treatment of CAP (Hahn and Beaty 1970, Ries, Levison and Kaye 1974, Flatauer, Chabalko and Wolinsky 1980, Boerner and Zwadyk 1982, Kalin et al. 1983). These studies however, have used sputum culture as reference standard. In two studies as reference standard was used blood culture, but only for *S. pneumoniae* (Gleckman et al. 1988, Musher et al. 2004). There are many factors which need to be borne in mind when considering the reliability and usefulness of Gram stain results. These are summarised below:

- Strict criteria for interpretation require appropriate operator training
- Validity of results is directly related to the experience of the interpreter (Fine et al. 1991)
- Sputum Gram stains correlate poorly with culture results in conditions other than CAP (Croce et al. 1998). This poses practical difficulties for laboratories that frequently have to interpret results with little or no clinical information
- Lack of availability: a survey of diagnostic microbiology laboratories in England and Wales (Roberts et al. 2008) revealed that, of 138 respondents, 53 laboratories (38%) do not provide a sputum Gram stain service at all and, of the remainder, 52 laboratories (38%) do so only on special request. Thus, ready availability of sputum Gram stain cannot be assumed. This lack of availability reflects the opinion of many microbiologists that sputum examination is rarely helpful in the diagnosis of CAP.

These studies support that performance of routine and reporting of sputum Gram stain on all patients is unnecessary, but can aid the laboratory interpretations of culture results. However, microscopic examinations using Gram stain may be useful for the assessment of quality of sputum samples (cytological content) with rejection of poor quality samples and it can also aid the interpretation of culture results and occasionally give an early indication of possible aetiology as shown in

Figure 1.5 The Gram stain (x1000) in this figure is an example of inadequate sputum specimen. It shows squamous epithelial cells, absence of inflammatory cells, and mixed bacterial flora, primarily consisting of Gram-positive organisms of multiple morphologies (including cocci in pairs, chains, and clusters) as well as Gram-negative rods and cocci.

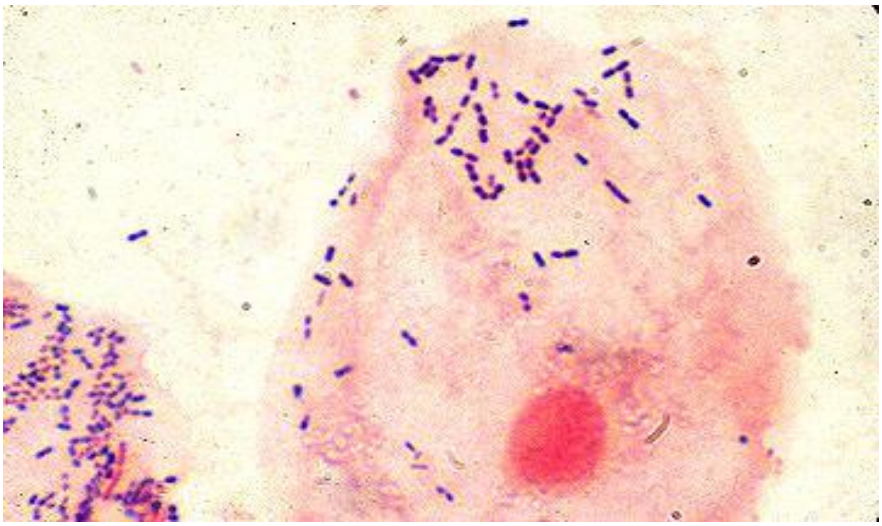

Figure 1.5: Sputum Gram staining from poor quality specimen

Determining the quality of the specimen is based on the numbers of polymorphonuclear leucocytes and squamous epithelial cells (SECs) present: purulent specimens may be selected for culture and non-purulent specimens or specimens contaminated with squamous epithelial cells may be rejected. A number of authors based rejection of sputum on an absolute number of SECs and/or leucocytes per field (Isenberg 2004, Sharp et al. 2004). Others based their rejection criteria on leucocyte/SEC ratio (Sharp et al. 2004). The advantage of using a ratio is that it compensates for the possibility of uneven distribution of cells in the smear. The microbiology laboratory automatically rejects sputum specimens such as this one shown in Figure 1.6. This Gram staining indicates poor quality sputum specimen full of squamous epithelial cells.

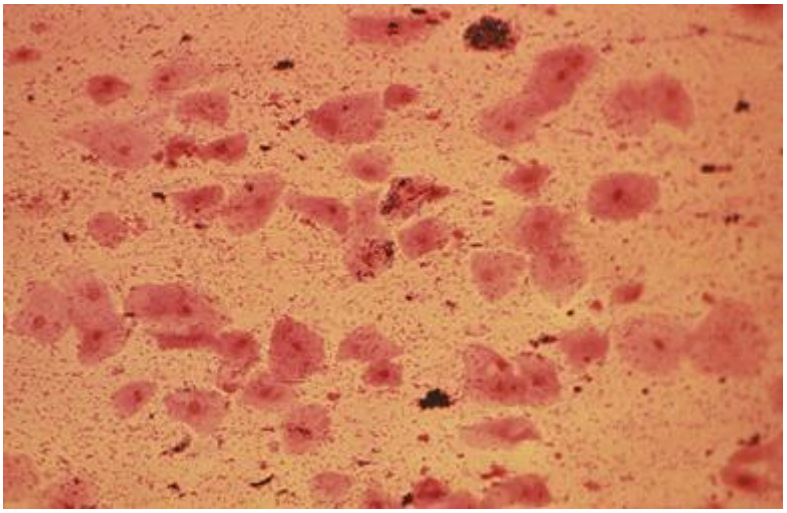

Figure 1.6: Gram staining of sputum with squamous epithelial cells

However, a useful guide to the quality of a sputum specimen can be obtained by its macroscopic appearance. Few studies have examined the relationship between macroscopic cues and specimen quality. Since 1974 no empiric studies related sputum specimen quality to macroscopic appearance. A quality of most expectorated sputum can be predicted from their appearance, this fact has not been emphasised in the literature.

For the macroscopic examination of an expectorated sputum sample is often sufficient to indicate whether it is primarily sputum or entirely or predominantly saliva. Sputum is customarily described macroscopically as mucoid (mostly mucus), mucopurulent (green looking with pus and mucus) or purulent (green looking, mostly pus), mucosalivary (mucus with a small amount of saliva) whilst the presence of frank or altered blood provides additional valuable information as described in Appendix 1.2.

The close macroscopic examination of sputum physical or gross appearance shows the presence of saliva, mucoid, blood and pus as detected with the naked eye. The other sputum macroscopic appearance includes the fleck, blood, and amount of froth or bubbles. The sputum consistency is described according to its physical factors of watery, mucoid, mucopurulent and purulent.

Salivary samples are watery expectorated sputum specimen with heavy froth and bubbles. On microscopic examination they show predominance of epithelial cells and on Gram stain a variety of micro-organisms typical of the normal oropharngeal

bacterial flora. This contrasts with the appearance of good quality sputum samples from a patient with pneumococcal pneumonia where the Gram stain provides valuable information on the presence of pus cells, and typical staining appearance of pneumococci as shown in Figure 1.7. The Gram stain in this figure shows abundant inflammatory cells and Gram-positive diplococci which are *Streptococcus pneumoniae* and this is an example of good quality sputum specimen.

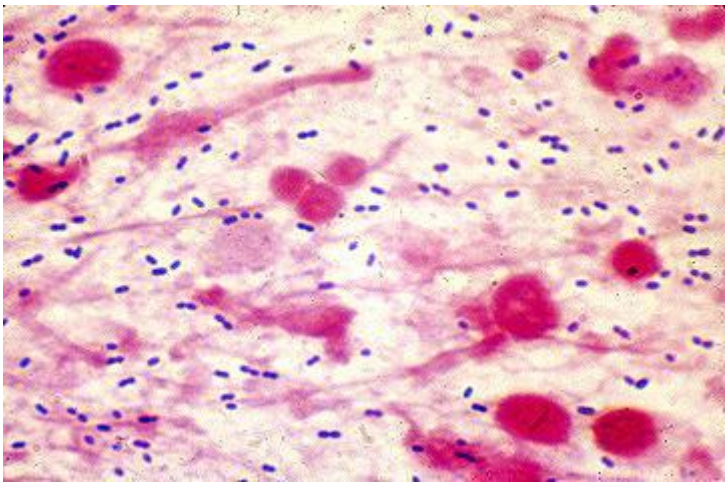

Figure 1.7: Gram staining of sputum from good quality specimen

Some microbiology laboratories will discard sputum specimens which are mucoid on naked eye examination, but this may be unreliable and those for examination for mycobacteria should be processed. Most laboratories discard specimen which appear to be only saliva and request a further sample. There is great variation in the method of processing sputum and, because there is no clear consensus. Based on the macroscopic and microscopic evaluation of sputum specimen, there is no reason to culture spit. The sender should be notified to recollect an appropriate specimen and this needs timely communication. The culture plate in Figure 1.8 is an example of culture of expectorated sputum showing different colonial morphologies on blood agar, which represents mixed flora; this result is common, even in the absence of a bacterial lower tract respiratory infection.

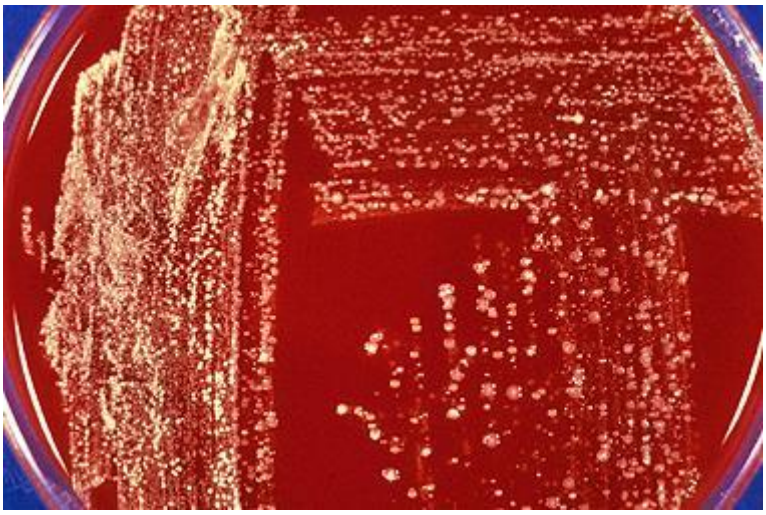

Figure 1.8: Sputum culture showing growth of mixed flora on blood agar

In addition to sputum quality assessment, sputum culture and sensitivity, many clinical microbiology laboratories do not pass judgment on the significance of isolates from patients specimens and instead report to clinicians all of their microbiologic findings. This policy leaves the responsibility for interpretation in the hands of the physicians. One of the important functions that a microbiologist performs is to decide what is clinically relevant regarding specimen work up, what organisms to look for and report, what organisms are pathogenic, what constitutes normal flora. Inadequate reporting may lead to unnecessary action, reporting without a comment may lead to inappropriate antimicrobial therapy. Therefore, sputum culture results should be interpreted based upon the quality of the specimen, quantisation of growth (light, moderate, or heavy), clinical correlation and if possible correlation with the Gram stain.

The sputum normal results from a healthy person would have no growth on culture. A mixture of microorganisms, however, normally found in a person's mouth and saliva, often contaminates the culture. If these micro-organisms grow in the culture, they may be reported as normal flora contamination. The normal respiratory tract flora includes Coagulase-negative staphylococci, Micrococcus species, *a* Diptheroids, Non-pathogenic Neisseria species, Alpha-haemolytic Streptococcus species, Non-haemolytic Streptococcus *species.*

From these accounts and reviews, the proper management of respiratory tract specimens is important for microbiological testing to inform the diagnosis as bacterial and indicate the key pathogen in the respiratory tract infections so that therapy can be pathogen directed, when possible, because of the public health benefit of making a specific diagnosis that allows recognition of epidemiologically important pathogens, contact tracing, and more rational use of antibiotics, and to promote further development of knowledge base producing guidelines and improving diagnosis of respiratory tract infections. In light of these accounts, this study was aimed to assess the appropriateness of microbiological test utilisation based on sputum culture.

1.3 Aims and objectives of the study

The overall main aim of this study was to determine the appropriateness of clinical microbiology test utilisation, evaluate the clinical relevance, cost-effectiveness, and hence recommend better utilisation strategies. The following steps were used:

1. To assess the appropriateness of microbiology test requests and determine the proportion of tests that are appropriate and identify ways to eliminate unnecessary and inappropriate test requisitions in routine microbiology.

2. To evaluate the quality of sputum specimens and processing practices to identify those unsuitable for microbiological testing by assessing the sample acceptance/rejection/processing criteria.

3. Review the actual test results (negative and positive) and organisms detected and compare with the clinical profile of the patient's and available evidence base for the actual process.

4. To assess the reporting of microbiology results by evaluating the final report with reference to clinical relevance, appropriateness and service user's to interpret the results.

5. Determine the total cost of microbiology investigations and determine the cost of unnecessary tests to develop improved guidelines for working up of clinical specimens for microbiology testing.

Chapter 2 Methodology

2.1 Introduction

The present study was undertaken to evaluate the process of microbiology specimen management in order to assess microbiology test utilisation and the appropriateness of test ordering. From this work it was hoped to estimate the prevalence of inappropriate laboratory utilisation and identify the proportion of inappropriate tests. A systematic review of laboratory tests used showed up to 46% of ordered microbiology tests were inappropriate and unnecessary, as shown in the previous Table 1.1 (van Walraven and Naylor 1998). The current study investigated in more detail the inappropriateness of microbiology tests, particularly respiratory tract specimens using sputum microbiology as model for the microbiology service utilisation.

The aim of the sputum study was to investigate the quality of sputum specimens, appropriateness of test requisition, adherence to specimen collection principles and laboratory compliance with the standard operative procedures (SOP).

2.2 Ethical issues

Ethical approval was obtained from the Bart's and The London NHS Trust (BLT) Ethical Committee for the data collection phase of the study, which involved the retrospective collection of data from patients microbiology laboratory request forms and computer records during the study periods. The letter from the Ethical Committee is attached in the appendix section of the thesis (Appendix 2.1).

2.3 Hospital setting and study design

This study was conducted at the Microbiology Department of the Barts and The London NHS Trust, which comprises the three hospitals of St. Bartholomew's, The Royal London and London Chest Hospital. BLT hospitals are tertiary care and teaching hospitals as well as referral centres with a total number of 1,172 beds (at the time this study was started) offering all modern medical specialties. This Trust provides a service to a catchment area population of over 2.5 million people from the City of London, East London and further afield. The total number of patients

attending every year is more than 766,844. This consists of 97,329 inpatients, 507,599 outpatients, and 161,916 accident and emergency patients. The Trust data updates were obtained from BLT annual review 2005/06 at hospital web site (www.bartsandthelondon.nhs.uk).

Similarly, the BLT Microbiology Department provides comprehensive diagnostic services to the hospitals within the Trust described above, as well as General Practice, Community and Newham Healthcare NHS Trust hospitals and community practice. Laboratory services are extensive and the microbiology laboratory processes over 436,000 microbiological specimens per year. The annual workload of respiratory tract specimens is more than 20,000, approximately 5% of the total, of which the number of sputum specimens is 9,566 (60%) and make up the largest fraction.

The study retrospectively reviewed the microbiology laboratory request forms and computer records from the microbiology laboratory using standardised data collection forms. The research plan of the study proceeded in different phases and was conducted in three phases as described below.

During the first phase (Phase 1), the study initially screened and evaluated the total number of respiratory tract specimens that have been requested for microbiological examination. Respiratory specimens were drawn anonymously from all patients in which respiratory bacteriology culture were requested in one calendar year (2004) that were sent to the microbiology laboratory for microbiological examination. The aim of this phase was to evaluate the usefulness of routine microbiological investigations for respiratory tract specimens and to assess it according to relevance of organisms reported during the actual test results.

During the second phase (Phase 2), the study conducted in-depth analysis and detailed microbiological evaluation of representative respiratory tract specimens. Respiratory specimens were drawn from samples processed and cultured from March 12, to May 31, 2004 (three months). There were two aims in phase: 1. To review specimen-processing practices and criteria of specimen acceptability based on local standards (as described in the microbiology procedure manual of BLT microbiology department), national and internationally established guidelines and other available evidence-based practice. 2. To assess and evaluate clinicians/users

adherence to hospital microbiology laboratory guidelines and British Thoracic Society recommendations for microbiological investigation.

During the third phase (Phase 3), the study conducted post evaluation and follow up of representative respiratory tract specimens. Respiratory specimens were drawn from samples processed and cultured from July 9, to July 18, 2006 (two weeks). The aim of this phase was to evaluate and follow up the impact of departmental policy changes due to rationalisation of the microbiology service and the outcome of this study based on the results obtained during Phase 1 and Phase 2.

2.4 Inclusion and exclusion criteria

All the respiratory tract specimens requested for routine microbiological examination were included and assessed for their microbiological test appropriateness. These specimens were BAL, ear swab, ETT, mouth swab, nose swab, NPA, sputum, throat swab, tongue swab and tracheal aspirate. These specimens were selected to assure that the inclusion of specimens with the most commonly encountered in the diagnostic microbiology laboratory. Fifteen thousand and nine hundred and forty one respiratory tract specimens were studied during the period of this study. The respiratory tract specimens requested for AFB tests and samples for cystic fibrosis microbiological investigations were excluded and were not included in the present study.

2.5 Data sources and specimen types

The respiratory tract specimens were collected from various patients attending or treated BLT hospitals and Newham NHS Trust. The total respiratory tract workload activity in 2004-2005 was 18,915 (Barts and The London NHS Trust 2005, National Pathology Benchmarking Review 2005). 15,941 (84.3%) of the total workload was randomly selected for this study due to time consumed of the data accessibility**.** Table 2.1 provides a breakdown of the sources and the type of the respiratory tract specimens. The majority of the requests originated from BLT inpatients, followed by GP patients and were mainly sputum specimens followed by throat swab specimens.

Table 2.1: Sources and types of respiratory specimens in Phase 1

Specimen /Sources	AE	CL	GP	IP	OP	UNK	Total	(%)
BAL	1	59	0	43	4	0	107	0.7
Ear swab	85	319	746	152	88	3	1,393	8.7
ETT	0	0	0	425	6	0	431	2.7
Mouth swab	8	36	70	39	9	1	163	1.0
Nose swab	2	51	74	242	41	0	410	2.6
NPA	4	0	3	204	0	0	211	1.3
Sputum	198	538	655	7349	817	12	9566	60.0
Throat swab	640	194	1260	854	585	16	3549	22.3
Tongue swab	2	11	31	14	2	0	30	0.4
Tracheal aspirate	2	1	1	44	3	0	51	0.3
Total	942	1206	2840	9366	1555	32	15941	100.0
Percentage	5.9	7.5	17.8	58.7	9.7	0.20	15941	100.0

AE: accident & emergency, CL: chest/specialist clinics, GP: general practice, IP: inpatients, OP: outpatients and UNK: unknown.

During Phase 2 of the study period, of the 700 representative respiratory cultures that were studied in detail, 460 (65.7%) were obtained from inpatients, 113 (16.1%) outpatients, 89 (12.7%) GP patients, 21 (3.0%) accident & emergency department and 17 (2.4%) specialists' clinics as shown in Table 2.2.

Over the three month study period, out of 700 specimens, 511 (73.0%) were sputum specimens, 100 (14.3%) throat swabs, 63 (9.0%) ear swabs, 12 (1.7%) bronchial washings and there were smaller number of mouth swabs (6), nose swab (5) and few other respiratory specimens as shown in Table 2.2.

Table 2.2: Sources and types of respiratory specimens in Phase 2

Specimen /Sources	AE	CL	GP	IP	OP	UNK	Total	(%)
BAL	0	8	0	4	0	0	12	1.71
Ear swab	0	0	23	6	34	0	63	9.0
Mouth swab	0	0	1	2	3	0	6	0.86
Nose swab	0	0	1	2	2	0	5	0.71
NPA	0	0	0	1	0	0	1	0.14
Sputum	2	7	9	427	66	0	511	73.00
Throat swab	19	2	55	16	8	0	100	14.29
Tongue swab	0	0	0	1	0	0	1	0.14
Tracheal aspirate	0	0	0	1	0	0	1	0.14
Total	21	17	89	460	113	0	700	100.00
Percentage	3.00	2.43	12.71	65.71	16.14	0	700	100.00

During Phase 3 of the study period, 133 respiratory cultures followed up over a two week period, 119 (89.5) were sputum samples, 11 (8.3%) throat swabs and there were smaller number of mouth swab (2) and ETT (1) specimens as shown in Table 2.3. 76.7% of the total specimens were from inpatients, 9.0% were from GP's and followed by 7.5% from specialist clinics.

Table 2.3: Sources and types of respiratory specimens in Phase 3

Specimen /Sources	AE	CL	GP	IP	OP	UNK	Total	(%)
Sputum	2	8	6	99	3	1	119	89.47
Throat swab	3	2	5	1	0	0	11	8.27
Mouth swab	0	0	1	1	0	0	2	1.5
ETT	0	0	0	1	0	0	1	0.75
Total	5	10	12	102	3	1	133	100.00
Percentage	3.76	7.52	9.02	76.69	2.26	0.75	133	100.00

2.6 Data collection

In order to assess the microbiology test utilisation and appropriateness of the test ordering, suitable data collection kits were developed and structured in an appropriate format to review and evaluate the test utilisation practices and total testing processing as shown in Appendix 2.2. As stated before, data was collected from the laboratory request forms and computer reports using developed data collection tool designed to capture all relevant information.

The major data elements collected included patient's demographic details, microbiological test requisition of respiratory samples for M, C & S, patient's clinical diagnosis, site of infection, quality of processed specimens based on macroscopic inspection, age of the specimens when received in the laboratory, whether patients were on antibiotic treatment, culture results (negative or positive), whether organisms isolated were pathogens or non-pathogens, TAT, final report issued and the interpretation of results.

2.7 Data evaluation

At arrival in the microbiology laboratory a biomedical scientist examines the quality of sputum specimen and decides if it is acceptable or unacceptable to process.

Combining the data from request forms and the data from the microbiology result report review allowed the data evaluation and assessment for the appropriateness of microbiology test utilisations. Microbiology test ordering was evaluated and judged to be justified (appropriate) if its request was in accordance with the clinical episode and widely accepted disease management guidelines and reviews published in reliable, peer-reviewed and indexed journals as described below. The specimen collection, handling and transport were evaluated per individual request.

The criteria used for the assessing and determination of appropriateness of microbiological test requests and the appropriateness of sputum microbiological investigation is based on the criteria recommended by the British Thoracic Society guidelines in 2001, updated version in 2004 and 2009 guidelines as described in section 1.2.8 in the review of literature. The second criteria used were the BLT guidelines prepared by the respiratory and medical microbiology departments in 2003. The BLT guidelines provide a rational approach to the microbiological investigation of respiratory specimen and it is attached in the appendix section (Appendix 2.3).

In addition to these UK-based guidelines, other guidelines were taken into account. These included the other internationally recommended guidelines, including the recently updated guidelines of the Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) released in September 2007 (Mandell et al. 2007) and European Respiratory Societies (ERS) in 2005 (Woodhead et al. 2005) as explained in section 1.2.8 in the review of literature. The overall means of evaluation criteria based on the guidelines for microbiology laboratory testing (Murray 1999) and UK national guidelines as stated previously. Finally, the following key criteria have been used in this study which were based on the above stated guidelines, and recommendations.

1. Type of microbiology test ordering or requisition for example routine bacteriology for culture and sensitivity (C & S), TB investigation, fungi investigation and cystic fibrosis microbiology.
2. An accurate clinical detail to accompany any request for microbiological investigation since this determines the choice and conduct of laboratory tests.
3. Previous antibiotic exposure or therapy.
4. Quality of the sputum sample and contamination by normal oropharyngeal flora.
5. Delays in specimen transportation and age of the specimen.

In addition to these criteria, the study investigator used other criteria to investigate the clinical relevance, cost-effectiveness of clinical microbiology and appropriateness of microbiology test results using respiratory tract specimens as a model. These criteria are the following:

1. Microbiology laboratory findings and cultures.
2. Reporting of microbiology test results and final reporting appropriateness.
3. Interpretation of actual test results and use of interpretative comments.
4. Expected reporting times and test TAT for microbiology tests.

2.8 Data processing and statistical analysis

A Chi-square (X^2) test was used to compare the observed data with data we would expect to obtain according to a specific data analysed. This standard statistical method for categorical variables was used to detect significant differences between factors studied. It tests the null hypothesis that the intervention of Phase 3 of the study had no effect. Associations were considered statistically significant if the P value was < 0.05 which means that the null hypothesis was rejected at the 5% level.

The study investigated the cost implication of inappropriate test utilisation by conducting cost assessment. Microbiology laboratory costs were calculated by estimating the total pay cost/request and total non-pay cost/request of for each microbiology request. The total pay cost/request includes the medical salaries cost, clinical scientist salaries, biomedical scientist's salaries and other staff salaries cost. The total non-pay cost/request includes the cost of supplies, equipment, and overhead charges.

The microbiology laboratory charge fee of each laboratory test was obtained from the hospital finance department pricing list. However, the real microbiology test cost would not be disclosed due to confidentiality issues. For general microbiology test cost analysis, cost data was obtained from The Keele University microbiology benchmarking report (National Pathology Benchmarking Review 2005, National Pathology Benchmarking Review 2006, National Pathology Benchmarking Review 2007, National Pathology Benchmarking Review 2008), Lord Carter NHS Pathology Reviews Reports (Lord Carter of Coles 2006, Lord Carter of Coles 2008) and

Healthcare Commission's Report (CQC) in 2007 were used for data analysis where possible.

2.9 Evaluation of microbiological quality indicators

This study used a framework of microbiology quality indicators for the case of lower respiratory tract infection in a microbiology laboratory. The evaluation of microbiology quality indicators was based on the assessments of the key criteria's described in the data evaluation section (2.7) and summarised in Table 2.4. For each key area of the practice, data on a series of quality indicators was collected and defined to evaluate the current practice of microbiological test appropriateness as explained in Table 2.4. The definition of the microbiological quality indicators were described in the definition section (2.10).

2.10 Definition of microbiological quality indicators

Microbiological test utilisation and quality indicators results were described as "appropriate" if they were diagnostic or supportive of clinical diagnosis, a useful negative, or used in monitoring of treatment or disease progress.

1. Test requisition: The microbiology tests requisition form has been completed and provided all relevant details by the user and particularly stated the required microbiology test including the test name or name of test requested, for example C & S. The test requisition was considered as an appropriate microbiological test requisition.

2. Clinical diagnosis*:* Similarly, if the microbiology tests requisition form was completed and provided all relevant details by the user and particularly stated the patient's working clinical diagnosis and clinical indications for the pre-test probability of the condition being sought to indicate that a test result would be abnormal or positive. The test requisition was considered as appropriate microbiological test requisition.

3. **Antibiotic use**: The microbiology tests requisition form was completed and provided all relevant details by the user and particularly stated the patient's

previous antibiotic exposure or antibiotic use. The test requisition was considered as appropriate microbiological test requisition.

4. Quality of the specimen*:* The specimen has good quality with relevant test request and passed microbiology laboratory acceptability criteria, collected, selected appropriately and transported to the microbiology laboratory and received at the right time. The quality of specimen was considered as appropriate microbiological specimen.

5. Specimen age: The specimen has good quality with relevant test request and was collected appropriately, transported to microbiology immediately, and received by the laboratory in a reasonable time to process. The quality of specimen was considered as appropriate microbiological specimen.

6. Test turnaround times: If the turn-around times for each request were decreased and result reported in appropriate time. The TAT is considered appropriate.

7. Reporting results: The laboratory report is precise and clear. The test report is considered appropriate.

8. Result interpretation: The microbiological report has relevant comments and provides appropriate explanation of elements of the report and test to the clinician. The test report is considered appropriate.

Table 2.4: Evaluation of microbiological quality indicators

No	Appropriate quality indicators	Inappropriate process indicators
1	**Test requisition:** The microbiology tests requisition form has been completed and provided all relevant details by the user and the required microbiology test name has been stated, for example C & S.	The microbiological test requisition does not include the name of tests requested on the patients request form. This means, the patient's sample has no test requested.
2	**Clinical diagnosis:** The microbiology tests requisition form was completed and provided all relevant details by the user and the patient's clinical diagnosis and clinical information has been stated, for example pneumonia.	The microbiology test requisition does not include the patient's clinical diagnosis and relevant clinical information on the request form. This means, the patient's clinical diagnosis is unknown.
3	**Antibiotic use:** The microbiology specimen has been collected before the start of the antimicrobial therapy.	The microbiological requisition stated that the patient has been receiving antimicrobial treatment before the specimen collection.
4	**Specimen age**: The microbiology specimen has been transported properly and delivered to the laboratory as soon as possible after its collection.	The microbiological specimen is not transported properly to the laboratory within 24hoursof its collection. This means, the patient's specimen is too old to be processed.
5	**Quality of the specimen:** The microbiology specimen has been selected properly, collected properly and therefore has a good quality.	The macroscopic quality assessment of specimen has found that the sample has poor quality and therefore the specimen is unsuitable for microbiological investigation.
6	**Test turnaround times:** The result of microbiology test has been reported as soon as possible and has a decreased TAT for each request.	The reported microbiological test result has increased test turnaround times of more than 3 days, the reported test results is too late and has a less microbiological significance.
7	**Reporting results**: The microbiology test result has been reported clearly, precisely and in a standardised format in which clinicians able to understand easily.	The laboratory report is not clear, concise, and timeless and lacks clarity; the microbiology report creates confusion and misunderstanding for the clinicians and test users.
8	**Result interpretation:** The reports of microbiological test result has been interpreted with relevant comments which provide an appropriate explanation of the report to clinician.	The microbiological test result does not being properly interpreted for their significance and instead reported to the clinicians in all microbiological findings, the test results is difficult and clinicians could not able to use it.

Chapter 3 Results

3.1 Introduction

During the 12 month retrospective study period, a total of 15,941 respiratory cultures were processed by the microbiology laboratory, and 6,396 respiratory cultures (40.1%) were reported as positive (definition of positive report, see section 3.3). Of these respiratory cultures, 9,566 (60.0%) were sputum specimens, and 3,730 sputum cultures (39.0%) were reported as positive. During the three month period of detailed microbiological evaluation, a total of 700 respiratory specimens were studied, and 221 (31.6%) specimens were one day old and 81 (11.6%) were received after two days of collection. Of these respiratory specimens, 511 (73.0%) were sputum specimens, and a total of 306 (59.9%) of 511 sputum samples were considered to be of poor quality. During the two week period of post evaluation and follow up studies, a total of 133 respiratory samples were studied, and 119 (89.5%) were sputum specimens. Of these sputum samples, a total of 82 (68.1%) of 119 samples was considered of good quality and appropriate for bacteriology culture.

