

---

# Clinical Laboratory Techniques and Microtechnology

## Primary Knowledge (PK – reading unit) Participant Guide

### **Description and Estimated Time to Complete**

*This learning module is an overview of how microtechnology is used for standard clinical laboratory tests. It covers the advantages and challenges of taking clinical tests out of the laboratory to the point of care (POC). An activity allows you to dig deeper into a specific test or technique and discover how microtechnology is changing medical diagnostics.*

This reading unit introduces you to the Clinical Laboratory. You will learn about the testing that takes place in a clinical lab, the requirements of the technicians and equipment used to produce accurate and consistent results, and the possibilities of replacing some of these tests using microtechnology such as microelectromechanical system (MEMS) and bioMEMS.

When reading the following overview, ask yourself this question: "Which clinical laboratory tests have been modified or could be modified so they can be done in non-laboratory conditions such as at home or in the field?"

This is a new field for microtechnology, so there are many possibilities open for the creative mind.

If you run into medical terms you are not familiar with, check out the glossary at the end of this unit.

### Estimated Time to Complete

Allow at least 30 minutes to review this material and answer the questions.

## Introduction

Have you ever donated blood or had blood drawn as part of your annual physical? If so, in both cases, your blood would have gone to a clinical laboratory for analysis. The donated blood would have been for blood type and disease then prepared for a blood bank or other medical applications. The drawn blood for the physical could have been checked for components such as the number of red and white blood cells, platelets and various enzymes and possibly, antibodies.

Clinical laboratories perform several different types of procedures:

- Analyze body fluids, cells and other components like DNA and RNA.
- Look for the presence of pathogenic entities such as bacteria, viruses and other microorganisms.
- Analyze the chemical content of fluids.
- Match blood for transfusions.

In order to accurately perform these tests, the technicians must be properly trained and the tools and equipment used must be able to accurately test for the components being analyzed.



*Clinical Laboratory testing*

To understand which tests can be adapted with microtechnology, it is advantageous for one to understand what clinical laboratory personnel do, how they do it, and the regulations that govern their training and laboratory activities.

In this unit you will study the following:

- An overview of activities that occur in the clinical laboratory including a discussion on sampling, testing and required certifications.
- The advantages and disadvantages of using microtechnology for clinical laboratory tests.

## Objectives

- Summarize at least three procedures performed in clinical laboratories.
- Describe at least three possible micro-sized devices or bioMEMS that might be suitable for clinical laboratory testing.

## **MEMS for Clinical Laboratory testing**

Clinical laboratory techniques are increasing in number and changing in methodology. This is due in part to the [Human Genome Project](#) that is being accelerated with the use of microtechnology and bioMEMS technology. This technology is being used to accelerate genome sequencing and to convert desktop instrumentation into portable devices for testing such as on-the-spot DNA diagnosis of infectious diseases, paternity testing, and DNA typing.<sup>1</sup>

In clinical laboratories, the incorporation of microtechnology has several advantages:

- Decreased costs as a result of miniaturization
- Use of smaller samples size
- Ability to test at home or in the field (point of care (POC) testing)
- Ability to multiplex tests (test for several analytes in one sample)

One disadvantage of microtechnology in clinical laboratory testing is that the concentrations of some analytes are too low for the test to be miniaturized. Low concentrations of analytes require a fairly large sample. For example, if the goal is to identify and isolate, from whole blood, infected white blood cells (WBCs) that are present at an incidence of only 1 in 10 million uninfected WBCs, then quantities in excess of 10 mL of whole blood may be required to encounter just five cells. This does not provide the ideal situation for a microdevice.

However, for smaller sample sizes (microliters, nanoliters, picoliters) where higher concentrations of analytes are being tested, microtechnology is ideal for clinical laboratory testing equipment. Laboratory equipment can handle these smaller test samples by using micro-sized fluidic channels and chambers, valves and actuators. Microtechnology in clinical laboratories has led to a decrease in the equipment's footprint as well as a decrease in the amount of reagents required for testing, the amount of waste produced, and the amount of consumables.<sup>2</sup>

Let's look at an application that has adapted quite well to the implementation of microtechnology in clinical laboratory testing – testing for the human immunodeficiency virus (HIV) and hepatitis C virus (HCV).

