PART 1

Introduction

Chapter 1
INTRODUCTION TO CLINICAL LABORATORIES

Patients may be subjected to many investigative procedures. These range in complexity from ward or clinic-based measurements familiar to all nurses, such as determining body temperature, pulse and blood pressure, through monitoring of heart function by electrocardiographic (ECG) machines to complex body imaging techniques, such as X-ray, computed tomography (CT) and magnetic resonance imaging (MRI) scan. All of these require the presence of the patient; they are performed on the patient, if not by nurses, at least often in their presence. In contrast, all the investigations described in this book are performed on samples removed from the patient. The remoteness of patients from the site of laboratory testing helps to engender the understandable though misguided perception that laboratory testing has little to do with nursing care and therefore need not concern nurses. In fact, an understanding by nursing staff of the work of clinical laboratories is important for several reasons.

Nurses are in a unique position to satisfy the need that many patients express for information about the tests to which they are subjected. This may be to allay fears and anxieties among those who have never undergone such a test before, or it may simply reflect a right to know. Most laboratory tests are only minimally invasive but can only be done with a patient's informed consent. Of course many patients will express no interest but some have questions that must be addressed.

Nurses often have responsibility for the collection and timely, safe transport of specimens. It is vital that anyone collecting samples is aware of the importance of good practice during this pre-testing phase.

Some blood and urine tests (e.g. blood glucose testing and urine dipstick testing) are performed by nurses at the point of care. It is important that the pitfalls, limitations and clinical significance of such testing are appreciated by those performing these investigations. Development of technology has allowed the introduction of chemical analysers into intensive care and emergency room settings, and an already established trend of increasing point of care testing is set to continue, with more nurses becoming involved in the analytical process.

Nurses are frequently involved in the reception of laboratory results. It is important that they are familiar with the terminology and format of laboratory reports

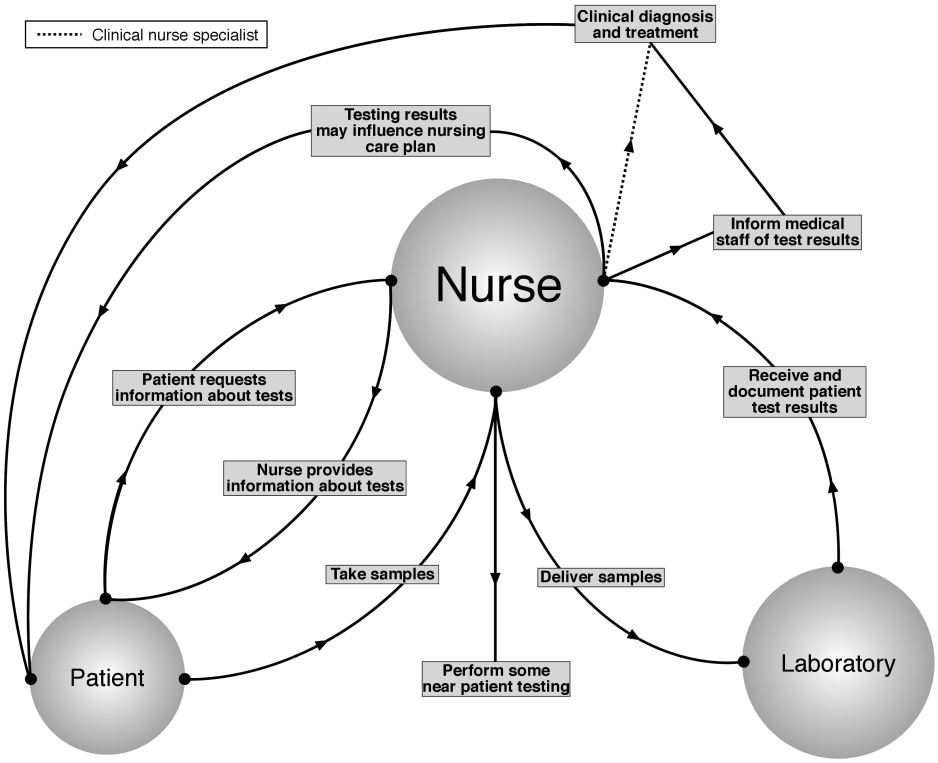

Figure 1.1 Nursing staff involvement in testing of patient samples.

and are able to identify abnormal results, particularly those that warrant immediate clinical intervention. Traditionally, doctors have had sole responsibility for both requesting and interpreting laboratory test results, but the developing role of the clinical nurse specialist and nurse consultant has required that nurses become involved in both of these processes. In any case, all qualified nursing staff have to make judgments about how the results of laboratory tests might impact on the formulation of nursing care plans for their patients.