3.2 Evaluations for appropriateness of microbiology test ordering

The analysis of the findings from the microbiological variables studied and information from the microbiology laboratory request forms is based on the microbiology quality indicators criteria described in Section 2.9. The evaluation of respiratory tract specimens for appropriateness of microbiological investigations by the designated quality indicators criteria are summarised in Table 3.1. Similarly, the summaries of the results from the respiratory tract specimens due to inappropriate test ordering practice are presented in Table 3.2. The analysis of these results is based on the detailed microbiological evaluation of representative respiratory specimens during the three month period in Phase 2 of this study.

Table 3.1: Evaluation for appropriateness of microbiology test utilisation

Evaluation criteria	Total RTS n (%)	Sputum n (%)	T/S n %)	E/S n (%)
1. Test request:				
C&S requested:	641 (91)	463 (91)	93 (93)	60 (95)
No test requested:	59 (9)	48 (9)	7 (7)	3 (5)
Total number:	**700**	**511**	**100**	**63**
2. Clinical diagnosis:				
With clinical diagnosis:	660 (94)	479 (94)	97 (97)	60 (95)
Without clinical diagnosis:	40 (6)	32 (6)	3 (3)	3 (5)
Total number:	**700**	**511**	**100**	**63**
3. Antibiotic use:				
With antibiotic treatment:	277 (40)	214 (42)	35 (35)	25 (40)
No antibiotic treatment:	188 (27)	135 (26)	33 (33)	12 (19)
Not stated treatment:	235 (34)	162 (32)	32 (32)	26 (41)
Total number:	**700**	**511**	**100**	**63**
4. Specimen age:				
Same day received:	398 (57)	309 (61)	32 (32)	42 (67)
I day old received:	221 (31)	145 (28)	46 (46)	19 (30)
≥ 2 days old received:	81 (12)	57 (11)	22 (22)	2 (3)
Total number:	**700**	**511**	**100**	**63**
5. Sputum quality:				
Good quality specimen:		205 (40)		
Poor quality specimen:		306 (60)		
Total number:		**511**		
6. TAT:				
< 3 days results reported:	322 (46)	251 (50)	35 (35)	27 (43)
Within 4 days reported:	127 (18)	94 (18)	23 (23)	5 (8)
≥ 5 days results reported:	251 (36)	166 (32)	42 (42)	31 (49)
Total number:	**700**	**511**	**100**	**63**

RTS: Respiratory tract specimen T/S: Throat swab E/S: Ear swab

Table 3.2: Summary of inappropriateness of microbiology test utilisation

Inappropriate test ordering practice due to:	**Total RTS** n (%)	**Sputum** n (%)	**T/S** n (%)	**E/S** n (%)
1. No test requested:	59 (9)	48 (9)	7 (7)	3 (5)
2. No clinical diagnosis:	40 (6)	32 (6)	3 (3)	3 (5)
3. With antibiotic treatment:	277 (40)	214 (42)	35 (35)	25 (40)
4. Prolonged transit time:	81 (12)	57 (11)	22 (22)	2 (3)
5. Poor quality specimen:	0	306 (60)		
6. Increased TAT:	251 (36)	166 (32)	42 (42)	31 (49)

RTS: Respiratory tract specimen T/S: Throat swab E/S: Ear swab

3.2.1 Microbiology test requisitions

On the examination of microbiology laboratory request forms in Phase 2 of representative respiratory tract specimens, overall, 641 (91 %) of 700 respiratory tract samples were requested the microbiology test of C and S. On the remaining 59 (9%) no request was made as shown in Tables 3.1 and 3.2. The data from these results indicates that sputum specimens have the highest proportion of specimens that have no test requested (9%) during the microbiological test requisitions. The ear and throat swabs have the lowest number of specimens with no test requested.

On further examination, it was found that the total number of respiratory tract specimens that were without microbiology test requests in the representative specimens that were assessed during the course of Phase 2 of this study have similar figures to that of the annual total workload; the difference found was only 1% (Table 3.25).

3.2.2 Patient's clinical diagnosis

On the examination of microbiology laboratory request forms in Phase 2 of representative respiratory tract specimens, overall, 660 (94.0 %) of 700 respiratory tract samples had the clinical diagnosis stated on the request form. In the remaining 40 (6.0%) of 700 samples, patients clinical diagnosis was not stated on the request form, as shown in Tables 3.1 and 3.2.

On further examination of sputum specimen requests, 479 (94.0%) of 511 patient requests for sputum microbiology had their clinical diagnosis on the request forms and 32 (6.0%) patients had not stated their clinical diagnosis. Where the patient's clinical diagnosis was stated, 14 (3.0%) patient's clinical diagnosis was illegible as explained in Table 3.3. The number of patients where their clinical diagnosis either was not stated or was illegible was 46 (9.0%) patients in total. The remaining 465 (91.0%) of the 511 patient's had stated their clinical diagnosis clearly.

Total number of patients with respiratory tract infections where only 65 (13%) out of the 465 patients stated their clinical diagnosis. There were only a few patients with the clinical diagnosis of pneumonia; most of the respiratory tract infections were patients with chest infections, bronchitis, URTI, throat infections, haemoptysis and coughs. This analysis of the results showed that (87%) sputum specimens showed no evidence of respiratory tract infections (Table 3.3).

The majority of the sputum specimens were from patients unlikely to have LRTI's and samples were collected from patients with respiratory tract conditions such as COPD, bronchiectasis, respiratory failure and asthma. The post-surgery patients had highest sputum culture request followed by the oncology/cancer patients.

Table 3.3: Patient's clinical diagnosis in sputum specimens in phases 2 and 3

Clinical diagnosis	Sputum culture in Phase 2 (n = 511) No. (%)	Sputum culture in Phase 3 (n = 119) No. (%)
Respiratory tract infections	65 (13)	19 (16)
Pulmonary TB/TB	17 (3)	3 (2.5)
Respiratory conditions	101 (20)	38 (32)
Non-respiratory tract infections	24 (5)	7 (6)
Oncology/Cancer	89 (17)	3 (2.5)
Surgery and trauma	32 (6)	5 (4)
Post-surgery	123 (24)	10 (8)
Other conditions	14 (3)	27 (23)
Illegible	14 (3)	1 (0.8)
No clinical diagnosis given	32 (6)	6 (5)
Total numbers:	511	119

For throat swab specimens, in 95 (95.0%) of 100 samples the clinical diagnosis was stated, and only three (3.0%) had not stated patient's clinical diagnosis. For two (2.0%) of the throat swab samples, it was not possible to read information in the request form. The majority of throat swabs have clinical conditions associated with throat conditions as presented in Table 3.4. More than 40% of the throat swab specimens were from patients with tonsillitis followed by patients with sore throats, and there were a few from patients with pharyngitis.

For ear swab specimens, in 57 (90.0%) of 63 samples had stated their clinical diagnosis and 3 (5.0%) were not stated while another 3 (5.0%) specimens contained their clinical conditions, but they were illegible. The majority of ear swab specimens have been collected from patients with clinical conditions related to ear conditions such as ear discharge, ear infections and otitis media as presented in Table 3.5.

Table 3.4: Patients diagnosis in throat swab specimens in phases 2 and 3

Clinical diagnosis	Throat swab culture in Phase 2 (n = 100) No. (%)	Throat swab culture in Phase 3 (n = 11) No. (%)
Throat infections	5 (5)	0
Sore throat	27 (27)	1 (9)
Pharyngitis	4 (4)	0
Tonsillitis	44 (44)	2 (18)
Throat conditions	2 (2)	0
Non-throat infections	2 (2)	4 (36)
Upper respiratory tract infections	3 (3)	2 (18
Other conditions	8 (8)	1 (9)
Illegible	2 (2)	0
No clinical diagnosis given	3 (3)	1 (9)

Table 3.5: Patients diagnosis in ear swab specimens in Phase 2

Clinical diagnosis	Ear swab culture in Phase 2 (n = 63) No. (%)
Ear infections	11 (17)
Ear discharge	32 (50)
Otitis media	11 (17)
Ear conditions	2 (3)
Non-ear infections	0
Other conditions	1 (1)
Illegible	3 (4)
No clinical diagnosis given	3 (4)

3.2.3 Antibiotic use

On the examination of microbiology laboratory request forms in Phase 2 of representative respiratory tract specimens, overall, 188 (27.0%) of 700 respiratory tract specimens were obtained before antibiotic treatment was given to the patients and for 235 (33.0%) of 700 samples it was not stated whether patients were given or not treated with antibiotics while 277 (40.0%) of 700 samples were collected from patients treated with antibiotics as presented in the Table 3.1.

The total number of patients that were either on antibiotic treatment or their antibiotic treatment status have not been stated on their microbiology request forms was 512 (73.0%) patients as compared to 188 (27.0%) patients that has been stated on their request form no prior antibiotic treatment. In sputum specimens, the total number of patients that were either on antibiotic treatment or not stated were 376 (74.0%) patients of the 511 sputum samples collected and only 135 (26.0%) patients has no antibiotic treatment.

The analysis of patient's antibiotic usage results has found that, if the microbiology specimen was collected before the start of the antimicrobial treatment and the microbiology laboratory request form stated the patient's previous antibiotic exposure or antibiotic use, then the test requisition was considered as appropriate microbiological test requisition. It has been also found, if the microbiology laboratory requisition form states that the patient's has been receiving antimicrobial treatment before the specimen collection, this practice was considered as inappropriate test requisition and would have no value for patients management.

3.2.4 Specimen age

On the examination of microbiology laboratory request forms, in Phase 2 of representative respiratory tract specimens, it was found that 398 (57.0%) of 700 specimens were transported to the microbiology laboratory within the day of sample collection and received by the laboratory on the same day and 221 (31.0%) of 700 specimens were transported to the laboratory after one day of sample collection, while 81 (12.0%) of 700 specimens were transported to the laboratory specimens aged more than two days after the day samples were collected from the patients as presented in the Table 3.1.

With regard to sputum samples, 309 (61.0%) of 511 sputum samples have been transported to the laboratory within the day of sample collection and 145 (28.0%) of 511 sample were received by the laboratory after one day of sample collection while 57 (11.0%) of 511 specimens were transported to the laboratory a more than 72 hours after the day collected from the patients. Total number of respiratory tract specimens that were received and processed by the microbiology laboratory either within hours or within 24 hours of sample collection were 619 (88.0%) of the 700 specimens in Phase 2 study.

The distribution of sputum specimen ages were similar to the total rate of respiratory tract specimens stated previously. However, the total number of sputum specimens that were received and processed by the microbiology laboratory either within hours or within 24 hours of sample collection were 92.0 % as presented in Table 3.6 in phases 2 and 3 studies.

On further examination, the age of specimen in throat swab and ear swab specimens indicates that 78 (78.0%) of throat swab were received within 24 hours and 22 (22.0%) received greater than 48 hours of sample collection. In ear swab, specimens received within 24 hours of sample collection was 61 (97.0%) and 2 (3.0%) of the specimens received greater than 48 hours of sample collection.

Table 3.6: Results of sputum specimen age (days) in phases 2 and 3 study

Specimen age days	**Sputum specimens** in Phase 2 (n = 511) No. (%)	**Sputum specimens** in Phase 3 (n = 119) No. (%)
0	309 (61)	62 (52)
1	145 (28)	48 (40)
≥ 2	57 (11)	9 (8)

Chi-square test analysis of sputum specimens age results has shown that the specimens received either 24 hours or more than 48 hours were more than 40% of patient's specimens as compared to those received within same day hence those

specimens were too old to process, X^2 = 7.29 (P = 0.026) and transported to the laboratory more than 24 hours after the date of sample collection (Table 3.6).

The analysis of specimen age results has shown if the specimen has good quality and is transported to the microbiology laboratory immediately and received by the laboratory in reasonable time to process, and then the quality of specimen was considered as appropriate microbiological specimen. It has been also found that if the microbiological specimen has not been transported properly to the laboratory within hours of its collection. The patient's specimen is too old to process and this practice was considered as inappropriate test requisition and would have no value for patient management.

3.2.5 Quality of sputum specimens

Of the 511 sputum samples macroscopically evaluated for quality by the microbiology laboratory, in 463 (92.0%) their gross appearance were described and 48 (8.0%) sputum samples had no macroscopic description as presented in Table 3.7. On further examination, a total number of 306 (60.0%) of 511 sputum samples were considered of poor quality and inappropriate microbiologically to process. The sputum specimens described as poor quality included those described as mucoid, salivary and sputum specimens that have no description.

The number of sputum specimens that were suitable for processing was obtained only from 205 of 511 patients (40.0%) and was considered of good quality and appropriate for microbiological investigation. Good quality sputum specimens included those described as mucopurulent and purulent sputum specimens.

The rate of good quality sputum specimens received and processed by the microbiology laboratory was improved in 2006 as data from Phase 3 study shows from 40% to 69% and the rate of inappropriate or poor quality sputum specimens received and processed by the microbiology laboratory decreased from 60% to 31% as presented in Table 3.7. Sputum specimens that were processed in Phase 3 study were of good quality and considered appropriate as compared with sputum specimens processed in Phase 2 studies.

Statistical analysis of results from sputum specimens quality description showed that there were significantly large differences between the quality of sputum

specimens in Phase 2, 40% (good quality) and those in Phase 3, 69% (good quality), X^2= 35.04 (P = 0.0001) as presented in Table 3.7.

Table 3.7: Results of sputum macroscopic description in phases 2 and 3

Description	**Sputum specimen** in Phase 2 (n = 511) No. (%)	**Sputum specimen** in Phase 3 (n = 119) No. (%)
Salivary	35 (7)	13 (11)
Mucosalivary	2 (0.5)	6 (5)
Mucoid	186 (36)	13 (11)
Blood stained	35 (7)	0
Mucopurulent	155 (30)	80 (67)
Purulent	50 (10)	2 (1)
No description	48 (9.5)	5 (4)
	2004 Phase 2 (n = 511)	2006 Phase 3 (n = 119)
Appropriate	205 (40%)	82 (69%)
Inappropriate	306 (60%)	37 (31%)

The analysis of patient's specimen quality results has shown that if the microbiology specimen has been selected properly, collected properly and has a good quality, the quality of specimen was considered as good and appropriate microbiological specimen.

3.2.6 Microbiology test results turn round times

15,941 respiratory tract specimens were received by the microbiology laboratory, 15,718 (99.0%) of these specimens were reported their expected TAT and 223 (1.0%) of the total specimens were not reported to requested clinicians due to unknown reasons. The expected TAT of results was reported in all of the 700 respiratory tract specimens studied in Phase 2 of the study. 251 (36.0%) of 700 respiratory tract specimens their culture and sensitivity results were reported more than five days of received sample by the microbiology laboratory as presented in the Table 3.8.

Table 3.8 shows the overall TAT of respiratory tract specimens in all phases of the study. The data from Phase 3 study shows the decreased TAT in all days (from one to more than 5 days) as compared to the data from other phases of the study. Over 30.0% of microbiology results were reported more than five days in study Phases 1 and 2. While the 39.0% of results were reported in two days and 27.0% were reported in three days in Phase 3 study. The reported results in Phase 3 in more than five days were only 17.0% as compared to other two phases.

Table 3.8: Results of respiratory tract microbiology TAT (in all phases)

Turn around times (Days)	**Respiratory tract** specimens Phase 1 (n =15941) No. (%)	**Respiratory tract** specimens Phase 2 (n = 700) No. (%)	**Respiratory tract** specimens Phase 3 (n = 133) No.(%)
0	223 (1)	0	0
1	1511 (9)	68 (9)	16 (12)
2	3099 (19)	112 (16)	52 (39)
3	3371 (21)	142 (20)	36 (27)
4	3025 (19)	127 (18)	6 (5)
≥ 5	4712 (30)	251 (36)	23 (17)

Table 3.9 shows the details of the results of sputum specimen reported TAT in all phases of the study. 2,563 (27.0%) of the sputum specimens test results were reported after more than five days of received sample by the microbiology laboratory in phase 1 and 166 (32.0%) in Phase 2 of the study while in Phase 3 only 16.0% were reported after more than five days. Among the individual specimens of throat swab and ear swab their microbiology results TAT results were presented in Appendices 3.1 and 3.2.

Comparing the TAT results of all phases of the study, phases 1 and 2 has more or less similar pattern of TAT both in total respiratory specimens and among the individual specimens. The lowest TAT has been found in ear swab culture results in both phases where in Phase 1 40.0% of test results were reported more than five days and in Phase 2 49.0% of test results were reported more than five days.

Table 3.9: Results of sputum microbiology TAT (in all phases)

Turn around times (Days)	**Sputum** specimen Phase 1 (n = 9566) No. (%)	**Sputum** specimen Phase 2 (n = 511) No. (%)	**Sputum** specimen Phase 3 (n = 119) No.(%)
0	0	0	0
1	1374 (14)	63 (12)	11 (9)
2	1934 (20)	88 (17)	50 (42)
3	1939 (20)	100 (20)	33 (28)
4	1756 (18)	94 (18)	6 (5)
≥ 5	2563 (27)	166 (32)	19 (16)

Statistical analysis of results (Table 3.9) from sputum specimens TAT showed that there were significantly difference between the TAT of sputum specimens in Phase 2 and those in Phase 3, X^2= 58.86 (P = 0.0001).

The analysis of patients expected TAT of results has shown that if the TAT for each microbiology request was decreased and results reported the expected TAT. Then the TAT is considered an appropriate. It has been also shown that if the reported microbiological test result has increased test TAT of more than three days, the reported patients test results is too late and has a less microbiological significance and was considered as inappropriate test requisition and would have no value for patient's management.

3.3 Microbiological results of respiratory tract culture

Over the 12 month study period, the results of a total of 15,941 respiratory tract specimens were analysed. The microbiological findings and their cultural results were reported in each specimen type in their respected tables and figures both in this section and in the appendix section. Microbiology laboratory cultured the respiratory tract specimens and reported the culture results findings according to the growth of micro-organisms either positive or negative. This study defined and assumed that for the positive culture, if the cultured organisms have been performed with full identification testing, antimicrobial susceptibility testing on relevant organisms and the test result were reported to the clinicians. For the negative culture, the cultured organisms no further identification and susceptibility testing have been performed on the organisms and then test results were reported to the clinicians.

Overall, the average respiratory tract cultures were reported positive in 40.0% and negative in 60.0% for the cultured specimens in all phases of the study. Table 3.10 explains the summary of the culture results from main specimen groups in Phase 1.

The detailed microbiology culture results findings from the sputum specimens in all phases are presented in this section and the results from throat, ear and nose swabs are described here briefly. All microbiological findings from the other respiratory tract specimens are reported in the Appendix section of the thesis (Appendixes 3.3, 3.4 and 3.5).

Table 3.10: Summary of respiratory tract culture results in phase 1

Type of respiratory sample	Number of specimens studied	Number of positive cultures (%)	Number of negative cultures (%)
BAL	107	44 (41%)	63 (59%)
Ear swab	1393	996 (72%)	397 (28%)
ETT	431	249 (58%)	182 (42%)
Mouth swab	163	41 (25%)	122 (75)
Nose swab	410	183 (45%)	227 (55%)
NPA	211	128 (61%)	83 (39%)
Sputum	9566	3730 (39%)	5836 (61%)
Throat swab	3549	965 (27%)	2584 (73%)
Tongue swab	60	22 (37%)	38 (63%)
Tracheal aspirate	51	38 (75%)	13 (25%)
Total	15,941	6,396	9,545
Percentage	100	40	60

3.3.1 Sputum microbiology culture results

In this study, 9,566 sputum specimens were cultured for lower respiratory tract infections investigation in phase 1 of the study, 3,730 (39.0%) sputum culture results were reported as positive culture and the remaining 5,836 (61.0%) sputum culture results were reported as negative test. The overall sputum microbiology culture results of all phases presented in the Table 3.11.

Table 3.11: Summary of sputum microbiology culture results in all phases

Culture results	**Sputum** culture in Phase 1 (n = 9,566) No. (%)	**Sputum** culture in Phase 2 (n = 511) No. (%)	**Sputum** culture in Phase 3 (n = 119) No.(%)
Positive	3,730 (39)	161 (32)	48 (40)
Negative	5,836 (61)	350 (68)	71 (60)

Table 3.12 shows the number of positive culture sputum samples and the types of organisms isolated in each phase of the study. Based on data obtained from the Phase 1, the bacterial isolates from the positive cultures of 3,730 (39.0%), only less than 18.0% were respiratory tract pathogens while the other 72.0% were non-respiratory tract pathogens. The primary respiratory tract pathogenic species reported were *Streptococcus pneumoniae* (4.0%), *Haemophilus influenzae* (7.0%) and *Moraxella catarrhalis* (3.0%). Among the culture positive sputum samples the most commonly isolated non-respiratory pathogens were coliforms (27.0%), *Pseudomonas* species (17.0%), *Candida albicans* (12.0%), MRSA (8.0%) and *Staphylococcus aureus* (6%).

The micro-organisms listed in Table 3.12 were cultured from the sputum specimens; full identification testing and antimicrobial susceptibility testing has been performed. All were reported as possible potential respiratory pathogens with release of their susceptibility results. The microbiology reports were direct reporting; no comments or interpretations were used for results.

The analysis of frequency isolation of possible pathogens in all study phases remains very similar, and there were no significant differences and changes in proportion of positive sputum cultures, X^2= 0.042 (P = 0.838) as presented in Table 3.11.

Table 3.12: Sputum culture results reported as positive test in all phases

Microorganism/s	Sputum culture in phase 1 (n = 3730) No. (%)	Sputum culture in Phase 2 (n = 161) No. (%)	Sputum culture in Phase 3 (n = 48) No. (%)
Respiratory tract pathogens:			
Streptococcus pneumoniae	157 (4.2)	6 (3.7)	2 (4.2)
Haemophilus influenzae	275 (7.4)	20 (12.4)	5 (10.4)
Moraxella catarrhalis	102 (2.7)	2 (1.2)	0
Doubtful non-respiratory pathogens:			
Staphylococcus aureus	241 (6.5)	15 (9.3)	4 (8.3)
MRSA	317 (8.5)	20 (12.4)	2 (4.2)
Beta-haem.streptococcus *A*	31 (0.83)	2 (1.2)	0
Klebsiella species	76 (2)	1 (0.6)	1 (2.1)
Pseudomonas species	636 (17)	40 (24.8)	8 (16.7)
Beta-haem.streptococcus B	9 (0.24)	0	1 (2.1)
Beta-haem.streptococcus C	8 (0.21)	2 (1.2)	1 (2.1)
Beta-haem.streptococcus D	4 (0.11)	0	0
Beta-haem.streptococcus F	1 (0.03)	0	0
Beta-haem.streptococcus G	16 (0.43)	0	0
Streptococcus constellatus	1 (0.03)	0	0
Non-respiratory pathogens:			
Acinetobacter species	66 (1.8)	1 (0.6)	4 (8.3)
Aeromonas species	1 (0.03)	0	0
Aspergillus species	17 (0.46)	0	0
Bacillus species	2 (0.05)	0	0
Candida albicans	444 (12)	11 (6.8)	4 (8.3)
Candida glabrata	5 (0.13)	0	0
Candida tropicalis	6 (0.16)	0	0
*Citrobacte*r species	2 (0.05)	0	0
Coag. neg. staphylococcus	115 (3)	2 (1.2)	0
Organism of coliform group	1002 (27)	31 (19.2)	14 (29.2)
Corynebacterium species	4 (0.11)	0	0
Enterobacter species	19 (0.5)	0	0
Enterococcus species	24 (0.64)	0	0
Escherichia coli	15 (0.40)	2 (1.2)	0
Haemophilus species	3 (.08)	0	0
Haemophilus parainfluenzae	24 (0.64)	4 (2.5)	0
Haemophilus aegyptius	0	1 (0.6)	0
Moraxella species	5 (0.13)	0	0
Morganella morganii	4 (0.11)	0	0
Proteus species	66 (1.8)	1 (0.6)	2 (4.2)
Serratia marcescens	5 (0.13)	0	0
Stenotrophomonas maltophilia	27 (0.72)	0	0

Table 3.13 shows the sputum culture results from 5,836 (61.0%) patients that were reported as negative culture results. 5,445 (93.0%) of these cultures grew normal respiratory tract flora, while the 391 (7.0%) of the sputum grew no organism.

The most common organisms isolated from the sputum cultures in phase 1 of the study were mouth organisms, otherwise known as throat flora, and there were no differences in all phases.

Table 3.13: Sputum culture results reported as negative test in all phases

Microorganism/s	**Sputum culture** in phase 1 (n = 5836) No. (%)	**Sputum culture** in Phase 2 (n = 350) No. (%)	**Sputum culture** in Phase 3 (n = 71) No. (%)
Coag. neg. staphylococcus	1 (0.33)	0	0
Corynebacterium species	1 (0.02)	0	0
Enterococcus species	2 (0.03)	0	0
Mixed coliform	8 (0.14)	0	0
Mouth flora/Throat flora	5194 (89)	320 (91.4)	56 (78.9)
No growth	391 (6.7)	23 (6.6)	6 (8.5)
Organism of the coliform	155 (2.7)	1 (0.3)	3 (4.2)
Pseudomonas species	9 (0.15)	0	0
Yeast species	57 (1)	6 (1.7)	1 (1.4)
Not processed	0	0	5 (7)

Table 3.14 shows the relationship between the quality of the sputum specimen and the types of organisms isolated. In Phase 2 of the study, out of the 511 sputum culture reports analysed, sputum culture reported as positive were 161 (32.0%) sputum samples. Out of the culture positive samples only 67 (42.0%) were from good quality sputum specimens while the remaining 94 (58.0%) sputum sample reported positive cultures were from poor quality sputum specimens.

There were six samples positive for *Streptococcus pneumoniae*, only one isolated from the good quality specimen and five were isolated from poor quality specimen sputum. Whilst twenty sputum samples were positive for *Haemophilus influenzae,*

thirteen were cultured from good quality sputum and seven were from poor quality specimens. Out of the culture positive samples reported in both good and poor quality sputum samples, the commonest group of organisms isolated were organism of Coliform group and *Pseudomonas* species, both group are non-respiratory pathogens.

The majority of possible potential respiratory tract pathogens were cultured from poor quality specimens. This raises the question of whether they were significant or normal throat flora.

Table 3.14: Sputum quality and results reported as positive in Phase 2 study

Organisms reported	**Good quality sputum** (n = 67) No. (%)	**Poor quality sputum** (n = 94) No. (%)
Streptococcus pneumoniae	1 (0.5)	5 (5)
Haemophilus influenzae	13 (6)	7 (7)
Moraxella catarrhalis	1 (0.5)	1 (1)
Staphylococcus aureus	8 (4)	7 (7)
MRSA	7 (3)	13 (14)
Beta-haem.streptococcus A	0	2 (2)
Klebsiella species	1 (0.5)	0
Pseudomonas species	16 (8)	24 (26)
Beta-haem.streptococcus C	0	2 (2)
Acinetobacter species	0	1 (1)
Candida albicans	5 (2)	6 (6)
Coag. neg. staphylococcus	0	2 (2)
Organism of coliform group	11 (5)	20 (21)
Escherichia coli	0	2 (2)
Haemophilus parainfluenzae	2 (1)	2 (2)
Haemophilus aegyptius	1 (0.5)	0
Proteus species	1 (0.5)	0
Total	67 (42)	94 (58)

Table 3.15 shows the relationship between the sputum quality and culture results. Only 138 (39.0%) sputum cultures reported as negative tests were cultured from good quality sputum specimens and 212 (61.0%) reported culture negative were cultured from poor quality specimens.

There were 130 (94.0%) mouth flora or throat flora cultured from good quality sputum and 190 (90.0%) mouth flora cultured from poor quality sputum specimens. Yeast isolates were cultured in six sputum samples, one was from a good quality sample and the other five were from poor quality specimens.

Table 3.15: Sputum quality and results reported as negative in Phase 2 study

Organisms reported	**Good quality sputum** (n = 138) No. (%)	**Poor quality sputum** (n = 212) No. (%)
Organism of coliform group	1 (1)	0
Mouth flora	130 (94)	190 (90)
No growth	6 (4)	17 (8)
Yeast isolated	1 (1)	5 (2)
Total	138 (39)	212 (61)

3.3.2 Throat swab culture results

In this study, 3,549 throat swab specimens were cultured for throat associated infections investigations in Phase 1 of the study, 965 (27.0%) throat swab culture results were reported as positive culture and the remaining 2,584 (73.0%) were reported as negative tests. The overall throat microbiology culture results of all phases presented in Table 3.16.

Table 3.16: Summary of throat swab culture results in all phases

Culture results	Throat swab culture In Phase 1 (n = 3549) No. (%)	Throat swab culture in Phase 2 (n = 100) No. (%)	Throat swab culture in Phase 3 (n = 11) No. (%)
Positive	965 (27)	29 (29)	2 (18)
Negative	2584 (73)	71 (71)	9 (82)

The bacterial isolates from the positive cultures of phase 1, 67.0% were throat pathogens while the other 33.0% were non-throat pathogens. The primary throat pathogenic species reported was beta-haemolytic streptococcus A (67.0%) which is generally known as Group A streptococcus. There were two other possible throat pathogens reported, beta-haemolytic streptococcus C (9.0%) and beta-haemolytic streptococcus G (8.0%) (Table 3.17). The frequency isolation of beta-haemolytic streptococcus A in all study phases remains very similar and there were no much differences.

Among the culture positives throat samples, the most commonly isolated non-throat pathogens were *Candida albicans* (4.0%), Organism of coliform group (4.0%), *Staphylococcus aureus* (3.0%), *Streptococcus pneumoniae* (2.0%), beta-haemolytic streptococcus B (2.0%) and beta-haemolytic streptococcus F (1.0%). The other organisms reported as positive culture from throat culture included *Coagulase negative staphylococcus, MRSA, Pseudomonas* species, *Haemophilus influenzae, Moraxella catarrhalis* and *Enterococcus* species. These organisms are known common throat flora and normaly isolated from throat swab cultures.

The micro-organisms listed in Table 3.17 were cultured from the throat specimens and full identification testing and antimicrobial susceptibility testing has been performed. All were reported as possible potential throat pathogens with release of their susceptibility results. The microbiology reports were direct reporting and no comments or interpretations were used for test results.