### **Microtechnology for Individual HIV/HCV Testing**

Microtechnology has been developed for rapid HIV testing. This HIV testing can now be performed at the point-of-care (POC) with the results being sent to a clinical laboratory for analysis, or with some devices, analyzed in the field.

One example of a micro-sized testing device that is already on the market is the Multiplo HIV/HCV antibody test developed by Medmira Inc. The Multiplo is an antibodies testing device that simultaneously tests for the human immunodeficiency virus (HIV) and hepatitis C virus (HCV). The device is small enough to fit in the palm of your hand. Because of its size, only a very small sample of serum, plasma or whole blood is required to perform the test. All one needs is a small amount of blood drawn from a simple finger prick.<sup>3</sup> (Note: The [newest Multiplo device](#) simultaneously tests for HIV 1/2, Hepatitis B (HBV) and HCV.)



**The Multiplo HIV/HCV  
Antibodies Test**

*(drawing does not represent actual device)*

The test does not require refrigeration nor does it require a technician to interpret the results. For one type of Multiplo, the presence or absence of two lines and a dot indicate one of four results:

1. Possible exposure to HIV-1, HIV-2, and/or HCV
2. Possible exposure to HIV-1 and/or HIV-2
3. Possible exposure to HCV
4. Invalid results

This test can be performed at home, providing an immediate solution. (*NOTE: This particular device is not approved by the FDA and therefore cannot be sold or used in the USA. However, similar devices such as the OraQuick In-Home HIV Test have been approved by the FDA.*<sup>4</sup>)

## **Microtechnology for Point-of-Care Testing**

Over just the past few years, microtechnology has significantly increased the ability to provide point-of-care (POC) testing. Point-of-care testing devices are small devices that are used in the field by either health care professional, technicians trained to use the devices, or even individuals. Daily glucose monitoring by diabetics is a prime example. This POC microtechnology that has been tested, proven, and has been commercially available for several years. There are currently “hundreds of (POC) devices being sold around the world for other applications, such as drug screening, urine analysis, coagulation, cardiac assessment, virus detection (HIV), and all of these employ microtechnology.”<sup>5</sup>

Another example of POC testing is drug screening. During the 2012-2013 school year, OraSure, a manufacturer of a POC non-invasive drug testing device, screened 1,200 students in Texas, on location. The sample was oral fluid collected from the students’ mouths, eliminating the embarrassment and inconvenience of peeing in a cup. Each test took five minutes and costs considerable less than previous methods. However, the collected samples still had to be sent to the lab and it took 24-48 hours to get the results. The advantages of this tests were primarily in the collection method and the required sample size – a small amount of oral fluid, as opposed to a jar of urine.<sup>6</sup>

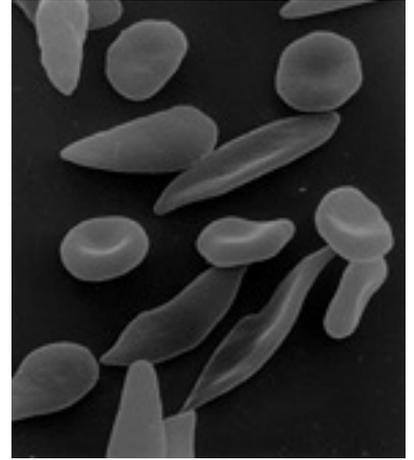
## **Clinical Laboratory Testing**

To better understand how microtechnology can be used for a multitude of laboratory testing, you need to understand what is actually done in a clinical lab. In the following sections we will discuss various aspects of clinical lab testing:

- The role of clinical lab personnel
- Sample sources and collection
- Typical clinical laboratory tests
- Training, licensure, and certification of personnel

## The Basic Principles of Clinical Testing and Laboratories

- Clinical testing uses analyte (biomarker) concentrations in bodily fluids to establish normal or reference values (e.g., The number of red blood cells in a sample).
- Clinical testing detects changes in the analyte concentrations in bodily fluids indicating a diseased state(e.g., A decrease of red blood cells).
- Cells have a particular physical appearance that is classified as either healthy or unhealthy. This can be seen in clinical testing. The picture shows sickle-shaped red blood cell from a patient with sickle cell anemia.
- Laboratory personnel are trained to take bodily samples, carry out tests on samples, analyze test results, and communicate results to physicians.
- Clinical laboratories and the personnel that work in the laboratories are certified and recertified in a timely manner to ensure quality results that are comparable from lab to lab.