Finally, there are those nurses whose professional role requires especially detailed knowledge of the work of the laboratory as well as close co-operation with laboratory staff. These include haematology nurse specialists, blood transfusion nurse specialists, infection control nurses and diabetic nurse specialists.

All the tests described in this book are performed – although not exclusively so – in clinical pathology laboratories. The final part of this introductory chapter serves to describe in outline the work of the five subdisciplines of clinical pathology, the range of patient types and samples tested (Table 1.1).

Table 1.1 Range of samples useful for laboratory investigation.

	Sample type
Chemical analysis	Usually blood or urine Less commonly: ● Faeces ● Cerebrospinal fluid (CSF): the fluid which surrounds the brain and spinal cord ● Pleural fluid: the abnormal accumulation of fluid in the pleural cavity of the lungs ● Ascitic fluid: abnormal fluid which accumulates in the peritoneal cavity
Haematological analysis	Usually blood only Occasionally bone marrow biopsy also useful
Microbiological analysis	Urine ● Blood ● Faeces ● Sputum Swabs from almost any accessible site including nose, throat, eye, ear wounds, vagina etc. Less commonly: ● Cerebrospinal fluid ● Pleural fluid ● Skin scrapings ● Nails ● Vomit
Histopathological examination	Tissue specimens only
Cytopathological	Cells recovered by scraping the surface of tissues (e.g. cervix) or aspirating abnormal fluids (e.g. cysts) Also urine and sputum are useful
Immunological analysis	Usually blood only

The clinical chemistry laboratory

(also known as chemical pathology, clinical biochemistry)

Clinical chemistry is concerned with the diagnosis and monitoring of disease by measuring the concentration of chemicals, principally in blood and urine. Occasionally, chemical analysis of faeces and other body fluids, for example cerebrospinal and pleural fluid, is useful.

Blood is a chemically complex fluid containing many inorganic ions, proteins, carbohydrates, lipids, hormones and enzymes, along with two dissolved gases, oxygen and carbon dioxide. In health, the blood concentration of each substance is maintained within limits that reflect normal whole body and cellular metabolism. Disease is often associated with one or more disturbances in this delicate balance

of blood chemistry; it is this general principle that underlies the importance of chemical testing of blood in the diagnostic process. The range of pathologies in which chemical testing of blood and urine has proven diagnostically useful is diverse and includes disease of the kidney, liver, heart, lungs and endocrine system. Some cancer cells release specific chemicals into blood. Measurement of these so-called tumour markers allows a limited role for the clinical chemistry laboratory in the diagnosis and monitoring of malignant disease. Nutritional deficiencies can be identified by chemical analysis of blood.

In addition to its diagnostic role, clinical chemistry is also involved in the monitoring of treatment. This role is most evident among patients receiving intravenous fluid replacement therapy or parenteral nutrition, who require regular monitoring of some aspects of blood chemistry. The blood concentration of some drugs must be monitored to ensure maximum therapeutic effect and minimum toxicity.

Most chemical testing of blood and urine is performed on highly sophisticated, automated machinery. A typical modern clinical chemistry analyser can process around 200–400 samples an hour with the option to perform up to 20 or more tests simultaneously on each sample. Results of the most commonly requested tests are usually available within 24 hours of receipt of the specimen. Some more specialised tests are performed only once a week. All laboratories offer an urgent 24-hour service for a limited range of tests; results of such urgently requested tests are usually available within an hour.

Intensive care patients often require frequent and urgent monitoring of some aspects of blood chemistry. In these circumstances, limited blood testing is performed by nursing staff using dedicated analysers sited within intensive care units; this represents one aspect of so-called point of care testing.