Table 3.17: Throat swab culture results reported as positive test in all phases

Microorganism/s	Throat culture in Phase 1 (n = 965) No. (%)	Throat culture in Phase 2 (n = 29) No. (%)	Throat culture in Phase 3 (n = 2) No. (%)
Possible Throat Pathogens			
Beta-haem.streptococcus A	644 (66.7)	21 (72.)	1 (50)
Beta-haem.streptococcus C	87 (9)	0	1 (50)
Beta-haem.streptococcus G	74 (7.7)	1 (3.5)	0
Corynebacterium diphtheriae	2 (0.2)	0	0
Non-Throat Pathogens			
Beta-haem.streptococcus B	12 (1.2)	1 (3.5)	0
Beta-haem.streptococcus D	0	0	0
Beta-haem.streptococcus F	3 (0.3)	1 (3.5)	0
Candida albicans	36 (3.7)	1 (3.5)	0
Streptococcus pneumoniae	16 (1.7)	0	0
Haemophilus influenzae	1(0.1)	0	0
Moraxella catarrhalis	3 (0.3)	0	0
Staphylococcus aureus	31 (3.2)	3 (10.4)	0
MRSA	9 (0.9)	0	0
Pseudomonas species	8 (0.8)	0	0
Streptococcus species	*1 (0.1)*	*0*	*0*
Aspergillus species	2 (0.2)	0	0
Coag. neg. staphylococcus	1 (0.1)	0	0
Organism of coliform group	29 (3)	1 (3.5)	0
Enterobacter cloacae	1 (0.1)	0	0
Enterococcus species	1 (0.1)	0	0
Escherichia coli	1 (0.1)	0	0
Neisseria meningitides	3 (0.3)	0	0

Table 3.18 shows the throat culture results from 2,584 (73.0%) patients that were reported as negative culture results. 2,543 (98.0%) of these cultures grew normal throat flora and no beta-haemolytic streptococcus (NBHS) was isolated. The remaining 41 (2.0%) grew no organisms.

Table 3.18: Throat swab culture results reported as negative test in all phases

Microorganism/s	Throat culture in Phase 1 (n = 2584) No. (%)	Throat culture in Phase 2 (n = 71) No. (%)	Throat culture in Phase 3 (n = 9) No. (%)
Throat flora	2123 (82)	71 (71)	5 (55.5)
NBHS	401 (15.5)	0	4 (44.4)
No growth	41 (1.6)	0	0
Organism of coliform group	19 (0.74)	0	0

3.3.3 Ear swab culture results

In this study, 1393 ear swab specimens were cultured for ear associated infection investigations in phase 1 study, 996 (72.0%) ear swab culture results were reported as positive culture and the remaining 397 (28.0%) were reported as negative tests. The overall ear microbiology culture results of all phases are presented in Table 3.19.

Table 3.19: Summary of ear swab culture results in phases 1 and 2

Culture results	Ear swab culture in Phase 1 (n = 1393) No. (%)	Ear swab culture in Phase 2 (n = 63) No. (%)
Positive	996 (72)	43 (68)
Negative	397 (28)	20 (32)

Of bacterial isolates from the 996 (72.0%), positive cultures of the most commonly isolated pathogens were *Streptococcus pneumoniae* (7.0%), *Haemophilus influenzae* (3.0%), beta-haemolytic streptococcus A (5.0%), *Staphylococcus aureus* (25.0%) *and Pseudomonas* species (38.0%) (Table 3.20).

Most of the other micro-organisms listed in the Table 3.20 are normally known to be doubtful pathogens and their clinical relevance is obviously difficult and case dependant, but those shown as of dubious significance are where clinical summaries did not indicate sensitivity according to Standard Operating Procedures for microbiological investigation of respiratory tract specimens. There were a few possible secondary pathogens that seldom cause ear associated infections in patients with normal ear. These include *Aspergillus* species, *Proteus* species, organisms of coliform groups and *Candida albicans.*

A total of 800 (80.0%) organisms were considered possible pathogens and reported with their susceptibility test results out of an overall total of 996 ear culture results reported as positive test from the total of 1,393 (72.0%) ear specimen processed in Phase 1. A total of 185 (18.0%) organisms reported with their susceptibility test results were of questionable value out of an overall total of 996. A total number of 11 (~2.0%) organism reported with their susceptibility had no microbiological values and were inappropriate to report as a positive test.

Table 3.20: Ear swab culture results reported as positive in phases 1 and 2

Microorganism/s	Ear swab culture in Phase 1 (n = 996) No. (%)	Ear swab culture in Phase 2 (n = 43) No. (%)
Possible Ear Pathogens:		
Beta-haem.streptococcus A	52 (5.2)	3 (7)
Beta-haem.streptococcus B	4 (0.4)	0
Beta-haem.streptococcus C	1 (0.1)	0
Beta-haem.streptococcus D	3 (0.3)	0
Beta-haem.streptococcus F	0	0
Beta-haem.streptococcus G	6 (0.6)	0
Streptococcus pneumoniae	70 (7)	0
Haemophilus influenzae	33 (3.3)	1 (2.3)
Moraxella catarrhalis	1 (0.1)	1 (2.3)
Staphylococcus aureus	246 (24.7)	9 (21)
MRSA	8 (0.8)	1 (2.3)
Pseudomonas species	376 (37.8)	14 (32.7)
Doubtful Ear Pathogens:		
Organism of coliform group	90 (9)	7 (16.3)
Candida albicans	16 (1.6)	1 (2.3)
Streptococcus species	*2 (0.2)*	*0*
Aspergillus species	24 (2.4)	2 (4.7)
Mixed anaerobes	9 (0.9)	1 (2.3)
Escherichia coli	1 (0.1)	0
Proteus species	42 (4.2)	1 (2.3)
Klebsiella species	1 (0.1)	0
Non-Ear Pathogens:		
Corynebacterium species	3 (0.3)	2 (4.6)
Coag. neg. staphylococcus	4 (0.4)	0
Enterococcus species	3 (0.3)	0
Bacillus species	1 (0.1)	0

Table 3.21 shows the ear swab culture results from 397 (28.0%) patients that were reported as negative culture results. 239 (60.0%) of these cultures grew normal skin flora, and the remaining 115 (30.0%) grew no organism.

Table 3.21: Ear swab culture results reported as negative in phases 1 and 2

Microorganism/s	**Ear swab culture** in Phase 1 (n = 397) No. (%)	**Ear swab culture** in Phase 2 (n = 20) No. (%)
No growth	115 (29)	8 (40)
No significant growth	11 (2.8)	0
Pseudomonas species	3 (0.8)	0
Coag. Neg. staphylococcus	3 (0.8)	0
Skin flora	239 (60.2)	11 (55)
Proteus species	0	1 (5)
Organism of coliform	5 (1.7)	0
Yeas*t* species	21 (5.3)	0

3.3.4 Reporting and interpretation of respiratory tract culture results

The report in Table 3.22 shows the typical microbiology result report from sputum culture. The left hand side (a) of the report shows a microbiological report from positive sputum culture, results that have been sent to clinicians and other microbiology laboratory service users. In addition to the patient's demographic data, the test report of *Escherichia coli* with a susceptibility report of relevant antibiotics was reported. The report indicates that this bacterium was isolated from the sputum culture with full identification and susceptibility of this bacterium to a number of different antibiotics.

No interpretation was offered on the significance of this finding. The report does not indicate whether this cultured bacterium was probably a potential pathogen or normal bacterial contamination due to bacterial colonisation of the upper respiratory tract. Similarly, it is not stated why antimicrobial susceptibility was performed and reported. The report generated by the microbiology laboratory should be written in a

way clinicians would understand and should be interpreted in the light of clinical diagnosis and culture findings.

The right hand side (b) of the report shows a microbiological report from a negative sputum culture, results that have been sent to clinicians and test results of throat flora was reported. The report indicates that this throat flora was isolated from the sputum culture and reported directly without any interpretation and further comments. The negative report generated by the microbiology laboratory should be written in a way clinicians would understand and should be explained in the light of clinical diagnosis and indicating why this culture is negative.

Table 3.22: non-interpreted microbiology report from sputum culture

Source: Sputum specimen (a)	**Source: Sputum specimen (b)**
▪ Status: Final ▪ Clinical diagnosis: Pneumonia ▪ Macroscopic description: Mucopurulent ▪ Culture: *Escherichia coli* ▪ Susceptibilities: - Sensitive: cefuroxime, gentamicin, augmentin, tazobactin, ciprofloxin - Resistant: ampicillin	▪ Status: Final ▪ Clinical diagnosis: Pneumonia ▪ Macroscopic description: Purulent ▪ Culture: Throat flora

(a): Final microbiology report from positive sputum culture.

(b): Final microbiology report from negative sputum culture.

3.3.5 Microbiology cost per request test

Table 3.23 shows the total cost per microbiology test request, including the total pay cost per request, the total non-pay cost per request, and the total capital charge cost per request where applicable (Table 3.23). The cost data used in this study were derived from the local hospital microbiology benchmark reports over the years, since the local cost data could not be used here due to confidentiality issues (National Pathology Benchmarking Review 2006, National Pathology Benchmarking Review 2007, National Pathology Benchmarking Review 2008, National Pathology Benchmarking Review 2005)

Table 3.23: Total expenditure cost per request

Sources of the cost	**Data years** 2005/2006	**Data years** 2006/2007	**Data years** 2007/2008
Total pay Cost/request	£5.91	£7.28	£4.57
Total non-pay Cost/request	£4.02	£4.69	£4.27
Capital charge Cost/request	£0.00	£0.00	£0.04
Total Cost/request	£9.94	£11.97	£8.88

The cost data indicated that during 2005 to 2007, the microbiology cost per test request was higher than cost data in 2007/2008. The salary increase of healthcare professionals was one of the reasons due to the Agenda for Change implemented from July 2005. The later data shows since increased productivity has led to reduction in overall cost per request of around 10%. The cost analysis of this study will be based on cost data from 2005/2006, total cost per microbiology test request of £9.94 (National Pathology Benchmarking Review 2006).

3.4 Impact of results on the NHS both locally and nationally

The current study results have major relevance to the NHS, both locally and nationally. It has an impact on microbiology workload activities, associated cost and clinical implication of patient care. The decreased workload activities indicate the reduction of inappropriate microbiology test utilisation. The appropriate test orderings practice reduces unnecessary tests, wasted costs and increases processing of properly collected good quality microbiology specimens which results in appropriate test results report.

3.4.1 Impact on microbiology workload activities

Table 3.24 shows microbiology benchmarking data for this Trust. This serves as a guide for optimal use of the microbiology laboratory service, indicating the total workload of respiratory microbiology activities from 2004 to 2008 and the gradual decreased number of specimens processed per year (Table 3.24). This study initiated and encouraged the use and application of microbiology quality indicators for the evaluation of specimen processing to minimise the processing of inappropriate specimens and performing unnecessary further testing.

Since the presentation of this study in the local hospital, the unnecessary workload decreased due to the new management rules that have been put in place. The first strategy was the rejection of duplicate sputum cultures and the use of comments for reporting duplicate sputum specimens received daily by the microbiology laboratory such as: “This test has been performed within the last three days. Therefore, in accordance with laboratory protocols it will not be tested again. If the patient's condition has changed since last testing, please contact one of the microbiology SpRs to request this sample is tested”.

The second strategy was the rejection of poor quality sputum specimens and issuing the appropriate statement, for instance, “mucoid sputum or salivary sputum specimen received, therefore, unsuitable for culture due to poor quality of the sample, please repeat if clinically required”. In addition to this, this policy became routine practice and is used daily presently at local hospital, BLT. Similarly, it has been also applied to other microbiology specimens including faeces.

Table 3.24: Total workload of respiratory tract microbiology activity

Workload Data (years)	**Respiratory tract** specimen	**Changes No. (+/-%)**
2004/2005	18,915	
2005/2006	19,618	703 (+4)
2006/2007	18,166	1452 (-7)
2007/2008	16,651	1515 (-8)

+/- indicates the % of increase or decrease for the workload

The respiratory microbiology workload decreased during the course of later years from 2006/2007 to present. This has been a significance development for the reduction of inappropriate microbiology test utilisation and if applied to other NHS hospitals in the country will decrease the processing of unnecessary microbiology specimens as well as wasted test costs.

3.4.2 Impact on cost to the local NHS and nationally

The rate of respiratory tract specimen received without microbiology test requests was 8%, which means that 1,594 of patients submitted respiratory tract specimens without stating the required microbiology test requested. This is described in Table 3.25. These figures and data were obtained from the main respiratory tract specimens assessed during the course of phase 1 of the study and specimens for TB investigation and cystic fibrosis microbiological tests were not included.

The results shown in Table 3.26 indicate the reasons for test inappropriateness and unnecessary number of respiratory tract microbiology specimens tested in the local hospital for various reasons. The data presented in this table was derived from the local hospital figures based on 2004/2005, 18,915 respiratory tract specimens and the study estimated the associated cost lost for the processing of inappropriate test orders.

Table 3.25: Total result of RTSs for microbiological test requisitions 2004-05

Test request	Respiratory tract specimen (n = 18915) No. (%)	Sputum specimen (n = 9566) No. (%)	Throat swab specimen (n = 3549) No. (%)	Ear swab specimen (n=1393) No. (%)
C & S requested	17321 (92)	8667 (91)	3301 (93)	1327 (95)
No test requested	1594 (8)	899 (9)	248 (7)	66 (5)
Total workload	18915 (100)	9566 (100)	3549 (100)	1393 (100)

Table 3.26: Summary of reasons for microbiology test inappropriateness

Reasons for test Inappropriateness	RTS local No.	RTS national No.
No test requested	1,594	182,931
No clinical diagnosis stated	1,081	124,124
Too old specimen received	2,188	251,069
Poor quality specimen received	5,728	1,306,123
Increased test turn around times	4712	540,547
Total	9,575	2,153,977

RTS: Respiratory tract specimen

In addition to the data shown in Table 3.25, the total number of bacteriology workload at local hospital and other associated hospitals was 436,151 samples during 2004/2005. The total number of respiratory tract workload was 18,915 (4.3%) out of the total bacteriology workload volume. Therefore, the respiratory tract specimen per bacteriology specimen from the hospital was 4.3% (18,915/436,151) respiratory request per bacteriology specimen.

As there are no national statistics for request rates within the NHS, it has been assumed that the request rate at this local hospital was representative of the NHS and extrapolated accordingly. Total microbiology request in England in a year 2005-2006 was 50 million requests (Lord Carter of Coles 2006.). The estimate of respiratory tract specimen requests in England from microbiology service users in that year was 2,170,000 (50,000,000 X 0.0434).

If we can assume that number of microbiology tests request rate of 8.4% is a typical representation, therefore, the number of respiratory tract specimens that has no microbiology test request in England in a year was 182,931 (2,170,000 X 0.0843). If these 182,931 respiratory tract specimens without microbiology test request assumed as inappropriate test order due to their lack of test request then this was an example of inappropriate utilisation of the microbiology laboratory service.

The average cost of processing microbiological specimens, including respiratory tract specimens, at local hospital microbiology departments was £9.94 as previously stated in Section 3.3.5. It has again been assumed that the missing test request rates within the department of microbiology at the local hospital was the same across the NHS hospitals and therefore the average cost of a respiratory tract test was the same across the NHS microbiology laboratories.

The cost of respiratory tract specimens without microbiology test request that has been processed in a year from microbiology services users in England was £1,818,334 (182,931 X £9.94). Similarly, the local cost of processing of unnecessary respiratory tract specimens was £15,844 (1,594 X 9.94) in the year 2004-2005.

On further cost analysis, it has been found that the cost of other inappropriate tests was similar to that of microbiological test requisitions as indicated the data presented in the Tables 3.26 and 3.27.

Table 3.27: Summary of cost for inappropriate microbiology test

Cost for inappropriate test	**local NHS** Cost/test X (£9.94)	**national NHS** Cost/test X (£9.94)
No test requested	£15,844	£1,818,334
No clinical diagnosis stated	£10,745	£1,233,793
Too old specimen received	£21,749	£2,495,626
Poor quality specimen received	£56,936	12,982,862
Increased test turn around times	£46,837	£5,373,037
Total	£152,111	£23,903,652

In terms of cost reduction, since this study began, the data from Phase 3 of this study has indicated good improvement in specimen transport, specimen quality and TAT of the test results. A significant amount of cost could be saved from this improvement as found in good quality of the sputum specimens from 40.0% to 69.0% (Section 3.5, (Table 3.7)). Hence, the rate of inappropriate or poor quality sputum specimens received and processed by the microbiology laboratory decreased from 60% into 31%.

The local costs associated with the processing of these inappropriate sputum specimens was decreased from £56,936 to £29,443 (2974 X £9.94) in 2006. Therefore, the local cost saved from the processing of appropriate and good quality specimen was a sum of £27,493 (£56,936 - £29,443) in 2006 after the intervention and staff education initiated.

3.4.3 Clinical implications for the patient's care

Further analysis of the study results indicates the clinical implications for patients care. Results from patients, clinical diagnoses and the quality of the sputum specimens indicates that 33.0% of patients with respiratory tract infections or respiratory conditions have produced a good quality sputum specimen, while a similar number, 35.0%, of these patients sent a poor quality sputum specimen to the laboratory (Table 3.28).

Table 3.28: Clinical diagnosis and sputum specimen quality in Phase 2 study

Clinical diagnosis	**Sputum quality** good (n = 205) No. (%)	**Sputum quality** poor (n = 306) No. (%)
Respiratory infection or condition	68 (33)	108 (35)
Other clinical diagnosis	137 (67)	198 (65)
Total	205 (100)	306 (100)

Looking at antibiotic use**,** results indicated that the majority of the respiratory tract possible pathogens have been cultured from the sputum specimens from patients that had no prior antibiotic treatment, whilst *Staphylococcus aureus*, MRSA, Pseudomonas species, organisms of coliform group, *Candida albicans* and yeasts were cultured from patients who had started antibiotic treatment before sample collection (Table 3.29).

This data indicated that the use of antibiotic treatments before sample collection reduces recovering of the possible respiratory tract pathogens while increasing the colonisation with non pathogenic organisms such as yeasts.

Table 3.29: Sputum culture results and antibiotic usage in Phase 2 study

Organisms recovered	No antibiotic treatment (n = 135) No. (%)	With antibiotic treatment (n = 214) No. (%)	Not stated treatment (n = 162) No. (%)
Streptococcus pneumoniae	3 (2)	1 (0.5)	2 (1)
Haemophilus influenzae	6 (4)	4 (2)	10 (6)
Moraxella catarrhalis	1 (0.7)	0	1 (0.6)
Staphylococcus aureus	3 (2)	4 (2)	8 (5)
MRSA	3 (2)	10 (5)	7 (4)
Beta-haem.streptococcus A	0	1 (0.5)	1 (0.6)
Klebsiella species	0	1 (0.5)	0
Pseudomonas species	7 (5)	23 (11)	10 (6)
Beta-haem.streptococcus C	1 (0.7)	0	1 (0.6)
Acinetobacter species	0	1 (0.5)	0
Candida albicans	0	11 (5)	0
Coag. neg. staphylococcus	0	2 (1)	0
Organism of coliform group	8 (6)	14 (7)	9 (5)
Escherichia coli	1 (0.7)	1 (0.5)	0
Haemophilus parainfluenzae	2 (1)	0	2 (1)
Haemophilus aegyptius	1 (0.7)	0	0
Proteus species	1 (0.7)	0	0
Organism of coliform group	1 (0.7	0	0
Mouth flora	93 (69)	122 (57)	105 (65)
No growth	3 (2)	16 (7)	4 (2)
Yeast isolated	1 (0.7)	3 (1)	2 (1)

Nearly all (94.0%) of the sputum specimens were collected from in-patients who had already been treated with antibiotics, as compared with specimens received from the out-patients department, where only 6.0% had received antimicrobial treatment, the results are present in Table 3.30.

Table 3.30: Type of patients and antibiotic usage in Phase 2 study

Type of patients (patients location)	**No antibiotic** treatment (n = 135) No. (%)	**With antibiotic** treatment (n = 214) No. (%)	**Not stated** treatment (n = 162) No. (%)
Accident & emergency (AE)	1 (1)	0	1 (1)
Chest/specialist clinics (CL)	2 (1)	0	5 (3)
General practice (GP)	1 (1)	0	8 (5)
Inpatients (IP)	107 (79)	202 (94)	118 (73)
Outpatients (OP)	24 (18)	12 (6)	30 (18)
Total	135 (100)	214 (100)	162 (100)

Assessing the age of specimens, the result in the Table 3.31 indicates that the majority of respiratory tract potential pathogens have been cultured from sputum specimens that had been received by the laboratory within day of sample collection. While *Staphylococcus aureus*, MRSA, *Pseudomonas* species, organism of coliform group and *Candida albicans* were cultured from the patients where their sample had been received more than one to three days after collection.

These specimens have questionable and limited microbiological value as the sample has been delayed either more than 24 or 48 hours of sample collection and it was too old to process.

Table 3.31: Sputum culture and effect of specimen age in Phase 2 study

Organisms recovered	specimen same day (n = 309) No. (%)	specimen 1 day (n = 145) No. (%)	specimen 2 days (n = 27) No. (%)	specimen >3 days (n = 30) No. (%)
Streptococcus pneumoniae	5 (2)	1 (1)	0	0
Haemophilus influenzae	13 (4)	4 (3)	0	3 (10)
Moraxella catarrhalis	1 (0.3)	1 (1)	0	0
Staphylococcus aureus	6 (2)	4 (5)	2 (7)	0
MRSA	9 (3)	11 (8)	0	0
Beta-haem.streptococcus A	1 (0.3)	1 (1)	0	0
Klebsiella species	0	0	1 (4)	0
Pseudomonas species	29 (9)	10 (7)	0	1 (3)
Beta-haem.streptococcus C	2 (1)	0	0	0
Acinetobacter species	1 (0.3)	0	0	0
Candida albicans	8 (3)	3 (2)	0	0
Coag. neg. staphylococcus	2 (0.6)	0	0	0
Organism of coliform group	17 (5)	6 (4)	4 (15)	4 (13)
Escherichia coli	1 (0.3)	1 (1)	0	0
Haemophilus parainfluenzae	3 (1)	1 (1)	0	0
Haemophilus aegyptius	1 (0.3)	0	0	0
Proteus species	1 (0.3)	0	0	0
Organism of coliform group	1 (0.3)	0	0	0
Mouth flora	186 (60)	93 (64)	19 (70)	22 (73)
No growth	17 (5)	5 (3)	1 (4)	0
Yeast isolated	5 (2)	1 (1)	0	0

Evaluating the quality of the specimen, the total number of sputum specimens that were judged macroscopically as appropriate (i.e. mucopurulent or purulent) and reported positive results were only 67 (42.0%) of the 161 sputum specimens from 205 described as good quality specimens. While 58.0% were from poor quality specimens as presented in Table 3.32. These 58.0% of the culture results reported positive were from poor quality sputum specimens.

Table 3.32: Quality of sputum culture reported as positive in Phase 2 study

Sputum quality	Positive culture report (n = 161) No. (%)
Good quality sputum	67 (42)
Poor quality sputum	94 (58)
Total	161 (100)

Analysing the results of TAT, the results of respiratory tract specimens culture positive test results that were reported of more than five days was more than 30.0% in the phases 1 and 2 of the study. Since this study, the TAT of microbiology results has been decreased. The TAT in Phase 3 of the study, the results that were reported more than 5 days was 17.0% and decreased dramatically as compared to the other two phases as described in the previous Section 3.2.6 (Table 3.8). Microbiology results with increased TAT have no clinical values for the patients care.

Since the presentation of the current study results, a new microbiology reporting system has been introduced and its interpretation is based on the clinical diagnosis of the patients, organism cultured and their clinical significance (Table 3.33). The introduction of comments and test result interpretation will improve the optimal utilisation of microbiology laboratory service.

Table 3.33: Interpreted microbiology report from positive sputum culture

Source: Sputum specimen (a)	**Source: Sputum specimen (b)**
▪ Status: Final ▪ Clinical diagnosis: Pneumonia ▪ Macroscopic description: Mucopurulent ▪ Culture: *Escherichia coli* ▪ Antimicrobial susceptibility report: Antibiotic Mic Interpretation Cefuroxime NP Sensitive Gentamicin NP Sensitive Augmentin NP Sensitive Tazobactin NP Sensitive Ampicillin NP Resistant ▪ Comment: The presence of coliforms may represent oral or upper airway contamination. Antibiotic therapy is only indicated in the presence of clinical signs of pneumonia. Contact (name/pager number of clinical microbiologist) if concerned.	▪ Status: Final ▪ Clinical diagnosis: Pneumonia ▪ Macroscopic description: Mucoid ▪ Culture: Throat flora ▪ Comment: Normal flora, which is probably colonising this site.

(a): Final microbiology report from positive sputum culture

(b): Final microbiology report from negative sputum culture

NP: Not performed

As previously stated in Section 3.3.4, the microbiology results were reported directly to the clinicians without interpretation comments (Table 3.22). The following microbiological comments have been introduced and have been in use for the last three years.

1. The microbiology report from sputum culture specimen growing with non-pathogenic organisms such as the organism of the coliform group, the following comments used with the report:

"The presence of coliforms may represent oral or upper airway contamination. Antibiotic therapy is only indicated in the presence of clinical signs of pneumonia." For clinical advice please contact if concerned.

2**.** The microbiology report from sputum culture specimen growing with *Staphylococcus aureus* or MRSA, this comments used with the report:

"The presence of *Staphylococcus aureus*, including MRSA, may represent upper airway colonisation. Antibiotic therapy is only indicated in the presence of clinical signs of pneumonia". For clinical advice please contact if concerned.

3**.** The microbiology report from sputum culture specimen growing with *Staphylococcus aureus* or MRSA with relevant sensitivity report, this comments used with the report:

"The presence of *Staphylococcus aureus*, including MRSA, may represent upper airway colonisation. Antibiotic therapy is only indicated in the presence of clinical signs of pneumonia". For clinical advice please contact if concerned.

4. The microbiology report from sputum culture specimen growing with same organisms from the repeat culture, this comments used with the report:

"Please refer to previous susceptibility test and as previously isolated". For clinical advice please contact if concerned.

3.5 Summary of study results

1. Ninety-one percent of the microbiology test requisition forms were completed by the service users provided in all relevant details and were considered as appropriate microbiology test requisitions. In 9% of the test requisition forms were not stated the name of the required test and this practice was considered as inappropriate test requisition.

2. Ninety-four percent of the respiratory tract samples were stated the patient's diagnosis and clinical details. The other 6% of the samples patients' clinical diagnosis was not stated on the request form. The total number of patients with respiratory tract infections was only 13%.

3. Twenty-seven percent of the microbiology specimens were collected before patients antibiotic treatment. 40% of samples were obtained from patients treated with antibiotics while the remaining 33% patient's status of antibiotic usage was not stated on the request form.

4. Fifty-seven percent of the specimens were transported to the laboratory within the day of sample collection. 31% of the respiratory tract specimens were received after one day of sample collection while the remaining 12% of the specimens were received by the laboratory after 2 days of sample collection.

5. Forty percent of sputum specimens were considered of good quality while the remaining 60% were considered as poor quality specimen.

6. The TAT of respiratory tract microbiology results was reported only 20% within three days in 2004/2005 and 27% in 2006. However, the total microbiology test TAT that was reported within three days in 2008/2009 was 90%.

7. Forty percent of the respiratory tract specimens were reported as positive based on the local hospital criteria of microbiology test reporting and 60% were reported as culture negative. In sputum culture, 39% were reported as positive and 61% were reported as negative. Of 39% of positive sputum specimens, less than 18% were positive with respiratory tract pathogens

while the remaining 72% were non-respiratory tract pathogens. The throat swab, 27% were reported as positive in which 67% were throat pathogens.

8. Prior to the present study, there was no microbiology test comments interpretation. However, from mid 2006 and onwards test interpretation comments have been used in all microbiology test result reporting.

9. The total cost/request of microbiology cost per request test was decreased from approximately £10.0 to £9.0 over the years from 2005/2006 to 2007/2008.

10. The total workload of respiratory tract microbiology activity was decreased from 18,915/year to 16,651/year over the years from 2004/2005 to 2007/2008, which is nearly down in 8%.

11. The total inappropriate RTS processed locally was 9,575, with 2,153,977 estimated nationally as derived figures from local NHS hospitals in 2004/2005.

12. The total cost of inappropriate respiratory tract microbiology test use was £152,111 in local NHS hospitals and £23,903,652 in national NHS hospitals as derived data from local hospital.

Chapter 4 Discussion

4.1 Introduction

This study was explicitly directed at respiratory tract specimens received routinely in the clinical microbiology laboratory, based on microbiological investigations at the clinician's requests. It provides insight into the importance of a rational approach to the microbiological investigation of lower respiratory tract specimens, particularly sputum samples. The study also addressed the rarely documented inappropriate utilisation of the clinical microbiology laboratory service by service users such as the clinicians and the other healthcare professionals. Several key factors responsible for the inappropriate utilisation of clinical microbiology laboratory test with reference to sputum cultures have been identified and studied in order to assess the ways to maximise the diagnostic yield from sputum cultures and other respiratory tract cultures. Finally this study illustrated cost control strategies in this clinical microbiology laboratory, the implications of the study outcome and the contribution of health economics to the evaluation of diagnostic strategies and microbiology testing both at the local health service level and the NHS at large, including the gaps, needs and challenges in UK clinical microbiology services.

The present study demonstrates the limited value of sputum specimens and other respiratory tract specimens as a diagnostic tool in the initial evaluation of patients with respiratory tract infections admitted to NHS hospitals or treated in health centres. From this study, eight main limitations have emerged. These are: the failure to state the required microbiology test requisition, patient's clinical diagnosis, to collect microbiology specimen prior patient's antibiotic treatment, to obtain a good quality sputum sample from most patients, delay in collection and laboratory processing of samples, to explain value of microbiology test results, delay in test turnaround times and failure to interpret microbiological test results.

All of these reported limitations cause low diagnostic yield and have minimal impact on therapeutic decisions. As no published results on the topic of microbiology laboratory test utilisation in UK are available, this study may serve as a departure point for discussion and future research.

4.2 Appropriate use of clinical microbiology tests

This study is one of the largest audits in the UK addressing the issues of inappropriate use of clinical microbiology tests. The main findings were as follows: 1) the clinicians and other healthcare professionals utilise the clinical microbiology service inconsistently by sending to the laboratory by inappropriate test requests and specimens; 2) in spite of numerous guidelines on appropriate specimens for microbiological examination, laboratories continue to receive and process large numbers of inappropriate sputum samples; 3) there was lack of adherence to specimen collections principles 4) lack of adherence to microbiology laboratory compliance with the laboratory working principles.

4.2.1 Appropriateness of test requisition

The results of this study has found that the frequency of missed or not stated type of required microbiology test during the microbiology test requisition was found to be 9% in 2004-05, as shown on the examination of patient's information on microbiology laboratory request forms. This disagrees with the fundamental requirement of test requisition. This study indicates that the value of stating proper microbiology test requisitions is underestimated whilst the importance of sending any microbiology specimen to the laboratory is overestimated. It is unfortunate how little attention is paid to the one process in clinical microbiology that has the most influence on accurate laboratory results and contributes so much to patient outcome and safety.

When a clinician decides to order a microbiology or laboratory test, a requisition slip (microbiology request form) is completed in writing or electronically and submitted with the specimen to laboratory. Thus, the clinical microbiology laboratory request form performs a pivotal role between the clinician and the laboratory, and it is indeed surprising that very little appears to have been published regarding this rather important aspect. It is the standard expectations of all clinical microbiology investigations should be requested the required tests. The microbiology test orders should be marked clear, specific, unambiguous and clearly marked on the requisitions and written legibly. The microbiology respiratory tract samples received without required test should be treated as an inappropriate test request and therefore the microbiology laboratory should not perform testing. Similarity, the

laboratory should not perform testing on any microbiology specimen without a valid order submitted in writing on the patient's microbiology request form.