*Sickle shaped red blood cells  
[Image courtesy of Drs. Noguchi, Rodgers, and  
Schechter of NIDDK.]*

## Duties of the Clinical Laboratory Technologist

Clinical laboratory personnel (technologists) perform several tasks. Here are a few of their primary duties:

- Examine and analyze body fluids, cells, and other biological components.
- Test for disease-causing microorganisms such as bacteria and parasites.
- Analyze the chemical content of fluids.
- Match blood for transfusions.
- Test for drug levels in the blood that show how a patient is responding to treatment.
- Prepare specimens for examination.
- Count cells in blood and body fluids.
- Look for abnormal cells, such as cancer cells, in blood and body fluids.

To perform these tasks, technologists use simple equipment such as microscopes, and more sophisticated equipment such as DNA sequencers. Some of the equipment is automated and computerized, but some is not. Some equipment can perform only a single test, while other equipment can perform several tests simultaneously.

Once a test is performed and the specimen examined, the technologist analyzes the results, records the findings and generally submits the reports to the physicians.

## Sample Sources

Your body is made up of many different types of cells. These cells are found in several of our bodily components such as blood, skin, urine, and hair. Almost all of these cells can be gathered and tested. The cells that are tested the most are found in the blood and urine; therefore, blood and urine are the two most common sample sources for clinical testing. Other sample sources, depending upon the clinical testing needed, include sweat, spinal fluid, joint fluid, sputum, hair, feces, oral fluids, bone marrow, nails, body scrapings and tissues from internal organs. The POC drug testing devices talked about earlier uses oral fluids extracted from the mouth.

## Sample Collection

For blood tests, two methods are used to obtain samples:

Finger prick (see picture) – Your finger is pricked for a small amount of blood. This blood is drawn into a tiny tube or smeared on a glass slide.



Blood draw - A vein on the inside of your arm is used for a venipuncture. Blood from the vein is drawn using a hypodermic needle with a small, glass vacuum tube. When the vein is punctured, the vacuum draws the blood into the tube.

*(Photo courtesy of the National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Health)*

Spinal fluid, joint fluid, bone marrow, and tissue samples are traditionally collected by a physician. Urine samples, feces, sputum, oral fluid, semen or other materials are collected at the laboratory or at home. For these samples, clinical laboratory personnel instruct individuals on the proper collection methods.

## Sample Preparation

Once the sample has been collected, it usually must undergo some biochemical processing in order to obtain the quantitative result that is needed for the patient. Commercial Clinical Laboratory instruments handle this processing in a highly automated fashion. The needed processes include sample cleaning and purification, cell lysing (i.e., destruction/decomposition), biomolecular capture, nucleic amplification, separation, and sample immobilization. Some BioMEMS tools for these processes include magnetic nanobeads, silica beads, electrophoretic sorting, magnetophoretic sorting. Following are brief descriptions of how a few of these processes work.