The haematology laboratory

Haematology is concerned principally with the diagnosis and monitoring of diseases that affect the number, size and appearance of the cellular or formed elements of blood. These are: the red blood cells (erythrocytes), the white blood cells (leucocytes) and platelets (thrombocytes). The full blood count (FBC) is the most frequently requested laboratory test, reflecting the range of common and less common disorders which affect both the numbers and appearance of these cells. It is in fact not one but a battery of tests.

The modern haematology analyser is able to process FBC tests at the rate of 100 samples per hour. The detailed information about the blood cells which these analysers provide has dramatically reduced the number of specimens which need to be examined under the microscope, but the microscope remains an essential tool to the haematologist for examination of bone marrow biopsy specimens and, in some circumstances, blood.

Apart from the cells in blood, haematology is also concerned with measurement of the concentration of some of the proteins present in blood which are involved in the process of blood coagulation.

Disorders of the blood in which haematology testing is important include: haematological malignancy (e.g. the leukaemias, Hodgkin's disease, myeloma), anaemia and diseases such as haemophilia in which disturbances of blood coagulation result in an increased tendency to bleed. Some haematology tests, including the FBC, are useful in the diagnosis or clinical management of some common, non-haematological diseases. For example, infectious disease is usually associated with an increase in the number of white blood cells. Anaemia is often a feature of many chronic inflammatory disorders such as rheumatoid arthritis, or may result from diseases of nutritional deficiency.

Many patients at risk of heart and blood vessel disease are given tablets, which tend to prevent the blood from clotting. This anticoagulation therapy must be monitored by regular blood testing to prevent excessive bleeding, a potentially dangerous side effect of such therapy.

Most haematology test results are routinely available within 12–24 hours. However, if the need is clinically justified, results of some haematology tests, including FBC, can be made available within an hour or so, at any time of the day or night.

The clinical microbiology laboratory

Clinical microbiology is concerned with the diagnosis of disease caused by infective agents, mostly bacteria but also viruses, fungi and parasitic worms. Much of the work involves isolation and identification of bacteria from many sorts of sample, including urine, sputum, faeces, blood, cerebrospinal fluid and swabs taken from a variety of infected sites. Bacteria can sometimes be seen by examining these specimens under the microscope, but more precise identification can only be made after culture, or growth of bacteria on nutrient-enriched media. One of the problems encountered by the microbiologist when dealing with clinical specimens is that many bacterial species are normally present in many sites around the body; indeed in some cases are essential for normal health. The microbiologist must isolate those that are pathogenic (i.e. cause disease) from those that are normally present, and from any environmental bacterial contaminant introduced during sample collection. Some body fluids are normally sterile; these include blood, cerebrospinal fluid, and fluid aspirated from joints and the pleural cavity. Bacteria isolated from these sites are always pathogenic.

Having isolated and identified a species of pathogenic bacteria, the next step is to test the sensitivity of the organism to a range of antibiotics. This information helps in deciding which antibiotic therapy is likely to be most effective in eradicating the infection.

Blood testing plays a limited but important and evolving role in detecting infections that are caused by organisms difficult to isolate by culture. During any infection the immune system produces specific antibodies directed at specific antigens present on the surface of the invading organism. A rising amount of the antibody in blood provides evidence of current infection.

Specific antigens present on the surface of organisms also provide a means of identifying infective agents. Testing blood for the presence of viral antigens is an important means of diagnosing viral infections such as those that cause hepatitis and acquired immune deficiency syndrome (AIDS).

Microbiological investigation may take from several days to several weeks to complete; this delay is governed largely by the speed of bacterial growth in culture. Initial microscopical examination can be performed immediately on receipt of the specimen if clinically necessary, and results can usually be made available on the day the sample is received in an interim report.

Clinical microbiology laboratories operate a 24-hour service for the rare cases when urgent culture and microscopical examination of samples is necessary. These include suspected cases of immediate life-threatening infections of blood (septicaemia) and central nervous system (meningitis).

Quite apart from their diagnostic role, hospital microbiology laboratories play an important role with infection control nurses in the monitoring and prevention of nosocomial infectious disease, that is infectious disease acquired by patients while in hospital, an ever present problem, which impacts on the working life of all nursing staff.