Inaccurate or incomplete requisitions have been reported to be the sources of errors which can affect the quality of laboratory testing. The CAP Q-Probes study in the US found that the 12.8% of test requisitions were improperly filled including the missing of test requisitions (Valenstein and Meier 1999). It also known that using a customised requesting of MC&S may result in the ordering of tests that are not required, reasonable or necessary. Hence, such requesting practice will increase the inappropriate utilisation of laboratory services and wasting millions of money.

The request (requisition) forms whether a hard copy or an electronic version from clinicians is the most important means of communication and clinicians should provide their requests by indicating the clinical question and the type of test and other information on the patient, thus enabling the clinical laboratory to select the appropriate tests, or test cascade. The advantages and disadvantages of electronic requesting of laboratory tests is not the scope of this study. Here, it is particularly important to stress the potential role of ward order systems in encouraging clinicians to select the most appropriate tests, in facilitating dissemination of protocols and guidelines and in effecting real time consultation by health professionals regarding specimen type, sample timings, and providing any other information useful for a state of the art specimen collection.

The microbiology laboratory requisition forms are designed to emphasise clinician choice. However, it is important that it only tests that are medically necessary for the diagnosis or treatment of the patient should be performed. The microbiology laboratory should deny the processing of specimens where there is insufficient key information to support the medical necessity of each of the ordered tests, as the information on the order forms can directly affect process and analysis of the specimens. The microbiology test requisitions are often made by the doctors; nurses are often responsible for providing patient's information both on the request form and specimen. Therefore, clinicians are accountable for selecting and ordering the inappropriate microbiology test and should sequence the test request, problem, complaint or other reason for the encounter as principal.

There should be developed a laboratory compliance programme or regular audit to ensure that regulatory policies for ordering, performing for microbiology laboratory

testing that are adapted and enforced. As part of the compliance programme, notice should be being provided to the service users to assist them in identifying their role in ensuring compliance. It should be outlined the shared responsibilities required of both service providers and service users to achieve compliance under the agreed guidelines for preventing of inappropriate test orders and specimens without required test.

The *Royal College of Pathologists* recently suggested the concept of intelligent requesting. “If we could stop doing unnecessary laboratory tests, we could at a stroke make efficiency savings that are probably greater than those that are currently being demanded”. However, too often laboratories find it easier to do a test than to argue that it is not necessary (Royal College of Pathologists 2010).

Apart from the clinical importance of test requisitions, there is a health and safety issue. The current study and other investigations have identified there has been a lack of sufficient relevant clinical details being provided on specimen request forms. This has resulted in samples being handled at the wrong biological containment level with resulting increased risk of infection to medical laboratory staff. In December 2011 the Health and Safety Executive (HSE) issued safety notice to alert health and social care services to potential risks to laboratory staff, if specimen request forms do not contain relevant details. It is important that medical staff and other healthcare professionals should ensure that appropriate information, including relevant travel history, clinical details and other relevant are provided in order to alert laboratory staff of potential dangers (Health and Safety Executive 2011).

4.2.2 Patients clinical diagnosis

The present study has found 6% of microbiological test requests were submitted without the patient’s clinical diagnosis. Patient’s clinical diagnoses are very important to laboratory staff. This is because they play an important role in setting the context for the test. Laboratory managers believe that this contextual information improves the laboratory’s input. For instance, it may help a microbiologist detect the need for more tests, or perhaps identify when a doctor may have asked for an inappropriate test. In addition to this, it may cause a dilemma to microbiologists for results reporting and interpretation. Hence, this may lead to misinterpretation of microbiology laboratory results.

The clinical information/impression should always come first and should always be used for proper interpretation of laboratory results. The culture and sensitivity result should be taken into consideration when clinical impression and adequacy of specimen are fulfilled. After all, the aim is to treat the patient, not the organism! If an organism name and sensitivities appear on a laboratory result, it is often interpreted as being the cause of the clinical problem.

This shows that providing appropriate clinical information, including the patient's clinical diagnosis and required microbiology test, will help the microbiology laboratory to do the appropriate microbiological investigations work that the clinicians and their patients want. Similarly, providing better clinical information will help the microbiology laboratory and microbiologists to produce an improved interpretative report and include comments with a beneficial effect on diagnosis and treatment.

The diagnosis of infectious disease conditions clinically starts with a good detailed history, followed by appropriate specimen collection and proper interpretation of results. The results of the present study show that there are still cases where a patient's clinical diagnosis and good clinical history is lacking. The clinical diagnosis and travel history is extremely important for infectious diseases and microbial infections in their epidemiological investigations, but is not always taken and entered on the microbiology laboratory request forms. In multicultural UK, due to migration from, and travel to, the tropics and the developing world, this aspect of the history and clinical diagnosis is extremely important.

It is well known that when proper clinical diagnosis is stated and appropriate investigation ordered, this would result in early patient treatment and where diagnosis was delayed or not started, would most likely cause patients to suffer with serious consequences and complications. Similarly, it is well known that inaccurate diagnosis leads to unnecessary deterioration of patients conditions leading to possible hospitalisation and prescription of inappropriate drugs. This adds enormous cost to already costly aspects of healthcare. Patients with correct clinical diagnoses lead to appropriate microbiological investigations and treatment. Hence, the diagnostic accuracy is the key for microbiological investigations (Wilson 2008).

This study underscores the important role that the provision and exchange of clinical information plays in microbiology laboratory processes. Clinical information helps to inform the laboratory of the type and urgency of tests required as well as assisting microbiology staff to add interpretative value to the information provided back to medical staff. The exchange and transfer of clinical information is underpinned by a complex variety of communication channels within the hospital. This study would suggest the use of computerised provider order entry (CPOE) systems. New CPOE systems can increase the efficiency of this process and enhance the richness of information exchange. To date, little attention has been provided to this issue. This study recommends that more research into this area be undertaken so as to make these channels of communication and information exchange more explicit, and as a means of providing information to enhance the design and implementation of CPOE systems (Wilson 2008).

Adoption of laboratory CPOE systems may offer institutions many benefits, including reduced test turnaround time, improved test utilisation, reduced costs, fewer errors, promote appropriate laboratory test selection, enhance the accuracy and efficiency of the entire laboratory testing process and better adherence to practice guidelines (Baron and Dighe 2011).

From the microbiological perspective, all microbiology tests require that the diagnostic information should be submitted in order to establish the medical necessity of diagnostic testing. The patient's clinical diagnosis should be indicated for each test ordered. Clinical diagnosis should be provided to the highest degree of accuracy or certainty on all tests ordered, both when the diagnosis is known and when the diagnosis is unknown. History, signs and symptoms of the patient may be used when a definitive diagnosis has not been established.

4.2.3 Specimen quality

This study assessed the quality of sputum specimens and has found that only 40% of samples were judged to be of good quality when standard macroscopic examination criteria were applied, thereby substantially reducing the number of sputum specimens appropriate for microbiology investigation. With reference to quality of sputum specimen, salivary and mucoid samples are unsuitable for culture and inappropriate in the investigation of pneumonia. Purulent or mucopurulent

sputum samples should ideally be collected before antibiotic therapy is started and should reach the laboratory with minimum delay; otherwise culture interpretation is difficult.

In this retrospective study of sputum cultures at our institution, based on the local criteria, the poor quality of sputum specimens were found to be 60%, and they have been considered as unacceptable and inappropriate samples for microbiological investigations. Sputum samples submitted for culture are often improperly collected and contain predominantly upper respiratory or oropharyngeal flora. Further more, the results of this study show a limited value of sputum culture as a diagnostic tool in the initial evaluation of patients with chest infections, as a majority of patient's sputum specimens has very poor quality and predominately consisted of saliva and were mucoid in their composition.

Many other clinical studies have demonstrated similar results. Roson et al. concluded that a good quality sample could be obtained in 39% of the patients with CAP admitted to a University hospital (Rosón et al. 2000). In a recent study, prospectively analysed hospitalised patients with CAP, a good quality sample was obtained in 36% of the patients admitted to hospital (Miyashita et al. 2008). This agrees with the rate of good quality sputum specimen as reported by the current study. Ewig and co-workers (Ewig et al. 2002) have shown that in primary care hospitals sputum has low diagnostic yield (9%) and does not contribute significantly to patient management.

If this initial requirement for specimen quality fails to be met, subsequent processing and culture work up becomes irrelevant for meaningful patient management. The adage "garbage in results in garbage out" can be used to descriptively refer to the issue of specimen quality in the clinical microbiology laboratory. Therefore, good quality sputum specimen is recommended. If poor quality sputum or spit received and specimen rejected (even processed) then the consequence is delay in diagnosis and treatment and repeat specimens collected after antimicrobial treatment.

The results of the present study suggest that using the macroscopic criteria, a macroscopic purulent/mucopurulent appearance could be used to assess the quality of sputum for screening before accepting it to process for culture. It is also believed this method had a high true-positive rate of predicting validity and

appropriateness of subsequent growth in culture based on macroscopic appearance. However, in the present study there are no comparative studies with Gram staining reported. If these observations of macroscopic validation are confirmed with sputum Gram staining microscopic examination. Thus, it is simply possible to replace microscopic validation (Gram staining) by the use of more this readily available macroscopic criteria validation for assessing sputum quality.

However, the usefulness of sputum Gram stain in the initial management of pneumonia is still a matter of controversy. Arguments against its use include the low yield, cited in many reports, described in the review of literature section, the belief that performing adequate sputum studies on a routine daily basis is a difficult task, and the low cost-effectiveness. Another argument against sputum Gram staining has been the lack of documentation of its value in terms of cost or outcomes. Although this study was not specifically designed to evaluate cost-effectiveness of macroscopic and microscopic validation of sputum specimens, the macroscopic sputum observation is the most simple and cost effective method of sputum quality assessment. Like most of the UK other hospitals, at our institution, sputum Gram staining is rarely performed upon patients with suspected bacterial pneumonia unless medically requested (Roberts et al 2008).

However, there are many studies in the literature on the value of sputum in the evaluation and management of LRTIs and, nevertheless, its role remains controversial. Recent studies have shown that the Gram staining of sputum is of limited value in the management of CAP in adult patients (Loens et al. 2009, Ferre' et al. 2011, Campbell and Forbes 2011). Evidence-based guidelines for interpretive reporting of the sputum Gram stain will allow laboratories to provide accessible, clinically relevant information to guide the management of pneumonia patients (Campbell and Forbes 2011).

Proper specimen collection and handling is one of the most important factors, along with appropriate use of tests, in maximising the cost effectiveness and clinical relevance of microbiological testing. It is essential to appreciate that a microbiology laboratory report is only as good as the specimen collected. The microbiology laboratory would much prefer quality to quantity when it comes to specimen type, particularly lower respiratory specimens.

In addition to this, it is also important to indicate that litigation has now entered the sphere of microbiological diagnosis and patient treatment. A poorly collected specimen with an incorrect answer and inappropriate treatment resulting in patient dissatisfaction may be cause for legal examination and action. The indication for sputum culture is that sputum samples should be sent for culture and sensitivity from patients with pneumonia who are able to expectorate purulent sample and who have not received previously antibiotic therapy. Sputum microbiology is not indicated for specimens that are largely or wholly saliva which can only yield misleading information and should not be sent for culture.

Lower respiratory secretions may result in more unnecessary microbiology laboratory effort than any other type of specimen. For example, in only 50-60% of patients with pneumococcal pneumonia can the organism be recovered from expectorated sputum samples, suggesting poor sensitivity of the culture (Isenberg 2004). On the other hand, the absence of a pathogen does not exclude the presence of serious pulmonary infection. Therefore, the sputum culture undoubtedly is one of the most misleading of all specimens with regard to true clinical correlation.

4.2.4 Specimen transport

In the present study, the majority of the respiratory specimens were received by the microbiology laboratory within the first 24 hours of sample collection. However, the results of this study has found that the total rate of respiratory tract specimen received by the microbiology laboratory that were greater than 48 hours of sample collection was 12%. This indicates that these specimens have little microbiological value as the sample has been delayed and it is too old to process.

All microbiological specimens including sputum specimens should be transported to the microbiology laboratory as quickly as possible. Delay of microbiology specimens by more than 2-3 hours in transit time causes the overgrowth of commensal flora, resulting in false positives, and it also causes the loss of pathogen viability, again resulting in false negatives. Therefore, microbiology specimens such as the sputum specimens should be transported immediately to microbiology laboratory and cultured specimen as soon as possible. The other microbiology specimens have been suggested transportation in fewer two hours is recommended with refrigeration if delays anticipated. It should be transported the

specimen to the laboratory expeditiously or make sure that, if it must be stored, the storage conditions are appropriate for the suspected organism.

Delays in collection have resulted in antimicrobial pre-treatment, thereby affecting the specificity of culture results, leading to an increased recovery of coliforms and non-fermenters. Although this study was not designed to define exactly the impact of processing delays on the sensitivity of sputum cultures, it is known that common respiratory pathogens such as *S. pneumoniae* and *H. influenzae* are easily missed when samples are processed after more than four hours. In addition, it was evident that delays in processing were associated with an increase in the isolation of *Candida* species. Thus, the isolation of *Candida* species in sputum samples of non-immunosuppressed patients may be regarded as marker of overgrowth with colonising organisms and not true pathogens (Ewig et al. 2002).

Specimen quality can be compromised during delivery by excessive delay, adverse temperature, and contamination of specimens collected for bacterial growth due to the delay. Each specimen type has standards for timely delivery and conditions for transport in order to maintain its integrity. Specimens for urgent test orders such as those collected in the emergency room need to be delivered to the laboratory immediately. Most micro-organisms die quickly after removal from the body and should be transported quickly. Transporting and processing delays can render a specimen invalid for analysis.

The results of the present study have found that the adherence to specimen collection guidelines and specimen delivery to the microbiology laboratory within 2-24 hours is not working and more action suggested addressing this issue of specimen transport is needed. Prompt processing of microbiology specimens minimises the loss in viability of potential pathogens and insures a more accurate appraisal of flora present particular sputum specimens. Reducing the delay in set up should give clinical more accurate results (less lost of viability due to transport delays to the). Bringing microbiology specimens to the laboratory quickly will be a physician satisfier, it will reduce turnaround time, and it will probably reduce length of stay, and processing such a specimen adds cost to the laboratory.

The present study suggests that the most important contribution to the effectiveness of the microbiology laboratory is the specimen that is appropriately selected, collected and transported. Since specimens for microbiological analysis

are likely to contain living organisms, specimen collection, handling and transport to microbiology laboratory as soon as possible. The properly transported microbiology specimens are vital to obtaining the best results.

The prompt transport of specimens to the microbiology laboratory is essential in order to optimise the yield of cultures and the interpretation of results. Delays in processing may result in the overgrowth of some microorganims or the death of more fastidious ones. Desiccation of the sample must also be avoided. Rapid transport to microbiology laboratory is indicated otherwise death of delicate organisms and overgrowth of normal flora that mask the pathogen. Delay more than 24 hours need transport media for certain specimen but delay of sputum samples more than 2 hours may need refrigeration as some school of thoughts believe (Sharp et al. 2004, Isenberg 2004). Specimen transport is one of the microbiological challenges.

4.2.5 Antibiotic use

The number of patients on antibiotic treatment in this study was found to be 40%, as stated on patient's microbiology laboratory request forms, and therefore, the results of this study confirm the common belief in which microbiology suffers from prescribe first, test later. It is commonly assumed that most of the physicians prefer to prescribe (antibiotics) first and test second. Due to its slow turnaround time (usually more than 24 hours), an estimated 70% of all microbiology tests are not used to guide therapy (personal communication). The basic rules on how to take microbiological samples state that a sample should be taken before antibiotic usage starts.

Obtaining a precise bacteriological diagnosis before starting antibiotic therapy is, when possible, of paramount importance for the success of therapeutic strategy during infection and sepsis. It has been demonstrated that the outcome of sputum Gram stain and culture for the detection of *Strep, pneumoniae* is inversely proportional to the duration of antibiotic treatment (Musher et al. 2004). Ewig et al, (2002) demonstrated that prior ambulatory anti-microbial treatment was associated with a four –fold reduction in sputum diagnostic yield.

The results of another study also demonstrated that prior anti-microbial treatment decreased the diagnostic yield (Miyashita et al. 2008). In addition to this decrease, their results also demonstrated that Gram-negative bacilli were more frequently observed in patients who had taken antibiotic treatment compared with the entire group (71.0% vs 29.0%) (Miyashita et al. 2008). Thus, the sputum samples obtained after initiation of antibiotic therapy may be unreliable and should be interpreted carefully. In similar studies, it has been reported that sputum microbiological investigations added very little to the management and outcome of patients who received an appropriate initial antimicrobial regimen in different hospital settings (Woodhead et al. 1991, Ewig et al. 1996, Sanyal et al. 1999, Theerthakarai et al. 2001, Ewig et al. 2002).

The results of the present study support that of other studies that one of the commonest reasons for false negative microbiological investigations is the sending of samples for culture or direct examination after commencement of antibiotic therapy. If possible, all such initial investigations should be sent before antimicrobial treatment is begun. In many cases and particularly in emergencies, culture results will not be timely enough to influence initial empirical therapy - i.e. antibiotic treatment may need to be commenced prior to obtaining such results. Indeed, it is national policy to administer antibiotics to patients with suspected meningitis at the earliest possible opportunity and not to delay this, even to initiate a laboratory investigation. However, in almost every other case, including emergencies, there is time to draw baseline pre-treatment tests. Sputum culture, blood cultures and other clinical pathology investigations can all be obtained from the patients. Similarly urine from urinary catheters, tracheal secretions from endotracheal tube, throat swabs, petechial aspirates/swabs, CAPD effluent, wound discharge etc. are frequently immediately available for direct microscopy and culture. Baseline investigations such as these may be sent in emergencies without delaying the institution of antibiotic therapy at all.

The lack of productivity of post treatment cultures in comparison to those obtained prior to treatment cannot be over emphasised. Sending cultures prior to antibiotic treatment will save a lot of time and effort**.** It is also important to note that cultures from patients on inappropriate antibiotics may also be falsely rendered sterile, from a laboratory point of view. Such cultures, sometimes referred to as check cultures, may give a false sense of security.

4.2.6 Value of microbiology test results

This study attempted to assess the value of respiratory tract microbiology test results based on the cultural results and reporting practices. The study found that there were unexplained bacteriology culture results and antimicrobial susceptibility testing results that were reported to the clinicians and other microbiology laboratory service users. The majority of the positive culture results that were reported consisted micro-organisms that had no microbiological significance and are normal respiratory tract flora in which their findings are sign of contamination or otherwise of colonisation of respiratory normal flora. The reporting of these organisms with their antimicrobial sensitivity results was unnecessary.

For instance, the results of sputum culture would seem to indicate that the many of the reported micro-organisms were normally known to be doubtful pathogens or non-respiratory tract pathogens and their clinical relevance is obviously difficult and case dependant, but those shown as dubious significance are where clinical summaries did not indicate sensitivity according to Standard Operating Procedures for microbiological investigation of respiratory tract specimens (Table 3.12). There are a few possible secondary pathogens that seldom cause lower respiratory tract infections in patients with normal respiratory tracts, but are often occurring hospital acquired lower respiratory tract infections. These include *Klebsiella* species, Gram negative bacilli such as *Enterobacter* species, *Citrobacter* species, *E.coli* and *Acinetobacter* species and *Pseudomonas* species.

Gram-negative bacilli and gram-positive cocci like *Staphylococcus aureus* and *Streptococcus pneumoniae* from the throat and mouth area may contaminate the specimen, especially if there is a prolonged transit time. In this study, there were six *Streptococcus pneumoniae* that were isolated from the sputum culture out of the 161 positive cultures from 511 samples. Only one was isolated from a good quality sputum sample, while the other five were cultured from poor quality sputum.

Guidelines for identification and susceptibility testing of potential pathogens recovered in the culture are based on the relative numbers and types of bacteria that grow in conjunction with the direct Gram stain results. Even good quality specimens may be inconclusive. Previous antimicrobial therapy may alter yield of culture. In this study, of the six *Streptococcus pneumoniae* reported, only three were isolated prior to patient's commencement on antibiotic treatments. MRSA,

Candida sp, coliform groups and *Pseudomonas* sp were cultured from post antibiotic treatments. Gram-negative bacilli often colonise the respiratory tract of patients who are treated with antibiotics (Craven and Hjalmarson 2010). Thus, sputum cultures positive for such bacteria should be interpreted with caution.

This study was not designed to investigate the aetiology of lower respiratory tract infections, particularly the causative agents of pneumonia. However, the isolation of primary pathogens from respiratory tract samples helps the diagnosis and proper antimicrobial treatments for patients with lower respiratory tract infection. Valid samples of sputum growing predominant micro-organisms were considered for a very probable bacteriological diagnosis.

Other studies have reported that sputum culture is of little value in diagnosing community-acquired pneumonia (CAP). According to the results of a cohort study published in the Sept. 13 issue of the *Archives of Internal Medicine in 2004 (*Garcia-Vazquez et al. 2004).The investigators and editorialist recommend against routine use (Madison and Irwin 2004). "The role of sputum culture as a rapid diagnostic tool that could direct antimicrobial treatment of CAP is a matter of controversy," write Elisa Garcia-Vazquez, and colleagues from the Hospital Clinic in Barcelona, Spain. "Some of its limitations are the difficulty to obtain good quality samples, its lack of reliability due to possible sputum contamination by the flora of the upper airways, its low diagnostic yield (i.e, sensitivity), and, therefore, its low impact on treatment decisions."

In an accompanying editorial, J. Mark Madison, and Richard S. Irwin, from the University Of Massachusetts Medical School in Worcester, describe routine Gram staining and culture of expectorated sputum as a "hallowed, time-honoured tradition of dubious value" (Madison and Irwin 2004). "We only order tests on expectorated sputum if organisms not covered by usual empiric therapy and clearly not contaminants, such as *Mycobacterium tuberculosis*, are suspected," the authors write. "Unless new strategies for applying and interpreting these sputum tests can be devised, what may be needed most are studies assessing the effects that these tests have on treatment delays, co-infection outcomes, and the over prescription of antibiotics. If such studies document significant negative effects in real-world clinical settings, then everyone might finally be able to retire these poorly performing tests."

These reports and studies are very similar to the findings of the current study; the author of this study believes that there is a very limited value of sputum microbiological culture. 94% of the sputum samples processed in NHS local laboratories was collected from in-patients; most of these patients with non-respiratory tract infection conditions, only 13% of patients have a diagnosis of LRTI including pneumonia, in this study. In addition, the majority of them were receiving antibiotic treatments.

4.2.7 Interpretation of microbiological test results

Subsequent to specimen analysis, the next step in microbiology testing is report interpretation and verification. However, the results of this study show that there is a lack of interpretative comments and backup information to help the clinicians to use the results appropriately. All microbiology laboratory test results are reported directly, regardless of whether they are positive or negative. This study has found a lot of non-interpretative microbiology reporting with release of susceptibility results instead of a lot of interpretative microbiology reporting with susceptibility results withheld. The present result is similar to one survey of microbiology laboratory users that found that microbiology reports were “more allied to the laboratory than to the busy clinicians” (Morgan 1995).

When reports are released with antibiotic susceptibilities results, this may reflect a tendency to consider reports that include susceptibilities as warranting treatment, regardless of clinical indications. In microbiology there is rarely any interpretation of the microbiology results. This kind of reporting practice is causing confusion among the service users. The poor impact of microbiology reports on patients care may, in part, be due to confusion between accuracy and clinical relevance of results. A detailed report, such as the one shown in Table 3.33 in section 3.4.3 is entirely accurate. The organism is correctly named, the manner in which it was isolated is noted and qualitative susceptibility results are given.

Sending of a specimen to the microbiology laboratory is in essence a request for consultation and should form part of the consultative process between the primary care/secondary care physician and the microbiologists/infectious disease (ID) physician. The report should transmit clinical useful information about the pathogen and sensitivities provide appropriate clinical and infection control advice and encourage the primary care clinician to seek further advice if required.

The interpretation of microbiology reports depends on a number of factors, including: source of the culture, Gram stain results, organism, and likelihood of that culture was contaminated based by the organisms that are isolated, number of organisms that grow, patient's gender, patient's age, and type of patient (immunocompromised, etc). The amount of organisms present, source of culture, and patient's age may determine significance as pathogen. Post-analytical interpretation of the microbiological laboratory results, the microbiology results is put in the context with the patient's symptoms as well as the general epidemiological situation of the ward.

In addition, it has been found that the naming of a specific organism, in a situation where it was unlikely to be a pathogen (e.g. *Staphylococcus aureus* in a throat swab), often leads to inappropriate therapy, as does the reporting of susceptibilities for organisms of doubtful significance (Lee and McLean 1977). The turnaround time of results is very important, but so is an accurate result that provides useful information. It has been seen many times in culture results that list normal flora because there was not enough expertise to interpret the growth on the plate with the thought being "let the physician decide if it is important". This thought process is not in the best interest of the patient, and lack of useful information is of no help to the physician. In most cases this increases turnaround time because of extensive work up.

This study suggests that the microbiologists should think outside the traditional thoughts and patterns of reporting everything that grows from the cultured specimens. They should come to a middle ground that ultimately produces the best result at the right time for the interest of the patients.

There may be a role for using interpretative reporting for negative reports. If a negative report has a high positive predictive value for the absence of infection, clinicians should be made aware of this. For example a negative throat swab could prompt the comments "a negative throat swab correlates with a very low likelihood of bacterial pharyngitis and antibiotic therapy is rarely indicated in this setting". Interpretative reporting of microbiology results entails the addition of a comment to the report, giving the likely significance of the organism(s) isolated and, where necessary, specific advice on therapy. The use of interpretative comments

appended to microbiology reports has been shown to allow clinicians to make informed decisions based on such reports (Barnes 1980).

The clinicians primary requirement of the microbiology laboratory as “what micro-organism is responsible for my patients condition?” (Neu 1978). Answering this question is often difficult because microbiology reports do not have the same absolute validity as most biochemical or haematological reports (Ackerman et al. 1980). Therefore, this study suggests that the inclusion of interpretative comments can compensate for confusing reporting practices and produce more clinically relevant reports. The lack of such interpretation may cause misinterpretation of microbiology results by clinicians.

However, there may be reluctance on the part of some laboratories to add lengthy comments as they might be seen to make reports needlessly long. It has been suggested that longer comments, employing a conversational tone, are more likely to reflect clinical reality and therefore be accepted by microbiology laboratory users. Morgan found that 97% of hospital doctors approved of the inclusion of interpretative comments on microbiology reports and 72% requested more interpretation (Morgan 1995).

The role of a microbiologist is to take an active role and make a difference because microbiology laboratory produces so much of the information that is used to make medical decisions. It is, therefore, important that microbiology reports are readable, accurate, and credible. Expertise of microbiologists is important, as both physicians and patients rely on him. However, in microbiology laboratories, there are less guidelines necessitating reporting and interpretations of microbiology cultural results. While most laboratories provide some form of interpretative comments in anatomic pathology reports, this is not always the case with clinical microbiology reports. Thus, this study indicates there is clearly a need for education of clinicians regarding indications for sending specimens and applying results to patient management.

This study would suggest and encourage that the ideal microbiology laboratory report should be user friendly, employing terms that are readily understood and communicate clinically relevant information. The patient is the true end-user of the laboratory and this should be the guiding principle in ensuring that results are reported in a way that maximises clinical benefit. Nobody questions the fact that

radiology and anatomic pathology results are reported with interpretation and that further discussion is often required between the radiologist or pathologist and the primary care physician. Perhaps the clinical microbiologist should begin to think of microbiology results in the same way as radiologist or pathologist do.

GPs and hospital doctors rely on accurate information from clinical pathology services to help them make the right treatment decisions that will deliver the best outcomes for their patients. They need to be sure they are able to interpret the results of pathology investigations correctly. Up until now, there has been no way of reporting pathology test results in a consistent, standardised way across the country, meaning that different names in different settings could mean the same or different things. The NHS will soon test the National Laboratory Medicine Catalogue (NLMC). This is a unique data set, which will standardise the way pathology tests are requested and reported electronically in hospitals, clinics and medical laboratories across the UK. It will address a number of quality and patient safety issues in both requesting and reporting, and improve the reliability and effectiveness of pathology services (Barnes and Batstone 2012).

NLMC will be available from July 2012 and it is similar to the British National Formulary (BNF). NLMC is the first comprehensive standard for pathology services, enabling pathology test requests and results to be standardised in common and consistent formats. It will define a common terminology so that doctors across the country will use the same words when ordering laboratory tests or receiving results. This means that hospital doctors, GPs, nurses and other health professionals can be certain they are requesting the right test every time and can safely interpret the results of pathology investigations eve when they come from more than one source.

In addition to NLMC pathology data system, Electronic health record (EHR) systems are now a major topic in healthcare service. Use of EHRs in physician practices and in healthcare organisations directly impacts the communication and management of laboratory information in patient care, particularly reporting of laboratory results and test order management (Henricks 2011). Meaningful use of EHR and its relevance to laboratories will have substantial direct and indirect implications for laboratories and for pathology practice and this will lead to improved healthcare provision. There will be greater expectations for electronic interchange of laboratory information which will provide other opportunities for ways that laboratories can better serve their provider community.

4.2.8 Test turnaround times (TAT)

The published TAT times in most of the NHS microbiological laboratories is a target of three days. However, this study has found that over 30% of respiratory tract microbiology results had a TAT of more than five days in the period of 2004-05. While the repeated follow-up study in 2006 found that 66% of cultural results were reported in three days. The average TAT of local NHS laboratory in 2009-2010 was more than 95% of all microbiology test results.

The results of this study show there were increased TATs in the period 2004-05 and decreased TAT in the last part of the study, in 2006 and onwards. The main reason for the decrease in 2006 was due to the introduction of a new IT system called Winpath system in the Trust at the end of the 2005. The possible second reason for the decrease of BLT TAT was due to the awareness of microbiology staff of the importance of TAT in microbiology as a result of this study.

Typical expected TAT for microbiology, Gram stains, when appropriate, are resulted within 2 hours of receipt. Culture results are read and reported as pending everyday via computer. Results are finalised within 2-5 days depending on growth and organism isolated. For the diagnosis and management of bacterial infections, physician's relay on the results of identification and antimicrobial susceptibility testing (ATS) provided by the clinical microbiology laboratory. As soon as results are reported, empirical therapy that was started in anticipation of culture results can be adjusted in order to achieve the highest treatment efficacy for the patients, prevent the development of antimicrobial resistance, and reduce the cost of antimicrobial therapy.