### *Silica Beads and Magnetic Nanobeads Technologies*

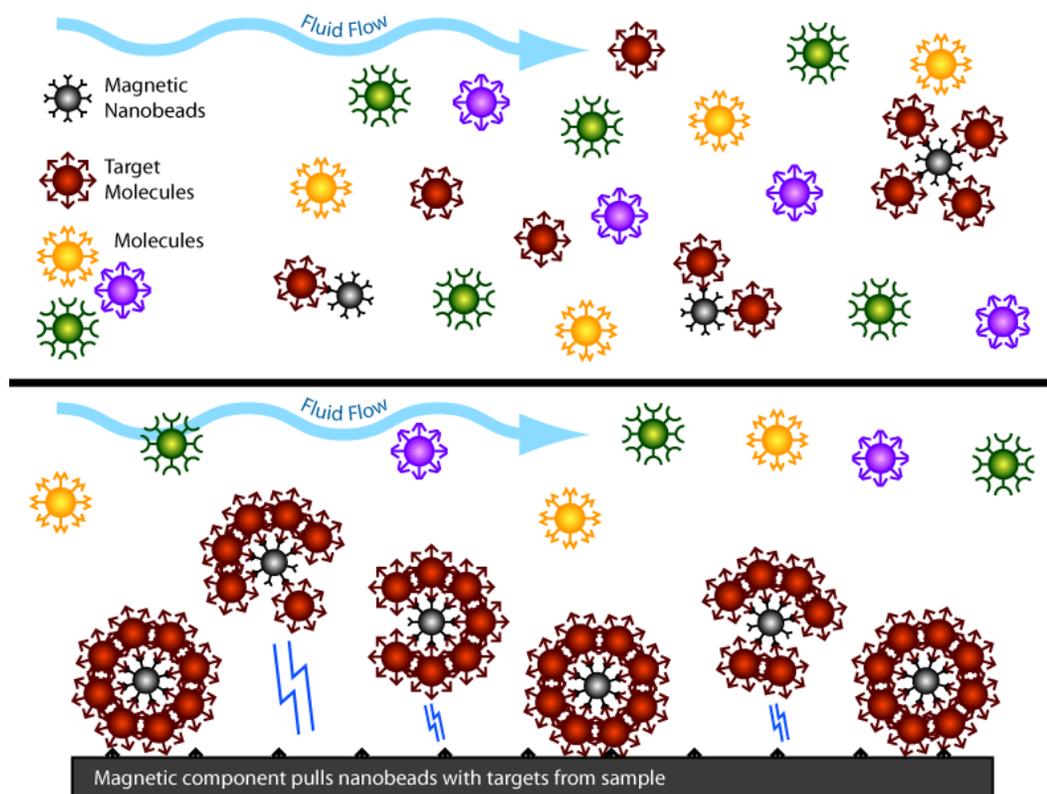
Beads are used as solid substrates that can bio-specifically capture molecules of interest, while discarding the vast majority of the sample, thereby increasing the effective sample concentration by many orders of magnitude. Magnetic and electrical forces are used in bioMEMS devices to perform these functions on samples that are both stationary and flowing.

In forensics, silica beads are being used to extract DNA from a sample by first being used to “beat up” the sample cells through mechanical lysis, and then attach to the extracted DNA. In a centrifuge, micro-sized silica beads are combined with the sample in an aqueous solution. Once the cell membranes are weakened through chemical lysis, mechanical lysis occurs by the silica beads physically breaking the cell membranes down even further. A salt solution is added that encourages the DNA to bind to the silica beads. Contaminates and other particles are extracted from the solution leaving the silica beads with the purified DNA. An elution buffer is then added that allows the DNA to separate from the silica beads and to be extracted from the solution<sup>7</sup>.

In medical applications, micro and nano-sized magnetic beads are being functionalized with probe coatings that provide analyte specificity. For example, IBA Solutions for Life Sciences uses magnetic nanobeads covalently linked with Strep-Tactin® to identify a specific antigen or type of strep on T-cells (MHC 1 Streptamers). These beads are currently sold on the commercial market.<sup>8</sup>

So how does this work? Below is one method that is being used.<sup>9</sup>

- The surfaces of the magnetic beads are functionalized with the specific probe molecules (molecules capable of detecting specific molecules). (See “magnetic nanobeads in graphic)
- The beads are added to the test sample where they detect and bind to the *target molecules* (the molecules to be detected).
- A magnetic field is applied that easily separates the bound beads/targets from the rest of the material in the sample. The unbound material is removed. (See graphic below.)
- At this point the solution can be adjusted so that the binding is broken between the beads and the target, and the beads are removed magnetically, leaving the target molecules. In some cases the target can be analyzed without being separated from the beads.



*Another example of magnetic nanobeads:*

“Researchers at Oregon State University have found a way to use magnetic "nanobeads" to help detect chemical and biological agents, with possible applications in everything from bioterrorism to medical diagnostics, environmental monitoring or even water and food safety.” This technology is very similar to the magnetic nanobeads previously discussed.

Specific probes can be attached to nanobeads that are inserted into a gaseous or aqueous solution, or just exposed to the surroundings. The probes identify specific analytes or targets (e.g., antigens, gas molecules, contaminate) while ignoring untargeted molecules in the solution. Once the analytes are detected, “a "ferromagnetic resonance" is used to relay the information electronically to a tiny computer and the information is immediately displayed to the user.” This is essentially a lab-on-a-chip or LOC, a device we’ll be talking about later on in this unit.<sup>10</sup>

*Magnetophoretic Sorting*

Magnetophoretic sorting is another method being used for sample preparation. Magnetophoretic sorting provides a method in which cells can be separated based on their magnetophoretic mobility (“a property related to the relative binding distributions of magnetic particles per cell”). Again, magnetic nanobeads are used that bind with specific cells in a sample. The sample is then exposed to a magnetic field that “separates” the cells into cell type.<sup>11</sup>

## **Testing**

Testing is the process of analyzing the sample for one or more specific item or "analyte". Testing can be quantitative, semi-quantitative, qualitative, or a descriptive physical or chemical analysis.