The blood transfusion laboratory

Blood transfusion is concerned with the provision of a safe supply of blood and blood products. In contrast to other pathology departments, blood transfusion has limited diagnostic function. In some senses its function more resembles a pharmacy in that its main purpose is to supply therapeutic products. With the possible exception of very severe blood loss involving more than half the total blood volume, the transfusion of whole blood is rarely necessary. The most frequently needed blood product is red cells, to correct anaemia and to replace blood lost during surgery or as a result of trauma. Much less commonly, the white cells of blood, platelets and the proteins present in blood plasma are therapeutically useful.

The National Blood Service (NBS) is responsible for the collection and supply of safe (disease free) donated blood to hospital blood transfusion laboratories. Here, each donated unit of red cells must be tested for compatibility with the patient's blood before it can be transfused. The transfusion of incompatible blood products can have very serious health consequences and is potentially fatal. Advances in compatibility testing have ensured that compatible red cells can be made available for transfusion usually well within an hour of a patient's blood sample arriving in the laboratory; this service is available 24 hours a day.

The blood transfusion department also has an important specific diagnostic role for some forms of haemolytic anaemia, in which the body produces antibodies against its own red cells. One important aspect of this work is haemolytic disease of the newborn, a potentially fatal condition in which the red cells of the developing fetus are destroyed by antibodies present in the mother's blood. All pregnant women are routinely tested for the presence of such antibodies.

The histopathology laboratory

(also known as morbid anatomy, cellular pathology)

Histopathology, the oldest of all pathology disciplines, is concerned with the diagnosis of disease by microscopical examination of tissue samples (biopsies). The rationale for this approach is that disease processes, e.g. malignancy, inflammation, infection, etc. are characterised by specific changes at the tissue and cellular level which are evident when tissue is viewed under the microscope. There are many ways of recovering tissue samples from the body. Tissue from the gastrointestinal tract, lungs and urinary tract are commonly sampled at the time of endoscopic examination. An endoscope is an instrument used to visually examine internal organs directly by fibre optics. The instrument includes small forceps, which can be used to remove small pieces of tissue during the examination. Tissue may be taken during surgery by incision or excision biopsy. Incision biopsy is the removal of a sample cut from an area of diseased tissue, whereas excision biopsy involves removal of the whole area of diseased tissue.

Before transport to the laboratory, biopsy samples must be 'fixed' in a chemical fixative, usually formalin, to preserve structure. This process can take from a few hours to a whole day depending on the size of the specimen. In the laboratory, 'fixed' specimens are impregnated with paraffin wax, allowed to harden and then cut into very thin sections just 3–5 μm thick. These wafer thin sections are then mounted on glass microscope slides and stained with chemicals, before examination under the microscope. The whole process from reception of specimen to issue of a histopathological report can take from one to three or four days depending on the size of the biopsy sample. Sometimes it is important to make a diagnosis very quickly, and in these circumstances a frozen section is performed. Tissue is 'fixed' immediately by freezing. This process allows sections to be cut almost immediately the sample is removed from the patient. The sections are stained and examined under the microscope. This rapid technique allows a diagnosis of, for example breast cancer, to be made in a half an hour or so while the patient remains anaesthetised on the operating table. Armed with a laboratory report that confirms malignant disease, the surgeon can proceed immediately to surgical treatment.

Microscopical examination of tissue removed from the patient is probably most widely used in the diagnosis and staging of malignant disease in organs throughout the body. It is also used in the differential diagnosis of non-malignant disease of the liver, kidney, lungs and gastrointestinal tract. It has a role in the diagnosis of connective tissue and skin disorders. More recently it has been used in the early diagnosis of tissue rejection among patients who have received transplanted organs.

All histopathological tests are invasive, often requiring surgical intervention to recover samples. Both financial and patient safety considerations ensure that, unlike other laboratory investigations, histopathological investigations are reserved for those patients in whom there is a strong suspicion of serious disease. In many cases, this suspicion will have been raised by the abnormal results of blood and urine tests performed in other pathology laboratories, so histopathology can represent the final stage in laboratory diagnosis.

Finally, post mortem examinations, to determine cause of patient death, are conducted in the hospital mortuary, which is administratively part of the histopathology department.