Faster reporting of microbiological results enables the clinicians to start appropriate treatment sooner, which is associated with an improved clinical outcome (Barenfanger, Drake and Kacich 1999, Bruins et al. 2005). It has been shown that if results are available earlier, significantly more changes in therapy are made, resulting in either a more effective or a less expensive treatment. Therefore, shortening the TAT of microbiological procedures is associated with an improved clinical outcome. However, most TAT studies have focussed on inpatient and emergency care settings, though a few researchers have ventured to outpatient

and general practice settings. TAT varies depending on the location of the laboratory.

TAT microbiology laboratory practices, and specimen characteristics such as the type of specimen and microbiological results findings. TAT varied substantially according to specimen type. Technically it is difficult to assess and determine TAT the difference between recorded starting times (test ordering) and ending points (test reporting time). Clinicians consider turnaround times from the time test is ordered to results reporting, whereas the laboratory professionals usually use specimen receipt to reporting of results as the turnaround times.

Currently, the measurements of TAT do not reflect whether the microbiology services meet the expectations of the clinicians using the microbiology service. Also, improving TAT can be challenging, not only because of the contributing factors outside the control of the microbiology laboratory, but because laboratories frequently try to improve TATs for a specific test, location, or specific type by immediately identifying and testing those specimens in question, thereby extending the TATs of other tests (Howanitz 2005).

The increased TAT and the majority of the problems directly affecting TAT for microbiology tests are associated with preanalytic related test ordering and specimen collection. The second cause could be analytic related and technical problems, including delays in expecting reporting times and verification of final results. It is often not known whether the clinicians have received test result reports or not.

The timelines with which test results are delivered is one of the most prominent parameters of laboratory medicine, and a common indicator of performance (Novis et al. 2004). Common among these are test TAT and time for notification of critical results. The ways to improve TAT include the use of automation of various steps in the analytic phase, increased use of electronic results reporting, and development of automatic electronic alerting systems for critical values.

World class service healthcare organisations are characterised by their attention to reducing waits and delays. In contrast, timeliness of results reporting has not been a major focus in clinical laboratories. While laboratory professionals often overlook timeliness as an important attribute, clinicians judge the adequacy of laboratory

services by the speed with which results are reported. A few studies have explored the wishes, wants, and needs of clinicians for the time frame in which laboratory results are reported, and, for the most part, these studies indicate laboratories do not meet clinician's expectations (Howanitz and Howanitz 2001).

However, regardless of method, TAT is viewed as a quality measure that reflects the performance of the testing process as a whole. Prompt and predictable reporting of test results can increase efficiency of patient care and improve clinicians and patient satisfactions, even when it does not affect health outcomes (Valenstein 1996). Improved TAT can save time and money for the organisation.

Principles of appropriateness in laboratory medicine are embodied in selecting the right test at the right time for the right patient. Test appropriateness is inherent to an understanding of the specific clinical condition and the value of particular test to the respective patient. The ability to make these determinations varies among clinicians. Standard measures of appropriateness do not prevail currently, though their development is viewed as important. Instead, clinical guideline performance indicators of care quality and measures of test use (including underuse and overuse) have been the basis for drawing conclusions about appropriateness from the current study. These are the reasons the present study was under taken to assess the factors responsible for the inappropriate microbiology test utilisation in order to reduce the inappropriate test ordering and encourage optimal use of microbiology service.

4.3 Causes of inappropriate use of clinical microbiology tests.

From a patient's perspective, due to inappropriate or missed diagnosis, there can be increased morbidity (and occasionally mortality) inappropriate antibiotics, unnecessary testing and longer hospital stays also add to the overall cost of the health services. Several studies have shown that between 25% and 40% of all tests sent to the laboratory are unnecessary, yet few laboratories in the UK have managed to reduce these unnecessary tests (Fraser and Woodford 1987, Winkens et al. 1996, van Walraven and Naylor 1998). Even where such reductions have been achieved, it has been difficult to sustain them. So, what is it that makes it difficult to manage demand and prevent inappropriate test utilisation? Several reasons have been suggested (Axt-Adam, Van der Wouden and Van der Does 1993).

These include uncertainty of likely diagnosis (associated with junior and inexperienced doctors), lack of understanding of the basis, sensitivity, and specificity of the tests, and the desire for diagnostic completeness. Furthermore, recommendations of special interest groups, peer and commercial pressure, patient expectation, and more recently, fear of litigation, have led to increased demand for laboratory tests. With all these barriers, it is not surprising that although attractive in concept, demand management has failed to make appreciable inroads and causes of inappropriateness of test utilisation are not addressed accordingly.

Similarly, this study supports the above stated reasons and has identified from the results of the current study, three main factors that may be associated with the causes of inappropriate microbiology test utilisation. These factors are: 1. Clinicians request of inappropriate test (request that is not the required microbiology test and patients' clinical diagnoses). 2. Clinicians lack of adherence to specimen collections principles (Specimen quality, specimen transport and antibiotic use). 3. Non-compliance of the microbiology laboratory with the laboratory working principles (test results value, test results interpretations and test turnaround times).

The first two factors are associated with the responsibility of clinicians to an extent. It seems that the clinicians were too little reliance on their clinical skills, and too much reliance on laboratory investigations. Even when investigations are warranted, too many additional tests (nice to haves) are ordered that are not crucial for diagnosis resulting in ordering of inappropriate tests and irrelevant tests. The third factor is associated with the responsibility of clinical microbiology laboratory to a larger extent. The first problem associated with laboratory staff is processing all specimens whether appropriate or not such as a specimens on a swab marked ear, sinus or wound and poor quality sputum specimens. The clinical microbiologist must use interpretative judgement to lend significance and clinical relevance to the information conveyed to the physician whether the specimen is easy or difficult to obtain.

One of the major causes of inappropriate clinical laboratory test utilisation is the elimination of pathology and laboratory medicine from the curriculum in many medical schools and consequent lack of knowledge of basic science among the junior doctors which is jeopardising patient safety according to the report published in 2008 (Khromova and Gray 2008). This study raised one very important question: 'with no standardisation of the medical curriculum for teaching of basic science,

how will junior doctors become competent in requesting and interpreting investigations in laboratory medicine?' Although patients safety became a fundamental priority for the NHS in 2000, "most acutely ill patients are cared for by the most junior medical staff with the least knowledge and experience".

Due to the reduction in the amount of teaching of pathology and laboratory medicine, these doctors have little understanding of what tests to order and how they should be interpreted. It has been reported also that the junior doctors have little concept of how tests should be used, and their role in diagnosis. Moreover, many seem unaware that laboratories have staff able to help them, not only with interpretation, but also with advice on appropriate testing.

The findings of a survey by Khromova and Gray (2008) demonstrated the need for additional teaching in clinical biochemistry. It seems likely or reasonable that the teaching of clinical microbiology is the same as the teaching of clinical biochemistry and other laboratory medicine areas, and in the medical curriculum in the UK the practical application of microbiology is often lacking. Proper collection of specimens, optimal use of the clinical laboratory and interpretation of microbiology reports are not adequately covered or emphasised in medical and nursing education in UK, leading to sub-standard management of infections. The knowledge and skills required to manage an infectious disease efficiently are knowledge of infectious diseases, suspect and diagnosis an infection, optimal use of clinical microbiology laboratory to confirm the diagnosis and treat with appropriate antibiotics as per microbiology laboratory results.

There is some evidence that the use of laboratory services can be improved by educating clinicians. Bareford and Hayling (1990) showed that there was a definite and sustained reduction in inappropriate requests when certain measures, such as issuing guidelines, fact sheets and holding seminars, for example in clinical biochemistry were implemented. In a study under taken in 2000, (Mishra et al. 2000) 98% of doctors and medical students agreed that clinicians should be invited to seminars to improve their skills in interpreting laboratory investigations. When asked about the best method of delivering teaching on the subject, 93% preferred seminars with active participation to lectures or symposia.

Of course it has been known that, in general, fear is a very strong driver. In the case of laboratory test ordering, the fear of not having ordered what the consultant

wanted is part of what drives junior doctors to over-order and fear of the lawyers (and possibly the media) is part of what drives consultants to do the same.

Since about half of the overall increase in healthcare spending is the direct result of increased utilisation of medical services by physicians, a decrease in utilisation practices will directly reduce laboratory costs. There may be a variety of reasons for the increase in clinical microbiology laboratory utilisation by physicians (Bartlett 1974, Robinson 1994). For example, physicians may request unnecessary tests because of their insecurity in establishing a diagnosis, or because of poor turn-around time of the laboratory. Another cause for increased utilisation may be the practice of standing orders for routine laboratory testing on patients. This practice is for the convenience of the physician and nursing staff, but has been shown to greatly increase laboratory utilisation without improvement in patient care. Another cause for increased utilisation is the use of check-off boxes on laboratory requisition forms which, again, is for convenience of physicians and nurses, but requires little conscious thought about what test is actually needed. Another cause for increased utilisation may be the automatic ordering of fungal, TB, or anaerobic cultures on certain specimen types, even though the physician may not have originally ordered nor needed this extra test. Reviewing utilisation practices for appropriateness is essential for cutting costs in the laboratory.

One problem with testing which is not justified, is that it wastes money and time and, since the money available to the health service is finite, inappropriate testing takes resources away from more useful endeavours (such as new tests or other clinical services). Clinical laboratory staffs in the laboratories of NHS hospitals have no real control over demand for laboratory services, and no real capacity to charge for same. Therefore, laboratory service providers depend on their service users (“customers”) to think of the greater good of patients as a whole, as opposed to the narrow view of just your patients, when you devise test-ordering strategies.

During this study, it has been found one of the greatest wastes of microbiology laboratory resources is spending money pursuing tests ordered by the physician that have very little effect on patient care. As reported in the study results where the microbiology laboratory processed specimens without a test request, sputum specimens of poor quality, respiratory tract specimen of too old to process (> 1 or 2 days old), follow up and further work of microbiology culture without microbiological

values. Similarly results shows also reporting of test results with increased TAT and microbiology report without interpretation of test results.

A major obstacle to successful implementation of appropriate laboratory test utilisation from the user's perspective is "consumer resistance". In the UK, neither the clinician nor the patient directly pays for the laboratory tests. Thus, there is little incentive for clinicians to alter their current patterns for requesting laboratory tests. Marketing strategies have to be developed to "sell" the concept of demand management to clinicians (consumers). This will require paying attention to the product (identifying areas for clinical laboratory demand management in consultation with clinicians), placement (bidirectional ward test ordering systems), price (clear cost/benefit analysis), and promotion (use of advertising material that appeals to both senior and junior medical colleagues) (Gopal Rao et al. 2002). Changes in the configuration of clinical laboratory test ordering system are inevitable.

In addition to the stated causes, there are a number of more strategic issues that constrain the optimal use of laboratory medicine services. For example, it is rare that laboratory medicine is directly involved in strategic planning of health services, despite the role that the laboratory is acknowledged to play in delivering healthcare services. There is little importance given to the management role of audit, through commitment to continuous quality improvement and performance management in the context of the care pathway (Price 2012).

4.4 Implications of the study outcome at local NHS service

The present study highlighted inappropriate test utilisation in clinical microbiology laboratories. However, during this study period, substantial improvements were seen in several areas of microbiology laboratory activities, including the development and implementation of restrictive specimen workup, and a process policy for screening sputum specimens for acceptability, limiting the duplicate specimens, reducing the microbiology test turnaround times across the department, increasing the value of microbiology test results, reducing specimen transport delay, introducing microbiology comments for certain microbiology results and improvement of communications with the microbiology service users.

Similarly, the study recommendations have been very well accepted by all levels of staff after the presentation of the study results. Since then it has led to a greater ownership of work, staff have been gratified to see improvements in the quality of the microbiology service after the introduction of the microbiological rational policies through out the laboratory process. More recently, a multidisciplinary to a lean system approach has been introduced in order to eliminate the waste of the clinical pathology laboratory process including the microbiology laboratory using some of the data obtained from the current study as example and reference data. Hence, during the past few years, the Barts and The London NHS Trust department of microbiology has developed and implemented strategies to eliminate inappropriate tests and useless activities.

The microbiology laboratory has introduced and adopted a restrictive policy of screening and evaluating the quality of sputum specimens for acceptance by macroscopic examination prior their process and to acceptance. Sputum specimens with the appearance of watery/saliva and muoid has been rejected with the exceptions of certain patients groups such as the neonatal, ITU and neutropaenic patients. Poor specimens could potentially have important effect on the welfare of the patients with pneumonia and other lower respiratory tract infections.

The Barts and The London NHS Trust hospitals had total beds of 1172, 766,844 patients attended for treatment and admissions and had more than 19,000 routine respiratory tact cultures in 2004-2005. In the UK, there are many other hospitals with similar number of beds and admission for the period of 2004-2005. If other hospitals had routine respiratory tract culture rates similar to our institution (on the basis of number of beds, treatment or admission), between 2 and 3 million respiratory tract cultures would have been performed in 2000-2005. If 60% (Table 3.25) of the sputum samples from these cultures were poor specimens, 1 to 2 million poor specimens would have been sent for culture in 2004-2005. For the processing of these poor specimens, a total amount of between £10 and £12 million could have been used and wasted. Improving the adequacy of sputum specimens could therefore have a large impact on personnel time, expenditure, and timely diagnosis and treatment of patients with pneumonia.

For the impact on microbiology workload activities, the three day rule strategies have been introduced by the Barts and The London NHS Trust microbiology

laboratory to reduce the number of daily sputum specimens received for culture from each patient. This restrictive policy has been introduced and discussed with the clinicians and used routinely since 2006. This three day rule needed in order to reduce the number of duplicate specimens processed every day. When ever the microbiology laboratory received similar specimens collected within three days the microbiology computer will generate an information comments for the clinician requested the culture. The following comment will be sent immediately, the routine sputum culture on patients proceeded their sputum sample within last three days have not warranted, are not cost effective, and rejected by issuing notification comments to clinicians.

The effect of this three day rule and restrictive policy of sputum workup has been seen by the reduction of workload activities of respiratory tract specimens processed during the last benchmarking audit. The number reduced from 19,618 in 2005-2006 to 18,166 in 2006-2007. This certainly reduced the processing of inappropriate and duplicate sputum specimens by 7%. Similarly, the three day rule has been extended and applied to the other areas of routine microbiology specimens, such as faeces bacteriology culture.

For the clinical implications for the patients care**,** although timeliness of results reporting has not been a major focus in clinical laboratories, there is now increasing pressure from clinicians and government targets to report results rapidly and meet the reported TAT targets. Reducing turnaround time's strategies has been introduced for all microbiology tests against the department's published TAT. As a result of this strategy, the microbiology laboratory now routinely monitor monthly TAT and consider this to be an indicator of performance published widely to large users of the service. Barts and The London NHS Trust microbiology department has set the length of time that ideally it should take to issue a report depending on the specimen type. For example a positive sputum culture result should be available within three days but a positive TB result will take up to 44 days.

The Trust expects that 96% of microbiology samples will be available within microbiology laboratory stated TAT and therefore microbiology to monitor these on a monthly basis. It has looked at each bench/section or test type and used the traffic light system as shown in tables 1 and 2 in the appendix section. Currently whole departmental tests have an average TAT of 95% including respiratory tract

specimens. The service user's survey has reported 79% satisfactory with the TAT within the Trust pathology service in 2007.

The improving TAT that has been seen since 2006 where 60% of respiratory tract specimen culture results have now improved as compared to data obtained 2004-2005. One of the reasons for this improvement is due to the introduction of LIMS IT system known as the Winpath system in 2005 that has greatly improved the laboratory TAT. The Trust also implemented, in April 2008, a new CRS. This system will provide a full audit trail from specimen request, through collection, arrival in clinical pathology laboratories to the final result. It is hoped that by 2011 all pathology test requests will be paperless. Therefore, the use of technological advances has been embraced of at each step in the laboratory cycle.

In addition to these changes, Barts and The London NHS Trust microbiology laboratory has introduced MALDI-TOF technology in 2010 to reduce costs, TAT and increase the efficiency of the service (Eydmann et al. 2011). This technology has changed the way we think about microbial identifications and strain differentiation by providing results from plate to name in approximately five minutes for one isolate and around 90 minutes for 60 isolates at minimum costs. This has resulted in fast TAT and rapid identification of pathogens of public health significance such as multidrug-resistant bacteria (Van Veen et al. 2010, Eydmann et al. 2011, Wolk and Dunne Jr 2011).

Similarly, efforts by staff to reduce laboratory TAT, plus monthly monitoring of the TAT across the microbiology laboratory sections, has also resulted in reduced TAT. To further improve TAT the Barts and The London NHS Trust is in discussion on the implementation of a shift system in the near future. However, a short term solution is now operating for a late team to work extended time to process the late deliveries from BLT and from Newham Healthcare Trust which arrive after 5.30 PM.

As described earlier in Section 4.1, slow and increased test turnaround times can lead to duplicate test requests, increased hospital cost and patient's length of hospital stay and result in more unnecessary antimicrobial treatments and more microbiological test requests. Thus, improvements of laboratory test TAT is the key issue of current microbiology laboratory practice in order to provide appropriate laboratory service to service users.

Another strategy that has been introduced as a result of this study, was to improve the way microbiology test results are reported, and the value of microbiology results. It has been described previously that the results of this study highlighted the importance of value added reporting in clinical microbiology results, when compared to the traditional way of reporting in microbiology test results, which is report what you see and forget what is not appropriate.

BLT microbiology laboratory has now started to introduce an interpretative way of commenting on certain microbiology results. This will to lead an appropriate microbiology test reporting and interpretation. Currently there are selective reporting areas with normal bacterial flora and no significant results. There is a control of information based on patient's conditions and laboratory policy of appropriateness. There is now a limitation of reporting organisms, with no microbiological value and doubtful pathogens, which has grown from respiratory tract specimens. For instance there is no follow up and set up of susceptibility tests for organisms grown in sputum cultures such as coliform group, *Pseudomonas* species and coagulase–negative Staphylococcus species unless there is a clinical justification from the doctors.

Cultures with a clear predominance of a single potential pathogen relative to the oropharyngeal flora present would get complete identification and susceptibilities as appropriate. For the cultures with three or more potential pathogens, none predominating, mixed flora would be reported. In both cases this comment is issued with the report. "Further workup; contact the laboratory within 24 hours. Cultures having only organisms that are considered normal flora would be reported as normal respiratory flora".

Prior to this study the microbiology laboratory, like other NHS laboratories, used to report all the organisms that grow from sputum specimens. Few of the organisms that have been reported have a bacteriological significance, and the majority of these reported organisms could have been reported as throat flora or mouth flora.

In addition to this limitation of reporting, the microbiology laboratory has started using interpretation comments with respect to value of the culture results. It is used many areas of the laboratory including sputum culture, urine culture and blood culture. This will have an impact on the value of test results and help the clinicians to use the test results appropriately. It is important to ensure that the clinicians

appreciate they are receiving more clinically useful information than would be provided by raw microbiology laboratory data without interpretation comments.

This study has reported that there are many respiratory tract specimens that should not be processed due to delays of transport and processing of more than 48 hours. Since this study highlighted these problems, the department has introduced appropriate measures to minimise them. These measures include extending the microbiology laboratory opening hours in order to receive late collections from the health centres and the main hospitals as described earlier. The specimen collection times have been monitored and acted the reported delays as soon as possible and informed the concerned bodies.

Reducing specimen transport and processing delays has improved the quality of the specimen and the laboratory TAT. Currently the majority of all general specimens are now received in a scheduled time and transported into the microbiology laboratory in a good time compared to previous times. There are also another two new developments which contributed to the reduction of specimen transport; the lean system is now in operation at BLT pathology services, and all clinical pathology laboratories are housed under one roof with only one common specimen reception.

Currently, there is a good communication between the microbiology laboratory and its service users. The microbiology department of the BLT has taken all necessary measures to increase the awareness of the importance of clinical microbiology laboratory ordering process and forms between the healthcare workers have been applied, these measures included institutional user surveys, active enhanced communications, laboratory manuals, education and audits.

As a result of this study it was proposed that within the microbiology department at our institution, unacceptable sputum culture specimens would be rejected for inpatients, except those patients stated laboratory SOP, and ask that they be recalled. The initial specimen would be held refrigerated for up to 24 hours until a satisfactory specimen is resubmitted. Rejected specimens would only be processed by specific clinician or doctor’s request when clinically justified. If a specimen is rejected and not cultured, the sputum culture report will be issued with an appropriate comment to ordered clinicians.

The study results approaches were set up around the specimen management towards the clinical relevant and cost-effective microbiology service at the Barts and The London NHS Trust. However, these approaches could be easily amended and used to suit local practices in any NHS laboratory.

4.5 Cost implications to microbiology laboratory service

This study has found that the total inappropriate respiratory tract specimens processed locally was 9,575 and 2,153,977 nationally as derived figures from local NHS hospitals in 2004/2005. The associated total cost of inappropriate respiratory tract microbiology test use was £152,111 in local NHS hospitals and £23,903,652 in national NHS hospitals as derived data from local hospital. However, the follow up study in 2006, the cost of inappropriate sputum specimens were decreased from £56,936 to £29,443. As a result of this reduction, the local NHS microbiology laboratory has saved sum of £27,493 in 2006 after intervention strategies and staff educational initiates. Overall, the NHS laboratories can achieve more cost saving using the demand management rules and strategies that can be put in place to process appropriate clinical specimens and reject inappropriate specimens as present study suggested and advocated by many other researchers.

This study was initially designed to investigate and establish the cost of routine microbiological investigations in order to calculate the potential cost-savings when used the microbiology test appropriately. The result shows that the total cost of microbiology test may be higher than the cost stated the other sources; for instance, the cost of routine sputum microbiology investigation may be higher in this local NHS laboratory. Due to data confidentiality, the cost of local NHS microbiolology laboratory could not be discussed in this discussion. However, the author of this study believes that this is needed to inform national policy makers about the true cost of pathology tests and to inform the local NHS Trusts about possible cost reduction measures.

Although the true cost of pathology tests are not known, the other bodies compared the local cost data with other cost data sources, notable the Healthcare Commission's Report known as now Care Quality Commission (Healthcare Commission 2007), Lord Carter's Report (Lord Carter of Coles 2008) and the University of Keele Benchmarking Service (National Pathology Benchmarking Review 2008). These three data cost sources are very similar and their finding

shows that in the NHS pathology services there is a variation in cost. For example in clinical microbiology the variation cost is from £4.00 to £9.40, with a median cost of £6.10 (Lord Carter of Coles 2008).

The cost of pathology test is higher in London teaching hospitals as compared to the other teaching hospitals outside London. One of the main reason is they provide more specialist services and employ more medical staff as well as being in central London. This study tried to establish the true cost of microbiology tests using respiratory tract specimens; however, the study was unable to establish the true cost of microbiology tests. The cost of positive tests and the negative tests is equally priced/costed. The reason is that there is no official cost structure in the NHS clinical laboratories.

It has been well known for some time that the UK spends less per capita on healthcare than other European countries. What may be less well known is that the UK has had a pathology service where no one knows the cost per test in terms of the single test of microbiology, such as sputum culture and sensitivity. Due to this perspective, this study did not manage to obtain the true cost of microbiology tests. The reasons for these difficulties is thought to be associated with the lack of cost structure in the NHS pathology service. The lack of good and accurate cost information is the key constraint in obtained the correct cost. The pathology service running cost included microbiology service comes from the Local Strategic Health Authorities (SHAs) as a general budget for the whole hospital trust.

The Department of Health (DoH) is considering the introduction of a tariff for pathology services. The Government, hoping and anticipating that under this system a community tariff could set a level that reflects greater efficiency and lower cost achieved by larger networks following consolidation. Such a tariff should relate to the end to end service, which Lord Carter advocated in his second report. However, the providers who did not consolidate their service would become increasingly uneconomic according to the response from the service providers.

The use of data from respiratory tract tests appeared to reduce healthcare associated costs in our institution. Based on these results, the study estimated that potential savings of between 5 to 10% could be achieved. At a national level, this would be implying annual savings of between £130 and £210 million in total, based on figures for 2005. If savings from rationalisations of the test utilisation adapted

nationally these figures would be even larger. The cost reduction would increase when more samples are evaluated and cost-effectiveness determined and more cost savings will be achieved.

The Carter reviews (Lord Carter of Coles 2006., Lord Carter of Coles 2008) emphasise the need to save 10% of the pathology spending budget. The UK national budget for pathology amounts to some £2.5 billion per annum (4% of the NHS spending) which equates to an annual national saving of £20 million per annum in a climate where demand for diagnostic testing is rising 10% per annum over the years (Beastall 2004).

In order to ensure that savings can be made, it will be essential for the DoH, Pathology services, PCTs and SHAs to have tools that enable them to monitor and manage demand to ensure that uses of diagnostic services are focussed on appropriate testing, which is delivered equitably to the population. This is especially so given the new NHS commissioning arrangements. Such tools are needed because of the variation in requesting patterns and the concern over inappropriate testing raised by the current study.

The increased utilisation (test ordering) and workload does not match with the increased microbiology laboratory budget for testing increased workloads. This contributes financial uncertainty to the clinical laboratory. It has been determined that one half of the laboratory cost increase is the result of increased costs to perform the test, and half is due to increased utilisation and new services, not due to inflation. Further, authorities believe that 20-60% of laboratory tests may be unnecessary and inappropriate, and do not contribute to improved patient care (Bartlett 1974, Robinson 1994, van Walraven and Naylor 1998, Gopal Rao, Crook and Tillyer 2003). Therefore, changing test ordering practices without compromising the quality of patient care is an important aspect of cost-effectiveness in clinical laboratories.

Clinical laboratories, including microbiology laboratories, must adapt to these economic realities. Laboratory managers and supervisors must develop the skills to manage the laboratory efficiently and cost-effectively, critically analysing all stages of laboratory operations and making appropriate changes as needed. The challenge is to do this without jeopardising patient care. Significant reductions in pathology spend are possible without compromising patient care. This study

believes that there is a lot of wastage across the healthcare delivery chain, from clinicians through to the pathology laboratory services that had thus been identified and effectively addressed, would result in considerable savings.

The current study suggests there is a need for cost-effective strategies and changes to address this issue. Cost-saving strategies represent change, and change is typically met with resistance. Conflicts will inevitably develop in our changing environment regarding what comprises quality healthcare, as opposed to cost-efficient healthcare, and what financial changes are necessary from the hospital administration and from the clinical microbiology laboratory. The laboratory needs to take an important role in developing strategies that focus on desirable patient outcomes, yet limit unnecessary and inappropriate testing; otherwise, changes will be imposed that are not in the best interest of the patient. While it is true that times have changed and healthcare economics are different from years ago, quality patient care is still the goal, and cost savings in the clinical microbiology laboratory must address that goal.

This study suggests that cost control in the clinical microbiology laboratory can be achieved most efficiently if microbiology departments first sort their laboratory costs into discrete categories and then initiate reforms in each category. In addition to this, this study suggests to use the three (albeit arbitrary since there is no known true microbiology costs per test) cost categories described below (each is discussed in the next section, recommendation strategies).

1. Strategies related to the pre-analytical phase and patients testing which are the events that happen before the specimen is received in the laboratory. This includes utilisation (when/how/why tests are ordered), specimen collection, and specimen transport. Microbiology laboratories should particularly question their laboratory's utilisation practices by asking what test or tests should be requested, and how often? Are clinicians failing to request tests that actually should be ordered? Are clinicians ordering tests that do not contribute to patient care? Controlling utilisation (test ordering practices) is a crucial strategy for cost containment.

2. Strategies related to the analytical phase and laboratory technical operations which are the steps performed inside the laboratory after the specimen has been received. Questions to ask include what processing and reporting methods are being used? Does the laboratory assess the quality of the specimen prior to

culture? How extensively, how rapidly, and by what methods does the laboratory work up a specimen? Does the workup match the needs of the physician?

3. Lastly, strategies related to laboratory management operations, which are the methods used to analyse the specimen and compare it with others. Are laboratory resources (personnel and equipment) being used properly? Is the skill mix adequate for the laboratory? Does the laboratory know and monitor its labour and supply costs? Does the laboratory use automation properly and effectively? Is the laboratory productivity being monitored, compared with a reasonable standard, and other similar medical institutions? Should some laboratory work be transferred to another laboratory e.g. Virology or immunology laboratories? Should some tests be brought back into the laboratory? Are contracts with suppliers, vendors, and reference laboratories being evaluated for cost?

There is a trend to evaluate how laboratory personnel are used. One of the options is suggesting that a microbiology laboratory may reduce overall personnel expenses by hiring lower-qualified personnel, such as medical laboratory assistants, to perform non-biomedical scientist (BMS) duties. The negative side of reducing experienced microbiology BMSs is that they are hard to find again when you need them. Therefore, reducing the BMS staffing level is always “a no win” situation. There is another option, automation in the microbiology laboratory is often suggested as a means of reducing staffing, but in the opinion of this researcher, automation does not generally reduce staffing to the same extent it may in other departments of the clinical pathology laboratories such as clinical chemistry.

However, this study suggests that the use of the three day rule means there are additional practices that can reduce labour, materials, and overhead costs, including reducing the frequency of testing, reducing off-hour testing, reducing the on-call service, redistributing work into fewer workstations, and increasing the batch size. It should be kept in mind, however, that some microbiological tests can’t be delayed or postponed for technical reasons.

It is well known that microbiology is an expensive laboratory service because it is labour intensive. Staff salaries generally account for 60 to 70% of the microbiology laboratory’s operating budget. Most microbiology tests cannot be automated easily, so there is a direct relationship between workload and the number of Clinical Laboratory Scientists or Biomedical Scientists needed. The government’s pathology

tsar, Dr Ian Barnes, was recently reported in the *Health Service Journal* as arguing that pathology could save 15-25% of its costs by reducing the proportion of highly qualified staff that perform junior tasks (Dowler 2011).

Labour is the greatest expense in clinical microbiology laboratory technical operations. Most microbiology procedures are performed manually and certainly are not as automated as procedures in chemistry or haematology. Therefore anything the laboratory can do to reduce labour costs will help. The most conventional approach to cost reduction, especially by non-laboratory personnel, such as hospital administrators, is simply cutting some laboratory procedures and personnel. This approach, however, may affect quality and service.

From a cost effective clinical microbiology perspective, this study showed that using respiratory tract specimens, particularly sputum samples, to streamline the initial test appropriateness in microbiology would be associated with cost savings in our setting. However, cost-effectiveness of different microbiology samples and long-term effect on cost-effectiveness would show how more cost saving strategies in microbiology services could be effective. Moreover, difference in costs of microbiology samples and the proportion of evaluable and appropriate tests may lead to different amounts of cost reduction. Our estimation is an easy tool to calculate such cost-reduction.

4.6 Recommendations to reduce inappropriate test use

This study has found that there is inappropriate microbiology test utilisation happening in the clinical microbiology laboratories in similar patterns, as explained in the previous sections. Similar findings have been reported previously by other investigators, as reported in the review of literature in section one of the thesis. When further analysis of the results conducted and reviewed the practice of test utilisation in our local institutions and other similar clinical laboratories both nationally and internationally, as well as further analysis of current literature. It has been found that there is an existence of similar utilisation problems having with similar causes of inappropriateness. Therefore, in order to address this issue fundamentally, it is also very important to recommend common test utilisation strategies that are based on right test, right time and right patient.