Many test results use what is referred to as the "normal or reference range" for an analyte's concentration. This range is determined by the results expected from 95% of individuals tested by each testing laboratory. This range is not a national result or even state result, but a result developed by the clinical laboratory scientists in each testing laboratory. Having a range specific to each laboratory is due to the many variables involved in the testing process. Each variable can affect the outcome. Such variables include

- the type of instrument and reagents used,
- the principle or method for the test that is being performed, and
- the type of population being served.

For example with population, children usually do not have the same ranges as adults, and men often have different ranges than women. An example of this is the Erythrocyte Sedimentation Rate (ESR). This is a common blood test used to detect the amount of inflammation in the body. It is determined by the rate at which the red blood cells (erythrocytes) settle in the bottom of a test tube over a period of time. One method that is used is called the Westergren method. This method yields a range of 0 – 15 mm/hr for males and 0 – 20 mm/hr for females.<sup>12</sup> However, between laboratories this range can be affected by factors such as specific lab equipment and technicians, as well as the age of the subjects.

With the possibility of worldwide standardized testing on the horizon, the determination of normal ranges would have to be global and the variability of the factors affecting testing outcomes would have to be decreased.

## Types of Laboratory Tests

There are thousands of possible laboratory tests, with around 500 performed in most institutions. The most frequently requested tests are listed below.

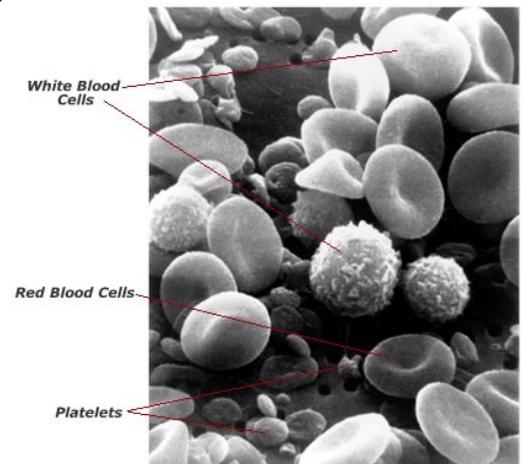
*While we review these tests, think about which tests could be modified for non-laboratory conditions (such as at home or in the field) using microtechnology?*

### Blood Tests (Hematology)

- 1) Red Blood Cell (RBC) - the number, structure, or function of red blood cells. RBC is used to evaluate anemia (a condition where the RBC count is less than normal)
- 2) White Blood Cell (WBC) - the number of white blood cells. WBC is used to look for infection or leukemia, as well as evaluate a person's response to a specific treatment.
- 3) Differential Count - the proportions of the different types of white blood cells. Infection, allergies, and a variety of illnesses can change the proportion of the different types of white blood cells.
- 4) Platelet Count - the number of platelet cells. Platelets provide the necessary hormones and proteins needed for proper blood clotting.
- 5) Coagulation (clotting) studies - Bleeding time, prothrombin time and other tests that determine the clotting process in the blood.
- 6) Hemoglobin - A measure of the oxygen-carrying capacity of the blood.

*This picture is a scanning electron microscope (SEM) image from normal circulating human blood. One can see red blood cells, several white blood cells including lymphocytes, a monocyte, a neutrophil, and many small disc-shaped platelets.*

*[Image Courtesy of the National Cancer Institute – Bruce Wetzel and Harry Schaefer (photographers)]*