Cytopathology is a sub discipline of histopathology. Whereas histopathology is concerned with microscopical examination of tissue samples, the focus of the cytopathologist is the cells that are normally exfoliated from the epithelial surface of organs. Sample recovery is less invasive than that required for histopathological investigation. Typically cells are scraped from the surface of organs such as the cervix of the uterus, the mucosal surface of the duodenum and stomach and lungs. Cells can also be recovered by aspiration using a fine needle and syringe, from the pleural and peritoneal cavities, or from solid tumours, for example in the breast. The cells are spread onto a glass microscope slide, fixed and stained and then examined under the microscope. Cytopathology is almost exclusively concerned with diagnosis of pre-malignant and malignant disease. The cervical smear test, used to screen women for cervical cancer, accounts for a large proportion of the workload of the cytopathology laboratory.

The immunology laboratory

Clinical immunology laboratories are concerned principally with blood testing for the diagnosis of autoimmune diseases, in which the body's normally protective immune system produces antibodies against its own tissue antigens. These self-reacting, destructive antibodies are called autoantibodies. The detection in blood of organ specific autoantibodies is helpful in the diagnosis of many diseases with an autoimmune component including some thyroid disorders, pernicious anaemia, and some forms of kidney and liver disease. More rarely, tissues may be microscopically examined for the presence of the complex formed when an autoantibody reacts with its complementary antigen. For example, the autoimmune disease systemic lupus erythematosus (SLE), which affects many organ systems, can be diagnosed by microscopical examination of a skin biopsy for the presence of such complexes.

Laboratory staffing

Clinical laboratories are staffed by graduate trained biomedical scientists (BMS) who are responsible for the analysis of samples. They are helped in this task by medical laboratory assistants (MLAs). Cytoscreeners are a specially trained group whose work is confined largely to the examination of cervical smears. Each pathology department is headed by a medically qualified doctor of consultant status who has specialised in one area of laboratory medicine (in some cases a non-clinical scientist fulfils this role). They provide a consultancy for clinicians on all aspects of laboratory medicine, so they might advise both on the

most appropriate laboratory investigation in particular cases, and the clinical significance of test results. Haematology consultants also have clinical responsibility for the care of patients suffering haematological disease (e.g. leukaemia). Medical consultants attached to clinical chemistry departments are often responsible for the clinical care of patients suffering diabetes and other metabolic and endocrine disorders, while a microbiology consultant is responsible with the control of infection nurse for the formulation and implementation of the hospital control of infection policy.

Histopathological diagnoses are made by a consultant histopathologist who also performs all post mortem examinations with the assistance of a mortuary technician

The future

Around 70% of patient diagnoses depend on the results of pathology laboratory tests. Recognition of the central role that pathology provides in the delivery of medical care to patients has led to a government-initiated programme of modernisation of pathology services.[1] One of the principal aims is 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) with nurses and other non-laboratory healthcare professionals becoming more involved in patient testing.

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.[2] In doing this work, pathology laboratories consumed an estimated 3.3% of total NHS expenditure.[2] Over the intervening years workload has continued to rise, currently at the rate of 10% per annum.[3]

As in all other areas of patient care, successful laboratory investigation depends on teamwork; nurses are important members of that team. Good communication between nursing and laboratory staff can help to ensure that resources consumed in delivery of pathology services are used to best effect for the patient.

References

1. Department of Health (2005) *Modernising Pathology: Building a Service Responsive to Patients*. London, The Stationery Office.
2. Audit Commission (1993) *Critical Path: An Analysis of Pathology Services*. London, HMSO.
3. Beastall G (2004) The impact of the General Medical Services Contract: national evidence. *Bull R Coll Pathol* **128**: 24–27.

Useful websites

www.ibms.org Institute of Biomedical Sciences – the professional organisation that represents biomedical scientists – the largest group of pathology laboratory staff.

www.rcpath.org Royal College of Pathologists – the professional organisation that represents pathologists – medically qualified laboratory staff.

www.acb.org.uk Association of Clinical Biochemistry – the professional organisation that represents non-clinical scientists working in clinical chemistry laboratories.

www.labtestsonline.org.uk website for patients about laboratory tests – includes a wealth of information about the work of pathology laboratories.