If there is a mantra for clinical microbiology laboratory testing, it is “order the right test at the right time for the right patient.” The wrong or unnecessary test done well is no better than the correct and necessary test done poorly. Ineffective and inappropriate ordering of tests has a major impact on the operations of a health system, affecting the quality of patient care, infection control measures, formulation of local antibiotic policy, length of stay, hospital cost, pfa (priorities for action), target for reduction of infection (MRSA, MSSA, *Cl. difficile* etc) and liability of healthcare organisations.

This study also pointed out that many investigations are composed of too many individual tests as a routine, and that rational, cost saving protocols/algorithms/cascades are not always in place. A fundamental requirement, in which this study found on to stress, is that tariff structures on the cost of tests needed to be radically detailed. Similarly, while test utilisation management plays an increasingly critical role in the clinical laboratory, nationwide, implementation has been slow. Now pressure from accreditation agencies, local strategic health authorities and changing the diagnosis related groups (DRGs) is driving the concept with more urgency.

Managing inappropriate microbiology test utilisations needs to promote appropriate ways of laboratory testing and provide more responsive and accessible alternative services in the community so as to prevent unnecessary laboratory test utilisation.

The support of physicians and other healthcare professionals will be critical to the success, and therefore test utilisation management will have added clinical value. Microbiology laboratory test utilisation aims to provide useful clinical information in the diagnosis, prognosis, treatment or management of patients suffering from infections. Hence, this study would recommend the following test utilisation management programmes that should provide useful clinical information, and appropriate and effective use of laboratory services, not solely focused on cost or test reduction without regard to clinical impact, not hinder a clinician’s ability to care properly for a patient, and improve the two way communication between the service providers and users. To achieve these appropriate test utilisation programmes, the following strategies and programmes are required.

1. **Evidence-based guidelines:** The use of evidence-based guidelines and testing protocols or algorithms to support, define and standardise the quality of medical microbiology laboratory processes. Such guidelines must be monitored, controlled and improved continuously. This study is proposing that the clinical microbiology laboratories and clinicians must work together, because the laboratories alone cannot successfully promote evidence-based guidelines without the co-operation of the ordering clinicians. The following are critical: support and endorsement by the executive clinician management, physician ownership of the process, physician sponsorship of the programme, physician management of the process and IT infrastructure and support. Ultimately, it is the responsibility of clinical microbiology laboratory staff to help clinicians understand the increasing complexity of tests and microbiological test uses.

2. Devise guidelines on protocols: It is important to devise guidelines on protocols for specimen procurement for the medical staff, since all cost-generating procedures and inappropriate tests originate with a physician's order. Some medical centres have established "best practices" or "clinical pathways" for physicians to follow. The teams that develop the clinical pathways are composed of physicians, nurses, and laboratorians. They should create a policy for specific microbiology laboratory testing protocols depending on diagnosis and/or clinical indications. These should be hospital-wide teams to reduce the confrontational component when utilisation is changed, as well as ensure that the clinical pathways agree with current medical practice.

Clinical pathway policies should include the best test to order, the number of specimens accepted per individual site, and how to properly collect and transport specimens. These policies set limitations on testing and specimen collection frequency, and contain clearly defined rejection criteria for the medical and nursing staff. These policies may also indicate tests the physician overlooked that might facilitate a rapid diagnosis. The goal of clinical pathways is to obtain the correct specimen and request the correct test. Laboratory utilisation in some medical centres has been improved by soliciting the support of Infectious Disease Physicians, hospital pharmacists, clinical microbiologists, and the chief of medicine. In the future, these clinical pathways or utilisation guidelines for each diagnosis will become the standard of care.

3. Establish an on going education programme: It is important to establish an on going education programme in order to keep knowledge of emerging micro-organisms, new microbiology laboratory techniques, antibiotics and emerging resistance up to date. To achieve this, modifying teaching of clinical microbiology is required in medical schools and at Universities. More emphasis should be placed on the practical aspects discussed above, especially in later clinical years, or during internship. Sessions in the diagnostic laboratory would be ideal. This will give the medical practitioners an insight into the working of the laboratory, will emphasise the importance of good specimen collection and improve their interpretation skills.

This study recommends that, if changing utilisation of the microbiology laboratory is to succeed, the impetus for this education programme must be envisioned by all participants as a cooperative educational venture. The educational design should be informational, not punitive. As stated earlier, in-service education of the medical staff may be one of the most important mechanisms of implementing effective changes in laboratory testing practices and providing specimen guidelines. It is imperative to get physician participation and involvement in the development of laboratory testing algorithms (pathways). If these guidelines are totally dictated by the microbiology laboratory they will fail. Physicians who do not understand the testing rationale may cost laboratory staff time and money in explanations, repeated tests, and stressful interactions. Cost containment alone cannot be used as the sole rationale for a cost containment programme. Instead, it is important to emphasise the improvement in the quality of care that will occur as a result of reducing over-utilisation, under-utilisation, and miss-utilisation of microbiology laboratory tests.

This study also recommends that good microbiology laboratory orientation programmes and frequent in-service sessions are a must for cost effective and relevant clinical microbiology. It is necessary to provide appropriate documentation for the changes microbiology laboratory propose—citing, for example: in-house laboratory data; Q-Probe data from the College of American Pathologists (CAP), CPA regulations; or recent research publications. It has been found it is effective to discuss laboratory policies at medical staff meetings. In-service presentations to small groups of physicians also seems to work well. Teaching tools, such as PowerPoint presentations, are beneficial; physicians are accustomed to this format.

4. Nursing staff training: In-service training for nursing personnel is crucial. It is important that nurses feel they are part of the solution, rather than to feel the microbiology laboratory is dictating to them. Nurses are often the ones to order the test, obtain the specimen, and submit the specimen to the clinical laboratory. Their buy-in is essential. Nurses can often represent the lab “de facto” because they interact with the physician more than the microbiology laboratory personnel. Clearly, a new role of the microbiologist is to be a resource to physicians and nurses, and laboratory managers and supervisors can only do this by getting out of the laboratory to interact with other hospital personnel, particularly the nursing staff.

5. Screen specimens for quality: It is essential to screen specimens for quality. Physicians often require guidance on the most appropriate specimens: how to collect them, the frequency of their submission, and methods of ensuring specimen quality. Also, physicians are often unaware of the detrimental effect on specimens of contamination with indigenous microflora. Therefore, the microbiologists need to provide information to the physicians. The concept that physicians can submit specimens and laboratories will run the requested tests without question is no longer valid. Specimens that are not collected or transported properly, even when handled optimally within the laboratory, are likely to provide misleading results, causing the physician to act on incorrect, misleading, or irrelevant data. Assessing specimen quality should be thought of as providing an essential service to the physician, and to the patient.

Once the specimen has arrived in the laboratory, the staff needs to screen the specimen (wounds and sputa for example) by Gram stain or gross appearance, to see if the specimen is adequate for culture. Further, the laboratory must ensure the proper storage of the specimen. A urine sample with just a few colony-forming units (CFUs) of bacteria left out at room temperature could easily yield a colony count that may be considered significant. This may necessitate full and expensive identification and susceptibility testing, and/or incorrect therapy, adding not only to laboratory costs, but also to overall hospital costs. The inappropriate storage of sputum specimens can result in the normal respiratory microbiota overgrowing potential pathogens and yielding misleading information.

6. Changing physician ordering practices: It is important to address the physician’s test ordering practices and behaviors**;** however, this changing is one of the most controversial and difficult tasks for the laboratory, because many aspects

of utilisation cannot be controlled directly by the clinical laboratory. Requesting unnecessary testing is a deep-rooted problem stemming from the early training of physicians; the pressure to test for unforeseen problems, and the fear of criticism for failure to consider certain unusual diagnoses. Also, unnecessary tests may be ordered because of academic curiosity, defensive medicine, and the fear of litigation. Often, attempting to change a physician's ordering practices leads to confrontation and unpleasant situations. It has been suggested that the place to actually start changing physician-ordering practices is with the physicians-in-training, rather than with currently practicing physicians. It may be easier to change the behavior of house officers, registrars, and fellows by performing audits and in-service training when physicians are employed by medical centres than when they have their own practices.

However, this study believes that microbiologists and clinicians may have different perceptions of what constitutes rational and necessary laboratory testing. In the clinician's view, a good microbiology test might be one that provides useful clinical information quickly. The microbiologist may recognise that such a test is labour-intensive, requires huge outlays of equipment or supplies, and is very costly. However, if the clinician believes this is the only way to make a diagnosis, then the test is justified to the physician. The differences between a clinician's and a microbiologist's perceptions and attitudes are important factors to consider when attempting changes in microbiology services.

7. IT infrastructure and support: There is a need for good hospital-wide and health centre computer system. One of the initial forays into utilisation management problems is due to a lack of system-wide computerised physician order entry (CPOE) in which clinical microbiology services and other clinical laboratories will need to be selected as test utilisation strategies that can be easily implemented and used.

A good hospital-wide computer system is essential to help reduce the frequency of laboratory testing and to improve utilisation. Physicians may be willing to abandon daily test-ordering if they are convinced that updates on the one culture specimen they sent in will be provided early each day, and that all clinically significant changes will be brought to their attention or flagged. The physician may not realise, for example, that multiple samples have been previously submitted, but a good

computer system will alert the requestor to them. Further, the initial requesting process is the ideal place to let the physician and other medical staff know about laboratory policies and guidelines for specimen submission, frequency, and transport. The laboratory's requesting system must provide clear definitions of what information, and exactly what specimen, is required. For example, a physician's request for a generic "wound culture" is not satisfactory. It fails to provide the microbiologist with adequate information for culturing procedures, resulting in inadequate results for the physician to evaluate. What is needed is a notation of the exact specimen source and location, for example, "abdominal surgical drainage", so that the specimen may be cultured appropriately.

8. Encourage communication: it is very important to encourage communication between the clinical microbiology laboratory, the physicians and with other healthcare professional to maximise the use of the microbiology services in management of infectious diseases.

Reviews of the literature and the personnel experience of this study author shows that it is easy to suggest these stated recommendations and restrictions, but harder to implement them. Therefore, it is recommended to implement the restrictions and changes slowly. As reported earlier, use of computer information flags that appear whenever someone tries to order these tests, hold in-service sessions with physicians and nurses to ensure everyone is informed. One of the ways to enhance good communications between service providers and service users is the use of posters and publishing a clinical microbiology newsletter, which conveys the appropriate laboratory utilisation and changes in the practice of laboratory medicine.

Some of the clinical relevant and cost-effective suggestions offered in this study may not apply to every microbiology laboratory. However, the strategy behind them, trying to generate essential laboratory information at a reasonable cost, is universal. As laboratorians we must change many of our approaches and thought processes. Change is uncomfortable. However, to be clinically relevant and cost-effective in the new healthcare environment, change we must. The modern medical microbiology laboratory should offer a comprehensive diagnostic service, designed to optimise specimen collection, to ensure quality of processing and to assist with the interpretation of microbiology reports.

Since the beginning of this study, the NHS pathology service has been undergoing major changes through reforms, the effects of the economic 'squeeze' and re-organisation of the service. The new Health and Social Care Bill will lead to a further intensification of these changes.

4.7 Conclusions

Sputum is the most common lower respiratory tract specimen received by the microbiology laboratory. It is also often the most problematic to assess due to contamination by oropharyngeal flora. In spite of numerous guidelines on appropriate samples for microbiological examination, laboratories continue to receive a large number of inappropriate sputum samples.

The aim of this study was to determine the appropriateness of clinical microbiology test utilisation, evaluate the clinical relevance, cost-effectiveness, specimen management and recommend better utilisation strategies. Respiratory tract specimens were used as an example and quality indicator for the examination of the total testing process.

In conclusion, this investigation has accentuated the real need for clear appropriate information, especially for test requisition, adherence to specimen collection principles, laboratory compliance with the standard operative procedures (SOP) and the use of interpretative comments to assist clinicians in interpreting microbiology test results.

From the results of the present study, it has been learned that clinicians and other healthcare professionals utilise the clinical microbiology services inconsistently, often by sending to the laboratory inappropriate specimens and test requests, as summarised below.

- Analysis of the findings showed that the usefulness of culture results was limited by the collection of inappropriate specimens and lack of clinical information on the microbiology request form.

- The crucial importance of the role of clinical and nursing staff is stressed if the clinical relevance of sputum culture is to be maximised.

- The increasing introduction of electronic pathology test requesting, gives new opportunities to restrict the collection of inappropriate specimens and make substantial savings in resources, both in the wards and the laboratory.

- In order to address this issue of inappropriate microbiology test utilisation, it is very important to recommend common test utilisation strategies that are based on right test, right time and right patient.

During the course of this study project the pathology service has undergone several changes and challenges, both locally and nationally, which has impacted and influenced the services of clinical microbiology laboratory. Challenges in healthcare that affect clinical microbiology are taking place on multiple levels. These challenges include changing infectious diseases, patient demographics, medical environments, technological revolution, economic environments and work force.

Changes in infectious diseases are directly affecting the practice of clinical microbiology. Newly emergent pathogens are playing an increasingly important role in the healthcare management of individuals and populations. The changes in patient demographics that most affect clinical microbiology are the increases in the populations of patients with greater susceptibility to infections. The aging of the population in the UK, Europe, USA and worldwide has increased the proportion of elderly patients who present with a broad range of new infectious problems caused by their declining resistance to infection. The change in the medical environment is particularly apparent in the increasing emphasis on evidence-based medicine and the use of guidelines. The emphasis on evidence-based diagnostics and the proven impact of diagnostic interventions on patient outcome will also put further pressure on clinical microbiology to prove its cost-effectiveness and clinical relevances.

The financial constraints imposed upon the healthcare providers are also influencing the practice of clinical microbiology. Driven to implement post-Carter recommendations, there is an expectation that significant savings, in the region of 20%, can be made by consolidating pathology services and so benefiting from economies of scale. The NHS, as a purchaser of healthcare, wants more value from pathology testing to optimise the cost-efficient use of the available resources. However, it is a challenge to understand and control the microbiology test costs because of there is no cost structure in the NHS, both nationally and locally, as

current study has revealed. Pathology modernisation also has an impact on the organisation of clinical microbiology laboratories. Two kinds of response are already clearly visible. The first is the consolidation of separate laboratories into bigger entities via mergers, acquisition of smaller laboratories by regional large laboratories, or the formation of networks. A second possible response is to streamline different sub-speciality laboratories into unified and integrated large-scale laboratories.

For the changing technological revolution, microbiology laboratory automation is emerging and processes are done faster than ever with more standardised and comparable tests. The introduction of MALDI TOF into the diagnostic microbiology laboratory has greatly reduced the time for identification of bacterial and fungi, and allowed the rapid identification of bacteria directly from blood cultures. There is a possibility that the trend toward increasing automation will reduce the need for highly trained microbiological staff. Thus, a technical workforce with less training could comprise a larger part of the clinical microbiology workforce. It is a matter of debate whether this will have an impact on the quality of the service. The introduction of, for example, molecular techniques, with their potential for miniaturisation and automation, will only strengthen this trend. However, Modernising Scientific Careers (MSC) will provide new education, training programmes and opportunities for scientists at a higher level.

The introduction of the National Laboratory Medicine Catalogue (NLMC), which the NHS will be testing in July 2012, will revolutionise pathology services in the way pathology tests are requested and reported in the UK. The activity of the clinical microbiologist would be towards the evaluation and interpretation of tests, including the determination of their sensitivity, specificity and predictive values; communication of results to clinicians, in particular, infectious-disease specialists; advising on antibiotic therapy and sampling strategy in conjunction with infectious-disease specialists; following trends in diseases epidemiology and reporting these trends to infection control teams.

The vision for the new NHS pathology service is modernising pathology which will create an efficient, lean and cost effective pathology service, managed and run by highly skilled healthcare scientists, who have knowledge and expertise in healthcare science and an understanding of the business of healthcare. From April

2013 clinicians will lead to the commissioning of clinical services, including community pathology.

The final conclusion from this study is that the microbiology specimen's management is the greatest challenge facing current and future microbiologists due to the nature of microbiology specimens and the process ranging from the collection to the reporting of results. This type of study and audit can give invaluable information about the rationale behind testing, and the appropriateness of sampling and transport time. Appropriate measures for corrective actions can be identified and implemented.

4.8 Future work

The data collection of this study was not designed to capture the entire process, from test ordering, specimen collection, storage, transport, processing to test reporting. To assess the impact on the total test process and generate new evidence, there is a need to investigate the entire current practice of clinical microbiology laboratory test utilisation from test order to test report. An academic analysis of current test-ordering practices might suggest that further research is needed into why doctors order tests the way they do, whether there really is such a high rate of unnecessary testing, and what value current ordering patterns add to our highly complex healthcare system. A pragmatic view, however, would suggest that there is enough published evidence that over-testing is a characteristic of healthcare systems in the developed world, and enough information in existing research to guide what should be done to reduce waste and harm resulting from inappropriate testing.

A multidisciplinary audit needs to be developed by a team of healthcare professionals (microbiologists, nursing, infection control, physicians, hospital managers etc) to assess the impact of sputum culture results on patient's outcome to improve quality of care and to reduce overuse of antibiotics.

Few studies have examined the relationship between macroscopic appearance and sputum specimen quality. Therefore, there is a need for further research work on the reliability of sputum macroscopic examination prior to sample processing in the microbiology laboratory, and its value in terms of cost or outcomes.

It is time that the focus of work in this area shifted to the development of practical, sustainable means of improving the appropriateness of testing. Future research may be best directed to understanding the place of sophisticated decision-analysis models, the role of point-of-care guidance and feedback systems, and effective clinical change-management strategies. As the UK grapples with the problem of funding healthcare due to the financial crises taking place around the globe, further research on cost effective microbiology laboratory practice in all areas of the microbiology laboratory should receive high priority.

Chapter 5 Professional and personal reflection

5.1 Introduction and reflective learning

5.1.1 Introduction

This part of the thesis describes the benefits of learning through reflection as part of a work-based professional doctorate study programme. The section is presented in two parts: The first describes the framework for reflective learning in higher education with reference to professional doctorate pathways and reflective practice. The second is an account of my own reflective learning, based within my academic context as a work-based doctorate student, and in my professional context as a Senior Biomedical Scientist and Microbiologist working in the hospital microbiology laboratory of one of the UK's largest teaching hospitals, Barts and The London NHS Trust. The journey of moving through a doctoral programme can be tedious and tiring. The personal journey of this particular doctoral student was weighted by the time and energy it has simultaneously taken to maintain a full time job, be an active participant in a 20 year marriage, and be a loyal, devoted and involved parent of five active teenage children, as well as keeping my present job through relocation and three recent restructuring processes that have taken place in our NHS Trust during this doctoral course.

5.1.2. Work-based learning and higher education

Traditionally, universities are viewed to conduct research to build up a body of knowledge that is then taught as a 'truth'. In this model, the subject matter knowledge is the defining characteristic. Students follow an existing curriculum. The content is fixed and determined. The methodologies used are disciplinary. The learning is individual. Problem solving is academic and timeless. The workload is uniform and fixed by the university. Learners attend an educational institution on a regular basis, or study from home. They sit examinations or complete set assignments. Reflection on learning occurs unintentionally and is non systematic. According to Costley (Costley 2000), this model has been questioned for some time.

When I started the professional doctorate programme, I had discovered that work-based learning represents a relatively new way of organising and learning in the

academy. It does not arise directly from the disciplinary frameworks in which knowledge has been traditionally ordered within the university, and in many instances it exemplifies more local knowledge, flowing from the particular spatial and temporal circumstances of work contexts and situations (Boud 2001). The content is flexible and individually determined. Knowledge is derived through a multidimensional, inter-professional, work-based frame of reference. It is constructing not absorbing knowledge (Costley 2000). Work-based learning is concerned with the knowledge gained by doing work and aims to be developmental for the practitioner, purposeful for the community of practice and useful in its contribution to academic learning and the knowledge stored in higher education. Work-based pedagogies focus on the creativity and reflexivity of individuals within a work-based context rather than the learning of a set syllabus (Costley 2000).

The methodologies used are transdisciplinary, applied and exploratory research methodologies (Boud 2001). They are influenced by contextual factors, the individual or community of practitioners who undertake practitioner research and development in organisation learning (Costley 2000).

5.1.3. Learning a new language, reflective learning

At the start of the doctoral programme, I had never heard of reflective learning. I soon discovered that reflection is an integral part of higher education work-based learning programmes. Since then, I have internalised this language to the extent that today, I can explain what I was unable to explain before I started the doctoral programme.

I have discovered that students in higher education are responsible for their own progress as independent learners. They take notice of and act upon formal feedback from their lecturers of course, but it is also important that they themselves think about (or reflect on) their learning. Numerous learning theories emphasise reflection as a key element of the learning process (Kolb 1984, Honey 1986). Increasingly, programmes of study explicitly require students to do this. Reflective learning is an integral part of work-based learning. In simple terms, reflection can be seen as ‘consciously thinking about and analysing what one has done (or is doing)’. It is a structured way to reflect upon one’s learning, to understand one’s learning processes, and thus allow becoming more autonomous. It is exploring one’s experiences of learning to better understand how they learn, ultimately with a

view to improving their further learning. During reflection-on-action (after you have done it) the learner looks back over an experience and reviews what was learnt. Reflection-in-action (while doing something) involves understanding new concepts through improvisation and experimentation during an exercise or experience (Schön 1983, Schön 1987).

Learners can develop into reflective learners by using methods such as creating a learning diary or portfolio, keeping reflective notes, making constructive use of feedback from advisors, consultants, examiners, etc., thinking positively about moving themselves and their skills forward (Cottrell 2003a, Cottrell 2003b). Engaging in reflective learning allows analysis of one's experiences and facilitates learning from this experience. It encourages critical thinking, and a questioning attitude and it promotes professional competences by encouraging recognition of mistakes and weaknesses.

5.2 Personal learning and reflection

5.2.1 Developing professionally

My motivation and interest in this doctorate has two dimensions. First, as a healthcare professional and healthcare scientist, I need to update and develop my knowledge to be able to perform to "best possible practice" for the benefit of the patients and their clinicians. Today there is an increasing demand that the clinical laboratory scientists have to take responsibilities and lead the service of clinical pathology. Second, to engage in lifelong learning and to gain additional skills, especially research and advanced qualifications. I started this programme of Doctor of Biomedical Science to develop my knowledge on the subject and to develop my professional practice.

The professional doctorate programme requires that candidates engage in reflective and planning activities explicitly during the early stages of their programmes through a review of their previous learning and the development of a detailed programme plan. These provide a foundation for the professional projects that candidates go on to undertake and engender a critically reflective stance from the outset.

When I was first asked to systematically undergo a reflective review of my previous learning as a biomedical scientist and doctoral student, I felt uncomfortable in doing so, I even felt it was irrelevant to what I intended to do in my studies, and I started, reluctantly, to describe and record my previous learning. I gradually started to identify the knowledge I have acquired during the years, skills, abilities and competencies. I learned to analyse, synthesise and evaluate it. The results were amazing and truly surprising to me. Although I knew I had worked and studied consistently all my life, I had never really realised what and how much I had done, had learned, and had developed in being able to do. I found it hard at the beginning to present all these in a comprehensive and cogently argued way, but by doing so, I gained this skill too. When I went through my previous learning and I recorded what I had previously done, what I had gained in terms of knowledge, skills, experiences, and capabilities, what I have accomplished, it was only then that I realised how that formed a solid background for my doctoral research studies and project, and it was only then that I realised the benefit of this activity.

I also undertook taught components of the course, such as professional review and development, advanced research techniques, publication and dissemination, the proposal for professional research and development. This also involved reflective learning and a presentation of course activities. During this module, I had to keep a learning diary as an ongoing record of the insights I gained in research, and write an overall reflection and evaluation of my learning at the end of the notes.

The module involved understanding the philosophical and theoretical issues in the professional doctorate, practitioner-led research, knowledge of appropriate methods, and their limitations and uses. It also included sessions aiming to enable all candidates to design and undertake research at doctoral level, devise and use appropriate research instruments, critically understand ethical issues in a range of contexts and be able to appropriately use approaches and tools in these contexts. I reviewed, evaluated and critiqued research approaches and methods in various contexts and selected and justified the selection of research methods chosen for my project work using research and development experience gained from the taught components.

The knowledge and skills acquired during the taught component were invaluable whilst writing up my doctoral thesis. For instance, critical evaluation of papers used as reference was enhanced through the advanced research techniques unit; this

facilitated more informed choices of which bibliographical sources to use for my reference and the review of the literature. My research project resulted in the presentation in academic meetings such as a short paper presentation at the IBMS congress in 2007 (Appendix 5.1). The presentation skills and experience gained from the Publication and Dissemination unit have helped me to present research findings to a wider audience.

At the end of part one of the course, I had achieved most of the knowledge and key skills that are required for the doctoral research project. The research project was work-based and professionally relevant. I have further learned more important skills. These skills included research methodology, data collection, data analysis, record keeping, critically thinking, project management and computer skills and other key transferable skills. I have also acquired a basic understanding of the fundamentals of financial management in healthcare facilities and the principles of medico-economic evaluation of laboratory tests. These tools, skills and theories, and the type of language to use were useful in the review of literature, discussion, evaluation of research findings and evaluation of the impact of the research on professional issues and implications on clinical pathology service. My supervisors provided me with valuable guidance throughout the course, on research project, the thesis preparation and final writing up.

5.2.2 Acquiring proficiency as a researcher

The second aspect I want to reflect on is my personal growth as a researcher. The research programme gave me invaluable experience in a work-based research project. I identified the overall direction of the research programme and the topic for my work-based project. I justified the relevance of both my own interests and those of my organisation, and professional field. I evaluated the ethical implications of my proposed project. I described and justified my choice of approach and methods for data collection and analysis using MS Excel.

I justified the feasibility of the project, indicated how the project was to be led and managed, and provided a realistic action plan for it. I produced a project proposal which took account of relevant professional and organisation issues (financial, human, etc.) necessary to complete the work-based project. I identified, and gained authority to use the resources necessary to complete the work-based project. I wrote a coherent learning agreement, which contained a summary of all

components of the intended programme, and a detailed project proposal, and I had a successful face to face discussion with the university faculty members about the importance of the topic of the project and research question. I explained the leadership role I intended to fulfil in the proposed project.

Reflection on and in action became a continuous valuable tool in this process, as previously explained in section 5.1.3. It made things clearer and pulled things together in a logical manner. It also drew my attention to the possible difficulties I would face during my research project, and made me start thinking about possible ways to address them. The intention here was to understand the project idea myself by working with meaning, which is deep approach (Entwistle 1996).

My research project involved the appropriateness of clinical microbiology laboratory investigations, and I had conducted a retrospective study of the cost and clinical relevance of microbiology specimen management and processing. The aim of this investigation was to determine the appropriateness of clinical microbiology test utilisation and evaluate the clinical relevance, cost-effectiveness and hence recommend better utilisation strategies. The key areas that my project was involved in have been stated and described in the previous sections of the thesis. However, the concept of the project was to provide valuable research information to establish an optimal clinical microbiology service based on the following concepts:

1. Good microbiology is clinically relevant microbiology (appropriate utilisation).
2. Exhaustively good microbiology may produce irrelevant or even misleading information (medical value of a laboratory test).
3. Good microbiology results only from a well collected, high quality clinical specimen, transported appropriately and received in a time frame that ensures proper testing (“garbage in, garbage out”).
4. Microbiology must be practised in a way that ensures adequacy of resources so that what needs to be done can be done without compromising quality (cost-effective microbiology).

During my research project I continued to keep a record of my reflective learning. I used the following methods: I kept notes during the project and I included reflective comments in my notes regarding the project investigation and writing up, taking into consideration the project expected outcomes and the formal programme criteria.

These reflective comments helped me to learn from experience and make sense of that experience. I made constructive use of feedback from my supervisors, microbiology consultant, staff and other stakeholders.

5.2.3 My personal reflections

Thinking back, I realised that following the University of Portsmouth work-based doctoral programme provided me with the opportunity to learn, as a lifelong learner, through equal and open access to high quality learning opportunities. Through the work-based learning, required by the nature of the doctorate programme, as a way of university level learning in the workplace, I was given the opportunity to (a) pursue academic research project study grounded within a work context and (b) to enhance the effectiveness of the clinical microbiology optimal test utilisation. I had the opportunity to be researcher in both my practice and profession. As an insider researcher, I learned to manage work and doctoral research projects together. I combined the work-based research project philosophy with that of demand management and appropriate test utilisation in clinical microbiology disciplines in the area of standardisation of laboratory rationalising. I also had the opportunity to introduce the concept for introducing a more interactive laboratory service. I established the needs of appropriate clinical microbiology test utilisation strategies, which were greatly needed by my workplace, and constituted as evidence of my work-based project. As a result, I gained knowledge, skills, abilities and experience in reviewing the existing microbiology laboratory test practices and establishing needs.

At the same time, I also learned how to lead a work-based research project in a busy NHS hospital staffed with more than 100 staff members (biomedical scientists, clinical scientists, specialist Microbiology registrars, consultants, faculty members, medical laboratory assistants, student, office personnel, and administrators) with constant work pressure issues. I have learned how to deal with unexpected complications of the project, find solutions to problems, make decisions, take responsibilities, negotiate, present and discuss the project progress and results.

I also learned to accept that some people are not prepared to accept something that does not suit them at the time, and as a result they can be difficult to work with. It can be very disheartening to continue working on a research project with such people. I learned to accept ignorance and tried to ‘educate’ stakeholders gradually

and as much as possible. I learned to accept that work-based research is a hard environment to work in because researchers have to prove themselves to many different people (colleagues, managers, fellow researchers, various microbiology consultants, ethical committees, and other stakeholders). Despite all that, I learned that at the same time, work based research is meaningful, motivating, challenging and worthwhile. This critical reflection on my practice, and that of team practice and development, enabled me to clearly identify achievements and strengths, recognise areas of weakness and make improvements. It helped me develop a more systematic awareness of all these. I learned to be responsible for my own learning, be autonomous, and practice continuous reflection on my learning experiences.

The professional doctorate programme has improved my knowledge of all aspects of clinical microbiology laboratory service, and I also feel that my exposure to work-based research projects will help to keep my options open as to possible career paths. It was great to meet other people from varying backgrounds working in the NHS or other organisations. Most of my intakes were other healthcare professionals with varying backgrounds and experience, including Chiropractics, Medical Imaging, Nursing and Pharmacy.

As for my work experience and professional developments, I feel so blessed for the opportunities that I have been given during the course. I have learned so many valuable skills that I will be able to use in future endeavours. I feel that I have not only gained knowledge, skills, experiences and capabilities during my studies, but I have also continued to do so in recent years. Through continuous work, improvement and implementation of the project outcome, through the feedback I keep receiving from colleagues and supervisors, and through continued presentations of various aspects of my research results, including journal club, academic meetings, etc. This experience has taught me leadership skills, project management skills, the importance of teamwork, and effective communication skills.