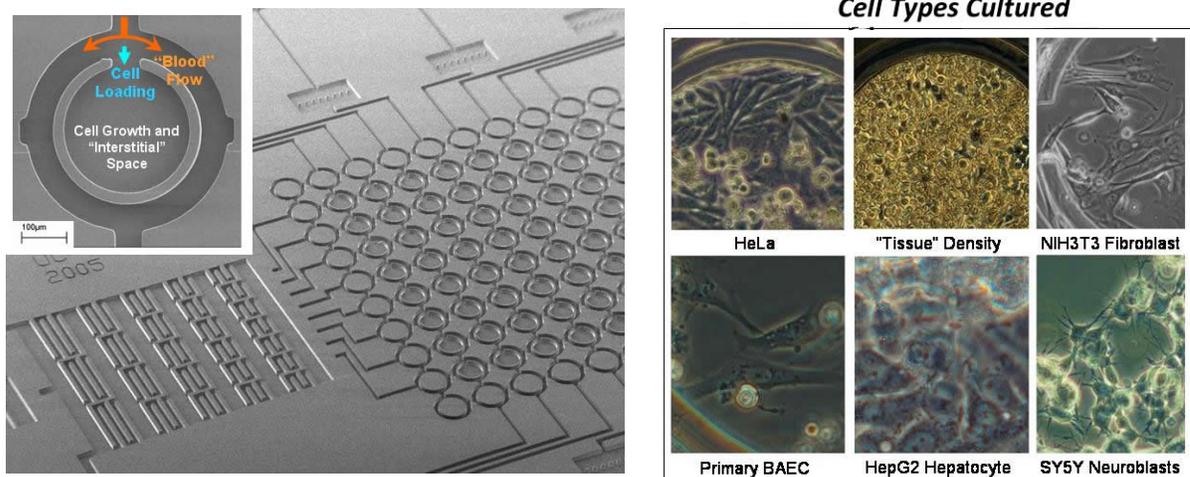
## Chemistry

- 1) Sugar (glucose) - the amount of sugar in the blood. This is a measurement for diabetes mellitus.
- 2) Electrolytes (sodium, potassium, chloride and carbon dioxide) - These substances maintain fluid and blood pressure balance, and are essential for the function of most body systems.
- 3) Enzymes – The enzymes aspartate amino transferase (AST) and alanine transaminase (ALT) help to diagnose liver disease. Creatine kinase (CK) and lactate dehydrogenase (LDH) help to diagnose heart disease.
- 4) Cholesterol - High amounts are associated with heart and blood vessel diseases.
- 5) Urea Nitrogen - Tests for kidney function.
- 6) Uric Acid – High concentrations may indicate gout. Levels are also monitored for chemotherapy and radiation therapy patients.

## Microbiology

Microbiology testing is the process of analyzing micro-organisms. There are three basic steps to microbiology testing:

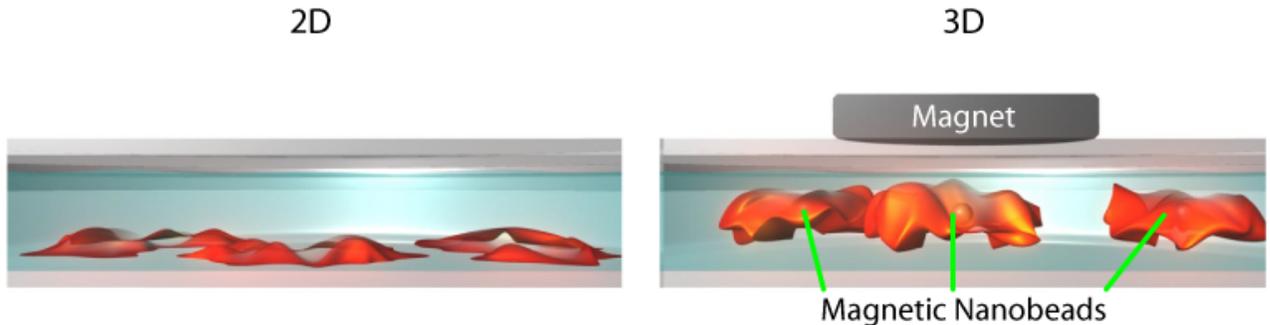
- 1) Culturing (growing) bacteria for the purpose of identifying the organism. (See *MEMS Culture Array below*)
- 2) Preparing a smear and stain of a bacterial culture for the preliminary evaluation of infection.
- 3) Sensitivity test - Testing bacteria with antibiotics to determine which drug is most effective.