The most significant part of my experience truly was working with my supervisors, mentors, colleagues and students of Portsmouth University. The professional doctorate programme has granted and rewarded me with better professional skills, greater confidence and a large step toward my education growth. Part of my research project has involved cost effectiveness of the microbiology tests. Thus, a thorough understanding of how UK healthcare services is organised and funded

made me aware of the competitive changes that pathology services have undergone, as well as the current trends and developments taking place in the microbiology profession. I can better understand the priority and importance of healthcare economics in the current financial situation.

5.2.4 Reflective conclusions

Becoming more reflective has helped me to achieve a better understanding of my own practice and an improved level of performance. Undertaking the DBMS has radically altered my professional practice and has enhanced my professional confidence and analytical abilities. The undertaking in research project and writing up the thesis became a fundamental and transforming process in my life, both professional and personal. Undertaking the DBMS enhanced my confidence and also my credibility, which gave me the time to think and forced me to articulate my ideas and to think analytically. The DBMS fundamentally changed my whole professional life; it was transformative and I would never have done a PhD, which seemed too academic. But the professional doctorate programme has really taught me to do research and to be interested in a much deeper approach to my practice and to carry out a research project based on professional practice to gain additional qualifications. Completing the programme allows me a sense of personal satisfaction as well as the knowledge that allows me to be a better microbiologist.

I can note two major contributions of this research project: to research in general and to my work organisation in particular. In theory, it offered new knowledge for highlighting the fact that there is a need to enhance the key concepts of microbiology specimen management, clinical relevance, cost effectiveness of diagnostic tests and optimal utilisation of the clinical microbiology laboratory service. The study gave invaluable information about the area of uncertainty between the clinician and the laboratory, and can identify appropriate measures for corrective action.

In practice, it provided change and improvement in the existing microbiology laboratory practice by developing and implementing improvement opportunities to ensure accuracy of test results, to improve quality of care and reduce unnecessary testing. Improvement opportunities that were identified to meet this goal focussed on reducing specimen delays, processing of poor quality sputum, reducing

microbiology test TAT, reducing unnecessary workload and cost, introducing test result interpretation comments and establishing new concepts which reduced costs and TAT.

On reflection, I was very pleased that such a positive outcome resulted from my contributions and research. It is my hope that the material that has been presented in this thesis demonstrates an ability to move forward with that goal, an ability to "stick to it" and see the project through from beginning to end. It is my hope that all who view this project and the accompanying materials will feel the same.

References

Ackerman, V., R. Pritchard, D. Groot Obbink, R. Bradbury & A. Lee (1980) Reporting practices of microbiology laboratories. *Journal of Clinical Pathology,* 33**,** 830-835.

Anon (2012) Reports - Understanding the value of pathology: The ultimate goal. *Biomedical Scientist,* 3**,** 157-159.

Aronson, M. D. & D. H. Bor (1987) Blood cultures. *Annals of Internal Medicine,* 106**,** 246-253.

Audit Commission. 1993. Critical Path: An Analysis of Pathology Services. London, HMSO.

Axt-Adam, P., J. C. Van der Wouden & E. Van der Does (1993) Influencing behavior of physicians ordering laboratory tests: a literature study. *Medical Care,* 31**,** 784-794.

Bareford, D. & A. Hayling (1990) Inappropriate use of laboratory services: long term combined approach to modify request patterns. *British Medical Journal,* 301**,** 1305-1307.

Barenfanger, J. (2001) Clinical Microbiology Laboratories Can Directly Benefit Patients-The effects of clinical microbiology labs on patient care and costs are often overlooked but can be quantified by the. *ASM News-American Society for Microbiology,* 67**,** 71-77.

Barenfanger, J., C. Drake & G. Kacich (1999) Clinical and financial benefits of rapid bacterial identification and antimicrobial susceptibility testing. *Journal of Clinical Microbiology,* 37**,** 1415-1418.

Barnes, I. & G. Batstone (2012) NHS to test new pathology data system. *The Guardian, 31 January*.

Barnes, M. (1980) Influence of laboratory reports on prescribing of antimicrobials for urinary tract infection. *Journal of Clinical Pathology,* 33**,** 481-483.

Baron, E. & L. Peterson (2001) Laboratory Response to the Challenge of Today's Medical Care Environment-Using the Laboratory Cost-Effectively to Enhance Patient Care. *Current Clinical Topics in Infectious Diseases,* 21**,** 172-189.

Baron, E. J. (2011) The Role of the Clinical Microbiology Laboratory in the Diagnosis of Selected Infectious Processes. *Journal of Clinical Microbiology,* 49**,** S25.

Baron, J. M. & A. S. Dighe (2011) Computerized provider order entry in the clinical laboratory. *Journal of Pathology Informatics,* 2.

Barr, J. (1999) Clinical laboratory utilization: Rationale. *In B.G. Davis, D. Mass, and M.L Bishop (ed.). Principles of clinical laboratory utilization and consultation. The W.B.Saunders Co., Philadelphia, PA:***,** 3-16.

Barr, J. & G. Schumacher (1995) The total testing process applied to therapeutic drug monitoring. *Therapeutic Drug Monitoring. Norwalk, Connecticut: Appleton & Lange*, 47-82.

Barr, J. & S. Silver (1994) The total testing process and its implications for laboratory administration and education. *Clinical laboratory management review:* official publication of the *Clinical Laboratory Management Association/CLMA,* 8, 526-542.

Barrett-Connor, E. (1971) The nonvalue of sputum culture in the diagnosis of pneumococcal pneumonia. *American Review of Respiratory Diseases,* 103, 845-8.

Barth, J. & R. Jones (2003) Indiscriminate investigations have adverse effects. *British Medical Journal,* 326, 393.

Bartlett, J. (2010) Respiratory infections in the community: evaluating current antibiotic options. Introduction. *The American Journal of Medicine,* 123, S1-S3.

Bartlett, J. G., S. F. Dowell, L. A. Mandell, T. M. File Jr, D. M. Musher & M. J. Fine (2000) Practice guidelines for the management of community-acquired pneumonia in adults. Infectious Diseases Society of America. *Clinical Infectious Diseases,* 31, 347-82.

Bartlett, R., M. Mazens-Sullivan, J. Tetreault, S. Lobel & J. Nivard (1994) Evolving approaches to management of quality in clinical microbiology. *Clinical Microbiology Reviews,* 7, 55-88.

Bartlett, R. C. (1974) A plea for clinical relevance in medical microbiology. *American Journal of Clinical Patholology,* 61, 867-72.

Bartlett, R. C. (1974). Medical microbiology: quality, cost, and clinical relevance. Wiley-Interscience, Division of John Wiley & Sons, Inc, New York, NY.

Barts and The London NHS Trust. 2005. Trust Annual Report 2004/2005.

Bates, J. H., G. D. Campbell, A. L. Barron, G. A. McCracken, P. N. Morgan, E. B. Moses & C. M. Davis (1992) Microbial etiology of acute pneumonia in hospitalized patients. *Chest,* 101, 1005-12.

Bates, M., D. Boyle & M. Rittenberg (1998) What proportion of common diagnostic tests appear redundant? *The American Journal of Medicine,* 104, 361-368.

Bauer, T. M., A. Lalvani, J. Fehrenbach, I. Steffen, J. J. Aponte, R. Segovia, J. Vila, G. Philippczik, B. Steinbruckner & R. Frei (2001b) Derivation and validation of guidelines for stool cultures for enteropathogenic bacteria other than Clostridium difficile in hospitalized adults. *Journal of the American Medical Association,* 285, 313-319.

Beastall, G. (2004) The impact of the General Medical Services contract:national evidence. *The Bulletin of the Royal College of Pathologists,* 128, 24-27.

Boerner, D. F. & P. Zwadyk (1982) The value of the sputum gram's stain in community-acquired pneumonia. *Journal of the American Medical Association,* 247, 642-5.

Bonini, P., M. Plebani, F. Ceriotti & F. Rubboli (2002) Errors in laboratory medicine. *Clinical Chemistry,* 48**,** 691-8.

Boud, D. (2001) Knowledge at work: issues of learning, . *in D. Boud and N. Solomon (eds) Work-Based Learning: A New Higher Education?, Buckingham: Society for Research into Higher Education and Open University Press.*

Branger, P., R. Van Oers, J. Van der Wouden & J. Van der Lei (1995) Laboratory services utilization: a survey of repeat investigations in ambulatory care. *The Netherlands Journal of Medicine,* 47**,** 208-213.

British Thoracic Society. (2006) The burden of lung disease:a statistical report from the British Thoracic Society**.** 2nd ed. London: *BritishThoracic Society*.

Broughton, W. A., R. M. Middleton, M. B. Kirkpatrick & J. B. Bass (1991) Bronchoscopic protected specimen brush and bronchoalveolar lavage in the diagnosis of bacterial pneumonia. *Infectious Disease Clinics of North America,* 5**,** 437-52.

Bruins, M., G. Ruijs, M. Wolfhagen, P. Bloembergen & J. Aarts (2011) Does electronic clinical microbiology results reporting influence medical decision making: a pre-and post-interview study of medical specialists. *BMC Medical Informatics and Decision Making,* 11**,** 19.

Bruins, M., H. Oord, P. Bloembergen, M. Wolfhagen, A. Casparie, J. Degener & G. Ruijs (2005) Lack of effect of shorter turnaround time of microbiological procedures on clinical outcomes: a randomised controlled trial among hospitalised patients in the Netherlands. *European Journal of Clinical Microbiology & Infectious Diseases,* 24**,** 305-313.

Campbell, S. & B. A. Forbes (2011) The Clinical Microbiology Laboratory in the Diagnosis of Lower Respiratory Tract Infections. *Journal of Clinical Microbiology,* 49**,** S30-S33.

Campos J.M, M. A. M., Howard, B.J. 1994. *Specimen collection and processing. In: Howard BJ, ed. Clinical and pathogenic microbiology. 2nd Ed. 213-242 St Louis: Mosby,* . Mosby Inc.

Carroll, K. C. (2002) Laboratory diagnosis of lower respiratory tract infections: controversy and conundrums. *Journal of Clinical Microbiology,* 40**,** 3115-3120.

Cherkaoui, A., J. Hibbs, S. Emonet, M. Tangomo, M. Girard, P. Francois & J. Schrenzel (2010) Comparison of two matrix-assisted laser desorption ionization-time of flight mass spectrometry methods with conventional phenotypic identification for routine identification of bacteria to the species level. *Journal of Clinical Microbiology,* 48**,** 1169-1175.

Chitkara, Y., K. McCasland & L. Kenefic (1996) Development and implementation of cost-effective guidelines in the laboratory investigation of diarrhea in a community hospital. *Archives of Internal Medicine,* 156**,** 1445-1448.

Cierny, G. & J. T. Mader (1984) Adult chronic osteomyelitis. *Orthopedics,* 7**,** 1557-64.

Cohen-Bacrie, S., L. Ninove, A. Nougairède, R. Charrel, H. Richet, P. Minodier, S. Badiaga, G. Noël, B. La Scola & X. de Lamballerie (2011) Revolutionizing Clinical Microbiology Laboratory Organization in Hospitals with In Situ Point-of-Care. *PloS one,* 6**,** e22403.

Costley, C. (2000) *The boundaries and frontiers of work-based knowledge*. *In: D. Portwood, Derek and Costley, Carol, (ed.) Developing work-based learning and the university: new perspectives and practices. SEDA paper (109). SEDA***,** 23-35.

Cottrell, S. (2003a) *Skills for Success: The personal development planning handbook*. Basingstoke: Palgrave Macmillan.

Cottrell, S. (2003b) *The Study Skills Handbook Second Edition*. Basingstoke: Palgrave Macmillan.

Craven, D. E. & K. I. Hjalmarson (2010) Ventilator-associated tracheobronchitis and pneumonia: thinking outside the box. *Clinical Infectious Diseases,* 51**,** S59-S66.

Croce, M. A., T. C. Fabian, L. Waddle-Smith, S. M. Melton, G. Minard, K. A. Kudsk & F. E. Pritchard (1998) Utility of Gram's stain and efficacy of quantitative cultures for posttraumatic pneumonia: a prospective study. *Annals of Surgery,* 227**,** 743-51; discussion 751-5.

Department of Health. (2004) Modernising Pathology Services, Department of Health, London.

Department of Health. (2005) Modernising Pathology: Building a Service Responsive to Patients. London, The Stationery Office.

Doern, G. V., R. Vautour, M. Gaudet & B. Levy (1994) Clinical impact of rapid in vitro susceptibility testing and bacterial identification. *Journal of Clinical Microbiology,* 32**,** 1757-62.

Dowler, C. (2011) 'Lower qualified pathology workforce ‘could make 25 per cent savings’. *Health Service Journal***,** 16 June.

Dumitrescu, O., O. Dauwalder & G. Lina (2011) Present and future automation in bacteriology. *Clinical Microbiology and Infection,* 17**,** 649-650.

El Helali, N., J. C. Nguyen, A. Ly, Y. Giovangrandi & L. Trinquart (2009) Diagnostic accuracy of a rapid real-time polymerase chain reaction assay for universal intrapartum group B streptococcus screening. *Clinical Infectious Diseases,* 49**,** 417.

Entwistle, N. (1996) Recent research on student learning and the learning environment. *The Management of Independent Learning***,** 97-112.

Ewig, S., T. Bauer, E. Hasper, G. Marklein, R. Kubini & B. Lüderitz (1996) Value of routine microbial investigation in community-acquired pneumonia treated in a tertiary care center. *Respiration,* 63**,** 164-9.

Ewig, S., M. Schlochtermeier, N. Göke & M. S. Niederman (2002) Applying sputum as a diagnostic tool in pneumonia: limited yield, minimal impact on treatment decisions. *Chest,* 121**,** 1486-92.

Eydmann, M., D. Ball, G. Sadler & Wilks. M (2011) Introduction of MALDI-TOF: a revolution in diagnostic microbiology. *The Biomedical Scientist***,** May: 329-332.

Ferre', C., F. Llopis, J. Jacob, A. Juan, X. Palom, I. Barde's & A. Salazar (2011) Is sputum Gram staining useful in the emergency department's management of pneumonia? *Emergencias,* 23**,** 108-111.

Fine, M. J., J. J. Orloff, J. D. Rihs, R. M. Vickers, S. Kominos, W. N. Kapoor, V. C. Arena & V. L. Yu (1991) Evaluation of housestaff physicians' preparation and interpretation of sputum Gram stains for community-acquired pneumonia. *Journal of General Internal Medicine,* 6**,** 189-198.

Fine, M. J., M. A. Smith, C. A. Carson, S. S. Mutha, S. S. Sankey, L. A. Weissfeld & W. N. Kapoor (1996) Prognosis and outcomes of patients with community-acquired pneumonia. A meta-analysis. *Journal of the American Medical Association,* 275**,** 134-41.

Flatauer, F., J. Chabalko & E. Wolinsky (1980) Fiberoptic Bronchoscopy in Bacteriologic Assessment of Lower Respiratory Tract Secretions: Importance of Microscopic Examination. *Journal of the American Medical Association,* 244**,** 2427-2429.

Forbes, B. A., D. Sahm & A. Weissfeld. 1998. *Infections of the Lower Respiratory Tract in: Bailley and Scott's Diagnostic Microbiology. 10th edition*. Mosby, St. Louis.

Forsman, R. (2002) The value of the laboratory professional in the continuum of care. *Clinical Leadership & Management Review.,* 16**,** 370-373.

Fraser, C. & F. Woodford (1987) Strategies to modify the test-requesting patterns of clinicians. *Annals of Clinical Biochemistry,* 24**,** 223-231.

García-Vázquez, E., M. A. Marcos, J. Mensa, A. de Roux, J. Puig, C. Font, G. Francisco & A. Torres (2004) Assessment of the usefulness of sputum culture for diagnosis of community-acquired pneumonia using the PORT predictive scoring system. *Archives of Internal Medicine,* 164**,** 1807-11.

Geckler, R. W., D. H. Gremillion, C. K. McAllister & C. Ellenbogen (1977) Microscopic and bacteriological comparison of paired sputa and transtracheal aspirates. *Journal of Clinical Microbiology,* 6**,** 396-9.

Giuseppe Cornaglia. & René J. Courcol. 2012. *European Manual of Clinical Microbiology*. 1st edition. Basel, European Society of Clinical Microbiology and Infectious Diseases.

Gleckman, R., J. DeVita, D. Hibert, C. Pelletier & R. Martin (1988) Sputum gram stain assessment in community-acquired bacteremic pneumonia. *Journal of Clinical Microbiology,* 26**,** 846-9.

Gopal Rao, G., M. Crook & M. Tillyer (2003) Pathology tests: is the time for demand management ripe at last? *Journal of Clinical Pathology,* 56**,** 243-248.

Gopal Rao, G., A. Jeanes, M. Osman, C. Aylott & J. Green (2002) Marketing hand hygiene in hospitals--a case study. *Journal of Hospital Infection,* 50**,** 42-47.

Gopal Rao, G., A. E. Ozerek & A. Jeanes (2001) Rational protocols for testing faeces in the investigation of sporadic hospital-acquired diarrhoea. *Journal of Hospital Infection,* 47**,** 79-83.

Granato, P. A. (1993) The impact of same-day tests versus traditional overnight testing. *Diagnostic Microbiology and Infectious Disease,* 16**,** 237-43.

Greub, G. & G. Prod'hom (2011) Automation in clinical bacteriology: what system to choose? *Clinical Microbiology and Infection,* 17**,** 655-660.

Guerrant, R. L., T. Van Gilder, T. S. Steiner, N. M. Thielman, L. Slutsker, R. V. Tauxe, T. Hennessy, P. M. Griffin, H. DuPont & R. B. Sack (2001) Practice guidelines for the management of infectious diarrhea. *Clinical Infectious Diseases,* 32**,** 331-351.

Hahn, H. & H. Beaty (1970) Transtracheal aspiration in the evaluation of patients with pneumonia. *Annals of Internal Medicine,* 72**,** 183-187.

Hayden, R. & L. Frenkel (2000) More laboratory testing: greater cost but not necessarily better. *The Pediatric Infectious Disease Journal,* 19**,** 290-292.

Healthcare Commission. 2007. Getting results: Pathology services in acute and specialist trusts. London, England. (Accessed 15 December 2007). http://www.healthcarecommission.org.uk.

Health and Safety Executive. 2011. Provision of key clinical information on laboratory specimen request forms. In *Health and Safety Executive-safety Notice*. Health and Safety Executive, HID 5-2011. December 9.

Heineman, H. S., J. K. Chawla & W. M. Lopton (1977) Misinformation from sputum cultures without microscopic examination. *Journal of Clinical Microbiology,* 6**,** 518-27.

Henricks, W. H. (2011) "Meaningful use" of electronic health records and its relevance to laboratories and pathologists. *Journal of Pathology Informatics,* 2.

Hobbs, F. D., B. C. Delaney, D. A. Fitzmaurice, S. Wilson, C. J. Hyde, G. H. Thorpe, A. S. Earl-Slater, S. Jowett & R. S. Tobias (1997) A review of near patient testing in primary care. *Health Technol Assess,* 1**,** i-iv, 1-229.

Honey, P. a. M., A. 1986. *Using Our Learning Styles*. Honey Publications, London, UK.

Howanitz, J. H. & P. J. Howanitz (2001) Laboratory results. *American Journal of Clinical Pathology,* 116**,** 311-315.

Howanitz, P. J. (2005) Errors in laboratory medicine: practical lessons to improve patient safety. *Archives of Pathology and Laboratory Medicine,* 129**,** 1252-1261.

Howanitz, P. J., G. S. Cembrowski, S. J. Steindel & T. A. Long (1993) Physician goals and laboratory test turnaround times. A College of American Pathologists Q-Probes study of 2763 clinicians and 722 institutions. *Archives of Pathology and Laboratory Medicine,* 117**,** 22-8.

Ieven, M. & H. Goossens (1997) Relevance of nucleic acid amplification techniques for diagnosis of respiratory tract infections in the clinical laboratory. *Clinical Microbiology Reviews,* 10**,** 242-256.

Irwig, L., P. Bossuyt, P. Glasziou, C. Gatsonis & J. Lijmer (2002) Designing studies to ensure that estimates of test accuracy are transferable. *British Medical Journal,* 324**,** 669-671.

Isenberg, H. D., ed,. 2004. *Lower Respiratory Tract Cultures in: Clinical Microbiology Procedures Handbook. 2nd edition*. Washington, DC ASM Press.

Johansson, N., M. Kalin, A. Tiveljung-Lindell, C. G. Giske & J. Hedlund (2010) Etiology of Community-Acquired Pneumonia: Increased Microbiological Yield with New Diagnostic Methods. *Clinical Infectious Diseases,* 50**,** 202-209.

Joyce, S. M. (1986) Sputum analysis and culture. *Annals of Emergency Medicine,* 15**,** 325-8.

Kalin, M., A. Lindberg & G. Tunevall (1983) Etiological diagnosis of bacterial pneumonia by gram stain and quantitative culture of expectorates. Leukocytes or alveolar macrophages as indicators of sample representativity. *Scandinavian Journal of Infectious Diseases,* 15**,** 153-160.

Kassirer, J. P. (1989) Our stubborn quest for diagnostic certainty. A cause of excessive testing. The *New England Journal of Medicine,* 320**,** 1489-91.

Kelly, A. M. (1998) Clinical impact of blood cultures taken in the emergency department. *Journal of Accident and Emergency Medicine,* 15**,** 254-6.

Khromova, V. & T. A. Gray (2008) Learning needs in clinical biochemistry for doctors in foundation years. *Annals of Clinical Biochemistry,* 45**,** 33-38.

Kilpatrick, E. S. & S. Holding (2001) Use of computer terminals on wards to access emergency test results: a retrospective audit. *British Medical Journal,* 322**,** 1101-3.

Kolb, D. 1984. *Experiential learning: experience as the source of learning and development.* Englewood Cliffs, NJ: Pentice-Hall Inc.

Kuijper, E. J., J. van der Meer, M. D. de Jong, P. Speelman & J. Dankert (2003) Usefulness of Gram stain for diagnosis of lower respiratory tract infection or urinary tract infection and as an aid in guiding treatment. *European Journal of Clinical Microbiology and Infectious Diseases,* 22**,** 228-34.

Lee, A. & S. McLean (1977) The laboratory report: a problem in communication between clinician and microbiologist? *The Medical Journal of Australia,* 2**,** 858-860.

Lentino, J. R. & D. A. Lucks (1987) Nonvalue of sputum culture in the management of lower respiratory tract infections. *Journal of Clinical Microbiology,* 25**,** 758-62.

Lim, W., S. Baudouin, R. George, A. Hill, C. Jamieson, I. Le Jeune, J. Macfarlane, R. Read, H. Roberts & M. Levy (2009) BTS guidelines for the management of community acquired pneumonia in adults: update 2009. *Thorax,* 64**,** iii1-iii55.

Loens, K., L. Van Heirstraeten, S. Malhotra-Kumar, H. Goossens & M. Ieven (2009) Optimal sampling sites and methods for detection of pathogens possibly causing community-acquired lower respiratory tract infections. *Journal of Clinical Microbiology***,** 21-31.

Lord Carter of Coles. 2006. Report of the Review of NHS Pathology Services in England. An Independent Review for the Department of Health. London: Department of Health .

Lord Carter of Coles. 2008. Report of the Second Phase of NHS Pathology Services in England. An Independent Review for the Department of Health. London: Department of Health .

Lundberg, G. (1998) The need for an outcomes research agenda for clinical laboratory testing (Editorial). *Journal of the American Medical Association,* 280**,** 565-566.

Lundberg, G. D. (1999) How clinicians should use the diagnostic laboratory in a changing medical world. *Clinica Chimica Acta,* 280**,** 3-11.

Macfarlane, J. & D. Boldy (2004) 2004 update of BTS pneumonia guidelines: what's new? *Thorax,* 59**,** 364-366.

Macfarlane, J., T. Boswell, G. Douglas, R. Finch, W. Holmes, D. Honeybourne, W. Lim, R. Marriott, D. Nathwani & P. Saul (2001) BTS guidelines for the management of community acquired pneumonia in adults. *Thorax,* 56**,** 1-64.

Mackowiak, P. A., S. R. Jones & J. W. Smith (1978) Diagnostic value of sinus-tract cultures in chronic osteomyelitis. *Journal of the American Medical Association,* 239**,** 2772-2775.

Madison, J. M. & R. S. Irwin (2004) Expectorated sputum for community-acquired pneumonia: a sacred cow. *Archives of Internal Medicine,* 164**,** 1725.

Maki, D., C. Weise & H. Sarafin (1977) A semiquantitative culture method for identifying intravenous-catheter-related infection. The *New England Journal of Medicine,* 296**,** 1305-1309.

Mandell, L. A., R. G. Wunderink, A. Anzueto, J. G. Bartlett, G. D. Campbell, N. C. Dean, S. F. Dowell, T. M. File, D. M. Musher, M. S. Niederman, A. Torres, C. G. Whitney, I. D. S. o. America & A. T. Society (2007) Infectious

Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clinical Infectious Diseases,* 44 Suppl 2**,** S27-72.

Marston, B. J., J. F. Plouffe, T. M. File, B. A. Hackman, S. J. Salstrom, H. B. Lipman, M. S. Kolczak & R. F. Breiman (1997) Incidence of community-acquired pneumonia requiring hospitalization. Results of a population-based active surveillance Study in Ohio. The Community-Based Pneumonia Incidence Study Group. *Archives of Internal Medicine,* 157**,** 1709-18.

Matthews, S. & J. Deutekom (2011) The future of diagnostic bacteriology. *Clinical Microbiology and Infection,* 17**,** 651-654.

McFarland, L., C. Surawicz & W. Stamm (1990) Risk factors for Clostridium difficile carriage and C. difficile-associated diarrhea in a cohort of hospitalized patients. *The Journal of Infectious Diseases,* 162**,** 678-684.

Miller, J. 1999. *A guide to specimen management in clinical microbiology. ASM Press, 2nd edition. Washington, DC.*: American Society for Microbiology.

Mishra, V., S. Kumar, V. Siwach, N. Sharma, R. Angral, A. Mujumdar & A. Sharma (2000) Need for bringing in a change in biochemistry curriculum to make it clinically oriented? *The Journal of the Association of Physicians of India,* 48**,** 635-638.

Miyashita, N., H. Shimizu, K. Ouchi, K. Kawasaki, Y. Kawai, Y. Obase, Y. Kobashi & M. Oka (2008) Assessment of the usefulness of sputum Gram stain and culture for diagnosis of community-acquired pneumonia requiring hospitalization. *Medical Science Monitor,* 14**,** CR171-6.

Morgan, M. (1995) Perceptions of a medical microbiology service: a survey of laboratory users. *Journal of Clinical Pathology,* 48**,** 915-918.

Mulatero, F., V. Bonnardel & C. Micolaud (2011) The way forward for fast microbiology. *Clinical Microbiology and Infection,* 17**,** 661-667.

Murray, P. R., ed,. 1999. Specimen collection, transport and storage in chapter 4 and specimen processing in chapter 5 in: Manual of Clinical Microbiology. 7th edition. Washington, DC ASM Press.

Musher, D. M., R. Montoya & A. Wanahita (2004) Diagnostic value of microscopic examination of Gram-stained sputum and sputum cultures in patients with bacteremic pneumococcal pneumonia. *Clinical Infectious Diseases,* 39**,** 165-9.

Nahass, R. & M. Weinstein (1990) Qualitative intravascular catheter tip cultures do not predict catheter-related bacteremia. *Diagnostic Microbiology and Infectious Disease,* 13**,** 223-226.

National Pathology Benchmarking Review. 2005. Microbiology Benchmark Report 2004/2005. Microbiology Department, Barts and The London NHS Trust. Keele University 2005.

National Pathology Benchmarking Review (2006) Microbiology Benchmark Report 2004/2005. Microbiology Department, Barts and The London NHS Trust. Keele University 2006.

National Pathology Benchmarking Review.. 2007. Microbiology Benchmark Report 2006/2007. Microbiology Department, Barts and The London NHS Trust. Keele University 2007.

National Pathology Benchmarking Review. 2008. Microbiology Benchmark Report 2007/2008. Microbiology Department, Barts and The London NHS Trust. Keele University 2008.

Neu, H. C. (1978) What Should the Clinician Expect from the Microbiology Laboratory? *Annals of Internal Medicine,* 89**,** 781-784.

NICE (2008) National Institute for Health and Clinical Excellence. Respiratory tract infections-antibiotic prescribing. Prescribing of Antibiotics for Self-limiting Respiratory Tract Infections in Adults and Children in Primary Care. NICE Clinical guideline. *NICE Clinical Guideline,* 69.

Niederman, M. S. (2009) Community-acquired pneumonia: the U.S. perspective. *Seminars in Respiratory and Critical Care Medicine,* 30**,** 179-88.

Novis, D. A., M. K. Walsh, J. C. Dale & P. J. Howanitz (2004) Continuous monitoring of stat and routine outlier turnaround times: two College of American Pathologists Q-Tracks monitors in 291 hospitals. *Archives of Pathology & Laboratory Medicine,* 128**,** 621-626.

Ozerek, A. E. & G. G. Rao (1999) Is routine screening for conventional enteric pathogens necessary in sporadic hospital-acquired diarrhoea? *Journal of Hospital Infection,* 41**,** 159-61.

Pannall, P., W. Marshall, A. Jabor & E. Magid (1996) International federation of clinical chemistry:: A strategy to promote the rational use of laboratory tests. *Clinica Chimica Acta,* 244**,** 121-127.

Paxton, A. (2011) Fresh approach to microbiology front-end robotics. *Cap Today*.

Perry, C. R., R. L. Pearson & G. A. Miller (1991) Accuracy of cultures of material from swabbing of the superficial aspect of the wound and needle biopsy in the preoperative assessment of osteomyelitis. The *Journal of Bone and Joint Surgery American,* 73**,** 745-9.

Plebani, M. & P. Bonini (2002) Wrong biochemistry results. Interdepartmental cooperation may help avoid errors in medical laboratories. *British Medical Journal (Clinical research ed.),* 324**,** 423-424.

Plebani, M. & P. Carraro (1997) Mistakes in a stat laboratory: types and frequency. *Clinical Chemistry,* 43**,** 1348-51.

Price, C. P. (2012) Evidence-Based Laboratory Medicine: Is It Working in Practice? *The Clinical Biochemist Reviews,* 33**,** 13.

Reed, W., G. Byrd, R. Gates Jr, R. Howard & M. Weaver (1996) Sputum gram's stain in community-acquired pneumococcal pneumonia. A meta-analysis. *Western Journal of Medicine,* 165**,** 197-204.

Regan, M. & R. Forsman (2006) The impact of the laboratory on disease management. *Disease Management,* 9**,** 122-130.

Reller, L. B., M. P. Weinstein, L. R. Peterson, J. D. Hamilton, E. J. Baron, L. S. Tompkins, J. M. Miller, C. M. Wilfert, F. C. Tenover & R. B. Thomson (2001) Role of clinical microbiology laboratories in the management and control of infectious diseases and the delivery of healthcare. *Clinical Infectious Diseases,* 32**,** 605-610.

Ries, K., M. E. Levison & D. Kaye (1974) Transtracheal aspiration in pulmonary infection. *Archives of Internal Medicine,* 133**,** 453-8.

Rinsler, M. (1984) The appropriate use of diagnostic services:(I). Introduction to the series. *Health Trends,* 16**,** 73.

Roberts, M. E., J. T. Macfarlane, R. C. George & T. G. Harrison (2008) Microbiology investigations in community acquired pneumonia--most laboratories in England and Wales do not offer all those recommended in the British Thoracic Society guideline. *Journal of Infection,* 56**,** 291-4.

Robinson, A. (1994) Rationale for cost-effective laboratory medicine. *Clinical Microbiology Reviews,* 7**,** 185-99.

Rosón, B., J. Carratalà, R. Verdaguer, J. Dorca, F. Manresa & F. Gudiol (2000) Prospective study of the usefulness of sputum Gram stain in the initial approach to community-acquired pneumonia requiring hospitalization. *Clinical Infectious Diseases,* 31**,** 869-74.

Royal College of Pathologists. 2010. Reconfiguration of NHS Pathology Services - A Statement from the Royal College of Pathologists Available at http://www.rcpath.org/resources/pdf/reconfiguration_of_nhs_pathology_services.pdf.

Sanyal, S., P. R. Smith, A. C. Saha, S. Gupta, L. Berkowitz & P. Homel (1999) Initial microbiologic studies did not affect outcome in adults hospitalized with community-acquired pneumonia. *American Journal of Respiratory and Critical Care Medicine,* 160**,** 346-8.

Schifman, R. B., A. Pindur & J. A. Bryan (1997) Laboratory practices for reporting bacterial susceptibility tests that affect antibiotic therapy. *Archives of Pathology and Laboratory Medicine,* 121**,** 1168-70.

Schreckenberger, P. (2001) Questioning dogmas: proposed new rules and guidelines for the clinical microbiology laboratory. ASM News-*American Society for Microbiology,* 67**,** 388-89.

Schumacher, G. E. & J. T. Barr (1998) Total testing process applied to therapeutic drug monitoring: impact on patients' outcomes and economics. *Clinical Chemistry,* 44**,** 370-374.

Schön, D. 1983. *The reflective practitioner: How professionals think in action*. San Francisco, CA, US: Jossey-Bass.

Schön, D. A. 1987. *Educating the reflective practitioner: Toward a new design for teaching and learning in the professions.* San Francisco, CA, US: Jossey-Bass.

Seng, P., M. Drancourt, F. Gouriet, B. La Scola, P. E. Fournier, J. M. Rolain & D. Raoult (2009) Ongoing revolution in bacteriology: routine identification of bacteria by matrix-assisted laser desorption ionization time-of-flight mass spectrometry. *Clinical Infectious Diseases,* 49**,** 543-551.

Seng, P., J. M. Rolain, P. E. Fournier, B. La Scola, M. Drancourt & D. Raoult (2010) MALDI-TOF-mass spectrometry applications in clinical microbiology. *Future Microbiology,* 5**,** 1733-54.

Sharp, S., A. Robinson, M. Saubolle, M. Santa Cruz, K. Carroll & V. Baselski. 2004. Cumitech 7B, lower respiratory tract infections. Washington, DC: ASM Press.

Siegel, D., P. Edelstein & I. Nachamkin (1990) Inappropriate testing for diarrheal diseases in the hospital. *Journal of the American Medical Association,* 263**,** 979-982.

Skerrett, S. J. (1997) Diagnostic testing to establish a microbial cause is helpful in the management of community-acquired pneumonia. *Seminars in Respiratory Infections,* 12**,** 308-21.

Smellie, W. (2003) Appropriateness of test use in pathology: A new era or reinventing the Wheel. *Annals of Clinical Biochemistry,* 40**,** 585-592.

Smellie, W., M. Galloway, D. Chinn & P. Gedling (2002) Is clinical practice variability the major reason for differences in pathology requesting patterns in general practice? *Journal of Clinical Pathology,* 55**,** 312-314.

Solomon, D., H. Hashimoto, L. Daltroy & M. Liang (1998) Techniques to improve physicians' use of diagnostic tests: a new conceptual framework. *Journal of the American Medical Association,* 280**,** 2020-2027.

Steindel, S. J. & P. J. Howanitz (2001) Physician satisfaction and emergency department laboratory test turnaround time. *Archives of Pathology and Laboratory Medicine,* 125**,** 863-71.

Taylor, E., T. Marrie, M. Fine, D. Obroskyl, W. Kapoor, C. Coley & D. Singer (1999) Observations from a multicentre study on the use of the sputum specimen in patients hospitalized with community-acquired pneumonia. *Canadian Journal of Infectious Diseases,* 10**,** 39-46.

Theerthakarai, R., W. El-Halees, M. Ismail, R. A. Solis & M. A. Khan (2001) Nonvalue of the initial microbiological studies in the management of nonsevere community-acquired pneumonia. *Chest,* 119**,** 181-4.

Valenstein, P. (1989) Turnaround time. Can we satisfy clinicians' demands for faster service? Should we try? *American Journal of Clinical Pathology,* 92**,** 705-6.

Valenstein, P. (1996) Laboratory turnaround time. *American Journal of Clinical Pathology,* 105**,** 676-88.

Valenstein, P., A. Leiken & C. Lehmann (1988) Test-ordering by multiple physicians increases unnecessary laboratory examinations. *Archives of Pathology and Laboratory Medicine,* 112**,** 238-241.

Valenstein, P. & F. Meier (1999) Outpatient order accuracy: a College of American Pathologists Q-Probes study of requisition order entry accuracy in 660 institutions. *Archives of Pathology and Laboratory Medicine,* 123**,** 1145-1150.

Valenstein, P. N. & K. Emancipator (1989) Sensitivity, specificity, and reproducibility of four measures of laboratory turnaround time. *American Journal of Clinical Pathology,* 91**,** 452-7.

Van Veen, S., E. Claas & E. J. Kuijper (2010) High-throughput identification of bacteria and yeast by matrix-assisted laser desorption ionization-time of flight mass spectrometry in conventional medical microbiology laboratories. *Journal of Clinical Microbiology,* 48**,** 900-907.

van Walraven, C. & C. Naylor (1998) Do we know what inappropriate laboratory utilization is?: A systematic review of laboratory clinical audits. *Journal of the American Medical Association,* 280**,** 550-558.

Wheat, L. J., S. D. Allen, M. Henry, C. B. Kernek, J. A. Siders, T. Kuebler, N. Fineberg & J. Norton (1986) Diabetic foot infections: bacteriologic analysis. *Archives of Internal Medicine,* 146**,** 1935-1940.

Widmer, A., M. Nettleman, K. Flint & R. Wenzel (1992) The clinical impact of culturing central venous catheters: a prospective study. *Archives of Internal Medicine,* 152**,** 1299-302.

Wilson, M. (1997) Clinically relevant, cost-effective clinical microbiology: Strategies to decrease unnecessary testing. *American Journal of Clinical Pathology,* 107**,** 154-167.

Wilson, M. (2000) Cutting costs in microbiology. *Advance Administrators Laboratory,* 9**,** 27-32.

Wilson, M. (2002) Appropriate use of clinical microbiology tests. *Clinics in Laboratory Medicine,* 22**,** 491-504.

Wilson, M. L. (1996) General principles of specimen collection and transport. *Clinical Infectious Diseases,* 22**,** 766-777.

Wilson, M. (2008) Assuring the quality of clinical microbiology test results. *Clinical Infectious Diseases,* 47**,** 1077-1082.

Winkens, R. A. G., A. J. H. A. Ament, P. Pop, P. H. A. Reniers, R. P. T. M. Grol & A. J. Knottnerus (1996) Routine Individual Feedback on Requests for Diagnostic Tests: an economic evaluation. *Medical Decision Making,* 16**,** 309-314.

Wolk, D. M. & W. M. Dunne Jr (2011) New Technologies in Clinical Microbiology. *Journal of Clinical Microbiology,* 49**,** S62-S67.

Woodhead, M., F. Blasi, S. Ewig, G. Huchon, M. Leven, A. Ortqvist, T. Schaberg, A. Torres, G. van der Heijden & T. J. M. Verheij (2005) Guidelines for the management of adult lower respiratory tract infections. *European Respiratory Journal,* 26**,** 1138-1180.

Woodhead, M. A., J. Arrowsmith, R. Chamberlain-Webber, S. Wooding & I. Williams (1991) The value of routine microbial investigation in community-acquired pneumonia. *Respiratory Medicine,* 85**,** 313-7.

World Health Organisation. 1997. The World Health Report 1997: Conquering suffering enriching humanity. *World Health Organisation*, Geneva.

World Health Organisation (1999). WHO report on infectious disease*:* Removing obstacles to healthy development. *World Health Organisation*, Geneva.

Appendices

Appendix 1.1: Guidelines of respiratory specimens handling and collection

Type of Specimen	Method of collection	Volume	Transport and storage	Comments
Lower respiratory:				
Expectorated sputum Induced sputum	Sterile container/cup	> 1ml	≤ 2 h, RT[a] delay: ≤ 24 h, 4C^{o}	Rinse mouth first, use Gram stain to screen for suitability
Bronchoscopy fluid (bronchial washing, lavage, brush & endotrach aspirate)	Sterile container/cup or tube	> 1ml	≤ 2 h, RT delay: ≤ 24 h, 4C^{o}	
Upper respiratory:				
Nasal	Insert premoistened swab into nares place into transport media	Swab transport	≤ 2 h, RT delay: ≤ 24 h, RT	For detection of nasal carriage of S. aurous or Group A streptococci only
Nasopharynx	Insert calcium alginate Swab into posterior nasopharynx via nose, inoculate medium at bedside or transport swab	Direct media inoculation	Plates ≤ 15 min. Swab:≤ 2 h, RT delay: ≤ 24 h, RT	Routine swabs may not support growth of some organisms (e.g., B. pertussis). Use calcium alginate or dacron/rayon swabs
Throat	Swab posterior pharynx and tonsils	Swab transport	≤ 2h, RT delay: ≤ 24 h, RT	Inform laboratory if identification of organisms other than group A beta haemolytic streptococci is indicated (e.g., N. gonorrhoea)

[a] RT: Room temperature

Appendix 1.2: Useful guide for sputum macroscopic examination

1. Sputum definition:

Sputum is material coughed up from the lungs and expectorated (spit out) though the mouth. Sputum is a substance comprised of mucus, foreign matter, and saliva that is found in the lungs or bronchial tree.

2. Purpose of sputum culture:

A sputum culture is done to find and identify the microorganism causing an infection of the lower respiratory tract such as pneumonia (an infection of the lung). Infections of the lungs and bronchial tubes are caused by several types of microorganisms, including bacteria, fungi (molds and yeast), and viruses.

3. Common reasons of sputum culture:

The purpose of a sputum analysis is to help identifying microorganisms that are causing respiratory infection. The most common reason for obtaining a sputum specimen is to test for infectious tuberculosis, pneumonia, bronchitis, lung abscess, or other respiratory infections.

4. Sputum Description:

Based on the clinical condition of the patients, a patient with infections produces pus-like material and/or blood may have an infection of the lower respiratory tract, see the table for details.

5. Sputum processing:

A portion of the sputum is spread over the surface of several different types of culture plates, and placed in an incubator at body temperature for one or two days. During incubation, bacteria present in the sputum sample multiply and will appear on the plates as visible colonies. The bacteria are identified by the appearance of their colonies, by the results of biochemical tests, and through a Gram stain of part of a colony. The bacteria are tested against different antibiotics to determine which will treat the infection by killing the bacteria.

6. Sputum culture results:

a. Normal results: sputum from a healthy person would have no growth on culture. A mixture of micro-organisms, however, normally found in a person's mouth and saliva often contaminates the culture. If these micro- organisms grow in the culture, they may be reported as normal flora contamination.

b. Abnormal results: the presence of bacteria and white blood cells on the Gram stain and the isolation of a microorganism from culture, other than normal flora contamination, is evidence of a lower respiratory tract infection. Micro-organisms commonly isolated from sputum include *Streptococcus pneumoniae, Haemophilus influenzae,* and *Moraxella catarrhalis*.

Sputum Description:

Term	Description	Gram staining	Associated with
Salivary sample	Samples are watery with heavy froth and bubbles.	On microscopic examination it shows predominance of epithelial cells and on Gram staining a variety of micro-organisms typical of the normal oropharyngeal bacterial flora	Normal patients
Mucosalivary sample	Samples contain mucus with a small amount of saliva	Like salivary samples on microscopic examination contain large number of squamous epithelial cells and oropharyngeal bacterial flora.	Normal patients
Mucoid sample	Samples appeared as transparent or translucent with or without debris and contain with white flecks and moderate froth and bubbles. **Mostly mucus.**	Like salivary samples on microscopic examination contain large number of squamous epithelial cells and oropharyngeal bacterial flora. Epithelial cells in large numbers within sputum smears mean that the specimen is predominately oral saliva, rather than true sputum fron the lungs.	Not generally associated with broncho-pulmonary infection.
Mucopurulent sample	The mucopurulent samples are normally opaque and usually yellow color with no froth. **Green-looking with pus and mucus.**	On microscopic examination, the Gram stain shows a large number of pus cells or polymorphonuclear leucocytes representing sputum specimen	Acute and chronic infection
Purulent sample	A sample appears like pus, yellow or greenish sputum, rusty descriptive, often copious and thick. **Green-looking, mostly pus.**	On microscopic examination, the Gram stain shows a large number of pus cells or polymorphonuclear leucocytes representing sputum specimen. White blood cells indicate inflammation and possible infection.	Acute and chronic infection
Blood stained sample	Expectoration of blood or bloody sputum, amount may range from blood streaked to massive haemorrhage (haemoptysis)	Red blood cells in a direct smear are not usually significant?	A variety of pathologies
Fetid	Foul-smelling, typical of anaerobic infection		Bronchiectasis, lung abscess or cystic fibrosis
Rusty	Descriptive of the colour of sputum (also called prune juice)	Gram stain of sputum shows abundant inflammatory cells and Gram positive diplococci; Streptococcus pneumoniae.	Pneumococcal pneumonia

Sputum colour, consistency, quantity, time of day produced, odour, and presence of blood or other distinguishing matter are important for sputum description and quality. Character of sputum description may be indicative of a particular disorder/infection.

Appendix 2.1: Ethical approval letter

From: Burke Sandra [mailto:Sandra.Burke@nelondon.nhs.uk]
Sent: 18 August 2004 09:37
To: Abdi Yasin
Subject: Ethical approval for student project

Dear Mr Abdi

Further to your letter dated 26th July 2004 the Chairman of Committee 1 Dr A T Tucker has read through your draft copy and details of your proposed project and consider it to be audit, therefore it does not require ethical approval.

Yours sincerely

Sandra Burke

Acting Research Ethics Committee Manager

East London and the City Research Ethics Committees
****

****

Appendix 2.2: data collection forms

To assess the degree of completeness and appropriateness of clinical microbiology laboratory test utilisation and test ordering practice, the Yes/No were used to measure the response for the determination of test appropriateness and inappropriateness of test and test request.

Work Category/Bench……
Specimen type……
Hospital site…….
Hospital Number……
Clinical diagnosis……

Study Serial NO……
Sample Number……..
Ward/GP/Source……
Date……..

Section 1: Evaluation of microbiology request form designing

Q.1: Type of request form and designing format	Y	N
a. Does the laboratory use standardised request forms to order microbiology tests? If yes, specify the type of the request form used in BLT as follow:		
One page hard copy form/complete page dedicated to microbiology.		
One page hard copy dedicated one type of microbiology specimen.		
One page hard copy form for all pathology service.		
Multiple copy form for all pathology service.		
Or any other form, please state:		
b. What type of request form used in this Trust?		
Paper format request form		
Electronic format request form		
c. Does the request form provide enough spaces for the completion of test requisition?		
d. Does the request form contain appropriate instructions to assist in specimen collection, transport and test ordering criteria?		
Comments:		

Section 2. Review of microbiology tests requisitions

Q.2: The requisitions/test request order of entry	**Y**	**N**
a. Does the requisition include patient's first and last name?		
b. Does the requisition include date of birth and sex?		
c. Does the requisition include location of the patient ward/clinic/GP?		
d. Does the requisition include Name and address of requesting doctor/healthcare provider?		
e. Does the requisition include name of tests requested?		
f. Does the requisition include specific anatomic culture site and source of the specimen?		
g. Does the requisition include date and hour of specimen collection?		
h. Does the requisition include clinical diagnosis and relevant patient's history?		
i. Does the requisition include antimicrobial agents, if any, that patient is receiving?		
j. Does the requisition include the specimen collector's name if other then the ordering doctor/physician?		
Comments:		

Section 3. Evaluation of the sputum quality

Sputum quality is measured by macroscopic examination, as recorded on patient's request form during the specimen acceptance and processing.

Q.3: Gross macroscopic examination of sputum evaluation and assessment.	Y	N
a. What type sputum received?		
Expectorated sputum		
Induced sputum		
Any other as:		
Or just sputum stated.		
b. Is the sputum samples quality assessment of macroscopic examination appearance described? If yes, check one of the following or as appropriate		
Purulent		
Mucopurulent		
Mucosalivary		
Saliva		
Blood stained		
Other descriptions as:		
Not described		
c. Is the reporting of macroscopic examination described as:		
Interpretatively?		
Purely descriptive?		
d. Is the specimen was cultured/processed regardless of macroscopic evaluation findings?		
e. If macroscopic observation indicated unsuitable or unsatisfactory specimen such as saliva or mucoid culture was done due to type of patient as:		
ITU patient		
Paediatric patient		
Immunocompromise patient		
Or not stated but processed.		
Comments:		

Section 4. Processing practices and results

Q. 4: Specimen processing and test results	Y	N
a. Is the date specimen received stated on the request form? If yes, specify the date specimen received in the laboratory and processed as:		
b. Is the specimen received appropriate and match the requested test? If no, specify the reason if appropriate:		
c. Is the multiple test requests received from the same specimen? If yes, specify the type of investigations requested.		
d. Are other cultural and special investigations performed that did not stated on the requisition? If yes, specify the type of investigations.		
e. Is pathogen/s isolated from the specimen? If yes, specify the pathogen/s and how is it reported.		
f. Is significant organism/s isolated from the specimen? If yes, specify the organism/s and how is it reported.		
g. If there is no growth on the plates, how is it reported?		
h. If there is growth of commensals/normal flora on the plates, how is it reported?		
i. If there is a positive or pathogen/s isolated from the culture is any further work performed? If yes, specify the further work. If no, specify the reason if appropriate.		
Comments:		

Section 5. Final test report and results interpretation

Q.5: Microbiology report and interpretation of the final results/reports	**Y**	**N**
a. Do the reports include:		
Patient's first name and last name?		
Date of birth and gender?		
Name and location of the patient?		
Name of requesting doctor/healthcare provider?		
Date/time of collection, where necessary?		
Specimen type and source?		
Test name/name of test requested?		
The test performed?		
Date/time specimen received and date processed?		
The test results, if applicable, the reference values, comments and recommendation for the clinical importance of the findings?		
Accession number and patient's hospital number?		
b. Are the report/result interpreted in a clinical meaningful manner and provide the clinicians with clinically relevant information's?		
c. Are the results being properly interpreted their significance or instead reported to clinicians all of microbiologic findings (i.e. no interpretation)?		
d. Does the report evaluate normal flora with report as per laboratory protocol?		
e. Are the data overload leads to confusing or misleading clinicians and service users?		
f. Does the final result contain reflective reporting where laboratory clinician might add on further tests using their microbiological judgement?		
g. Is reflective testing used to inform the user when ordering or cancelling one test based on the result of another test or specimen?		
Comments:		

Appendix 2.3: BLT Guidelines for respiratory microbiology specimen

A rational approach to the microbiological investigation of respiratory specimens

Guidelines from the Respiratory and Medical Microbiology Departments BLT 2003

The aim of these guidelines is to rationalise the work of the Microbiology Department by placing greater emphasis on well-taken and clinically relevant specimens. The Microbiology laboratory can then give more time to service development such as a liquid culture system for tuberculosis.

Routine Gram stains will no longer be carried out on sputum specimens at the Royal London Hospital. Gram stains have not been carried out on sputum specimens at St Bartholomew's Hospital for some time.

Where it is felt that a Gram stain would be clinically useful, the medical team should telephone the laboratory respiratory bench (ext 2610 / 2009) to request it. A routine Gram stain is not necessary for every patient (Ref: BTS Guidelines).

N.B. Specimen Quality

For routine culture and sensitivity, no salivary or mucoid specimens are accepted from adult patients at either hospital (other than paediatric patients, neutropenic patients, ventilated patients or BAL specimens). This does not apply to specimens for AFB investigations. See point 7.

FURTHER ACTION FOR SPECIFIC CLINICAL CONDITIONS

1. Chronic Obstructive Pulmonary Disease

In stable COPD, or during exacerbations, there is little evidence that sputum culture or sensitivity is of any value and these should not be sent. If the clinical diagnosis only states COPD the specimen will not be processed. Appropriate reasons for sputum examination in patients with COPD are: if there is pneumonia, a suspicion of bronchiectasis or failure to respond to antibiotics. COPD specimens will only be processed if these particular reasons are stated.

2. Pneumonia

The importance of sputum examination is stated in the B.T.S. guidelines but these should be well-collected, expectorated (i.e. coughed up) sputum specimens or bronchoscopy specimens. As mentioned above, if it is considered that a Gram stain would be clinically useful for an individual patient, contact the laboratory respiratory bench (ext 2610/2009) to request it.

3. Bronchiectasis

Anaerobes are often the main causative organisms of infection in these patients. Greater emphasis regarding obtaining specimens representative of lower respiratory flora is necessary. Ideally these specimens should be obtained by a physiotherapist. Rapid transport of sputum specimens is necessary as anaerobes can die extremely quickly. Specimens will be incubated for 5 days.

4. Nasopharyngeal Aspirate Specimens from Children

These are normally collected for virological investigation and will only be accepted for bacterial culture if a telephone call is made to the respiratory bench (ext 2610 / 2009) to request it.

N.B. For the Neonatal Unit (Elizabeth and Constance Green Wards) routine bacterial culture is also carried out on 'deep' nasopharyngeal aspirate specimens and this will continue. Where Gram stains are also required for individual patients on these specimens, the ward should telephone the request to the respiratory bench (ext 2610 / 2009).

5. Other Sputum Specimens

Greater emphasis should be made on efficient transport of these samples to the laboratory. (Specimens which take a long time to arrive are unlikely to yield relevant pathogens.)

6. Ventilated Patients

It would be preferable for non-directed broncheoalveolar lavage specimens to be obtained from ventilated patients when clinically indicated (not routinely at weekends). Quantitative estimates of the organisms present could be undertaken and will give more relevant clinical information.

7. AFB Investigation (Direct line to TB laboratory ext 2652)

a) Sputum

Non-purulent as well as purulent specimens of sputum will be processed for AFB.

b) Lymph nodes or specimens from superficial sites

Biopsy specimens or specimens of pus are always preferable and will give the best results. As a last resort, where there is insufficient pus to be put into a container, normal swabs can be taken and placed in charcoal medium. This should be pre-arranged with the TB Lab Senior (ext 2652). Direct staining for acid fast bacilli is unreliable and should not be undertaken. The swabs will be decontaminated and subsequently placed in liquid media for rapid mycobacterial culture.

c) EMU specimens should only be taken in cases of suspected renal or miliary TB. The whole of three consecutive early morning urine samples should be collected (large containers are available from Clin Labs) and not just an aliquot.

d) Special blood cultures for AFB should be considered from immune suppressed patients and patients with miliary/disseminated disease.

For molecular investigations, discuss with Microbiology ext 7251 or 7249

8. General Comment

In the future molecular techniques may augment the clinical service and help elucidate the clinical relevance of organisms grown from respiratory samples. We also wish to encourage further research into this area. Results obtained using molecular techniques could be compared with those obtained from standard microbiological techniques (including near-patient testing).

Appendix 3.1: Results of throat swab TAT in days (in all phases)

TAT (Days)	**Throat swab** specimens Phase 1 (n = 3549) No. (%)	**Throat swab** specimens Phase 2 (n = 100) No. (%)	**Throat swab** specimens Phase 3 (n = 11) No. (%)
0	0	0	0
1	45 (1)	1 (1)	4 (36)
2	679 (19)	12 (12)	3 (27)
3	873 (25)	22 (22)	1 (9)
4	767(22)	23 (23)	0
≥ 5	1185 (33)	42 (42)	3 (27)

Appendix 3.2: Results of ear swab TAT in days (in all phases)

TAT (Days)	Ear swab specimens Phase 1 (n = 1393) No. (%)	Ear swab specimens Phase 2 (n = 63) No. (%)
0	0	0
1	14 (1)	0
2	264 (19)	9 (14)
3	301 (22)	18 (28)
4	252 (18)	5 (8)
≥ 5	562 (40)	31 (49)

Appendix 3.3: Summary of culture results from other RT specimens in phase 1 study

Culture results	Nose (n =410) No. (%)	ETT (n =431) No. (%)	BAL (n =107) No. (%)	MS (n =163) No. (%)	TS (n =60) No. (%)	T/S (n =51) No. (%)	NPA (n =211) No. (%)
Positive	183 (45)	249 (56)	44 (41)	41(25)	22 (37)	38 (76)	128 (61)
Negative	227 (55)	182 (42)	63 (59)	122 (75)	38 (63)	13 (25)	83 (39)

Nose swab ETT: endotracheal tube BAL: *Bronchoalveolar lavage* MS: mouth swab TS: tongue swab T/S: Tracheal secretion NPA: *nasopharyngeal aspirate*

Appendix 3.4: Culture findings from other respiratory tract specimens in phase 1 reported as culture positive

Microorganism/s	Nose (n =183) No. (%)	ETT (n = 249) No. (%)	BAL (n = 107) No. (%)	MS (n = 163) No. (%)	TS (n = 22) No. (%)	T/S (n = 38) No. (%)	NPA (n = 128) No. (%)
Beta-haem.streptococcus A	*6 (3.3)*		*1 (2.3)*	*1 (2.4)*			
Staphylococcus aureus	78 (42.6)	8 (3.2)	7 (15.9)	8 (19.5)	2 (9)	5 (13.2)	22 (17.2)
MRSA	11 (6.0)	5 (2)	2 (4.6)	2 (4.9)		7 (18.4)	
Beta-haem.streptococcus B	4 (2.2)	*2(0.8)*	*1 (2.3)*				1 (0.8)
Beta-haem.streptococcus C	1 (0.6)						
Candida tropicalis	1 (0.6)						
Candida albicans		4 (1.6)	2 (4.6)	26 (63.4)	15 (68.2)	2 (5.3)	3 (2.3)
Haemophilus influenzae		2 (0.8)	3 (6.8)				4 (3.1)
Streptococcus pneumoniae	14 (7.7)		5 (11.4)				8 (6.3)
Moraxella catarrhalis	3 (1.1)	1 (0.4)				2 (5.3)	3 (2.3)
Pseudomonas species	7 (3.8)	5 (2)	8 (18.2)	1(2.4)	1 (4.6)	7 (18.4)	7 (5.5)
Coag. neg. staphylococcus	18 (9.8)	135 (54.2)				3 (7.9)	31(24.2)
Organism of coliform group	28 (15.3)	77 (30.9)	12 (27.3)	2 (2.9)	4 (18.2)	6 (15.8)	43 (33.6)
Enterococcus species	1 (0.6)	3 (1.2)					
Escherichia coli	1 (0.6)	*2(0.8)*				1 (2.6)	
Enterobacter cloacae	1 (0.6)	1 (0.4)				1 (2.6)	
Acinetobacter species	1 (0.6)					*2 (5.3)*	1 (0.8)
Klebsiella species				1 (2.4)		1 (2.6)	1 (0.8)
Serratia marcescens			1 (2.3)				
Proteus species	8 (4.4)	1 (0.4)				1 (2.6)	4 (3.1)
Stenotrophomonas maltophilia		3 (1.2)					
Aspergillus species			2 (4.6)				

Appendix 3.5 :Culture findings from other RT specimens in phase 1 reported as culture negative

Microorganism/s	Nose (n = 227) No. (%)	ETT (n = 182) No. (%)	BAL (n = 63) No. (%)	MS (n = 122) No. (%)	TS (n = 38) No. (%)	T/S (n = 13) No. (%)	NPA (n = 83) No. (%)
No growth	72 (31.7)	137 (75.3)	6 (9.5)	6 (4.9)		7 (53.9)	49 (59)
No significant growth	2 (0.9)						
No staur/BHSA	6 (2.6)						
Coag. neg. staphylococcus	2 (0.9)	5 (2.85)					
Enterococcus species		1 (0.55)					
Organism of the coliform	5 (2.2)	4 (2.2)		4 (3.3)	2 (5.3)		7 (8.4)
Pseudomonas species	2 (0.9)						
Yeast species		2 (1.1)		9 (7.4)	3 (7.9)		1 (1.2)
Skin flora	138 (60.8)						
Mouth flora/Throat flora		33 (18.1)	57 (90.5)	103(84.4)	33 (86.8)	6 (46.2)	26 (31.3)

Appendix 5.1: Abdi, Y. (2008). Investigation of factors affecting quality of sputum specimen and culture results. *The Biomedical Scientist*, January: 27-33

Investigation of factors affecting quality of sputum specimen and culture results

Y ABDI
Department of Medical Microbiology, Barts and The London NHS Trust,
Royal London Hospital, 80 Newark Street, London E1 2ES, UK

Sputum is the most common lower respiratory tract specimen received by the microbiology laboratory. It is also often the most problematic to assess due to contamination by oropharyngeal flora. In spite of numerous guidelines on appropriate samples for microbiological examination, laboratories continue to receive large number of inappropriate sputum samples.

The aim of this study was to investigate the quality of sputum specimens, appropriateness of test requisition and adherence to specimen collection principles.

In this study 511 microbiology laboratory request forms from patients in whom sputum culture was requested in 3 months period were examined.

The factors studied included (a) sputum description based on macroscopic inspection (b) microbiological test requisition of sputum for microscopy, culture, and sensitivity (MC & S) (c) age of the specimen when received in the microbiology laboratory (d) whether patients were on antibiotic treatment (e) patients clinical diagnosis.

Analysis of the findings showed that the usefulness of culture results was limited by the collection of inappropriate specimens and lack of clinical information on the microbiology request form.

The crucial importance of the role of clinical and nursing staff is stressed if the clinical relevance of sputum culture is to be maximised.

The increasing introduction of electronic pathology test request gives new opportunities to restrict the collection of inappropriate specimens and make substantial savings in resources both in the ward and the laboratory.