*MEMS Cell Culture Array (left). This array creates a microenvironment for growing cells in vitro and in parallel, allowing for the analysis of multiple cell growth conditions. The inset left shows the microenvironment of each array component. The cells on the right were grown in the cell culture array developed at the BioPOETS Lab, UC-Berkeley. [Developed by and courtesy of BioPOETS Lab, UC-Berkeley]*

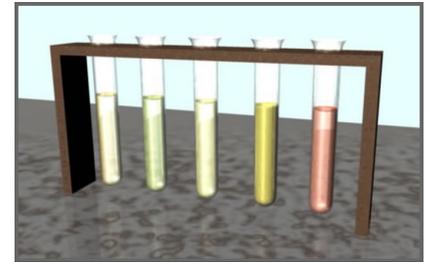
## Three-Dimensional Cell Culture Using Magnetic Nanobeads

In a study by a team of Houston scientists, magnetic iron oxide nanoparticles were added to a gel that contained phage (a virus that destroys bacteria by lysis). The phage caused the particles to be absorbed into cells over a few hours. The nanoparticle-loaded cells were then transferred to a Petri dish “filled with a liquid that promotes cell growth and division.” When a coin-sized magnet was placed on top of the Petri dish, the nanoparticles inside the cells were attracted to the magnet, lifting or “levitating” the cells off the bottom of the dish. This allowed the cells to grow and divide while being suspended in the liquid. This process of 3D cell culturing is more like the ways cells grow and divide in the body as compared to the 2D growth in the bottom of a Petri dish.<sup>13</sup>



## Urinalysis

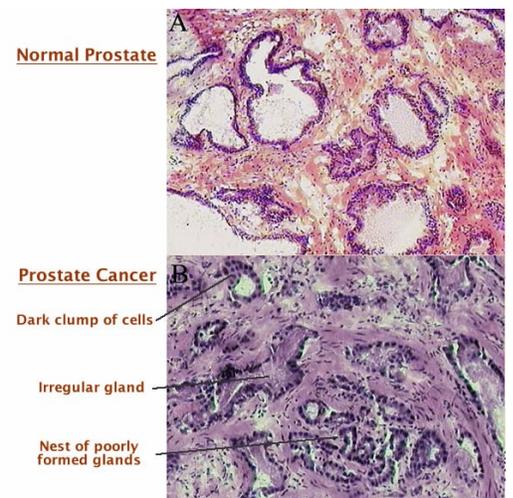
Many individual tests make up a urinalysis, such as measuring the amount of glucose, blood, and bacteria present in the urine. The results of a urinalysis provide the physician information about the kidneys, liver and other body processes. The color, lack of color, transparency, or cloudiness of the urine provides usable information about the patient.



Urine Samples

## Histology

Histology is the study of the microscopic anatomy of cells and tissue. In order to perform this test, a biopsy must be performed. A biopsy is the removal of a small section of the tissue to be studied. The type of cells and their chemical reactions are evaluated. For example, the picture shows a prostate gland biopsy from a normal prostate (A) and from a cancerous prostate (B). In the cancerous prostate one can see irregularly shaped glands and poorly formed glands.<sup>14</sup>



*[Photomicrographs courtesy of United States Government (Public domain)]*

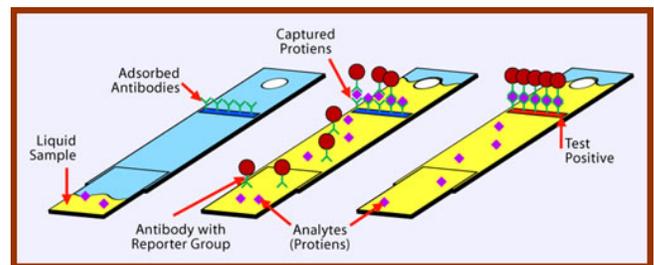
## Cytology

Cytology is the study of cells. Microscopic examination of cells is used to determine abnormal conditions or malignancy. An example is the Pap smear taken to detect cervical cancer in women.

## Immunology

Immunology is the study of all aspects of the immune system, such as its physiological functioning, malfunctions, and the physical, chemical and physiological characteristics of its components. Tests that fall under immunology include the following:

1. HIV test
2. Autoimmune disease tests (lupus, rheumatoid arthritis, and autoimmune thyroid diseases – Graves' and Hashimoto's)
3. Pregnancy test (confirms pregnancy)
4. Rubella test (tests for measles)



*Home Pregnancy Testing*

## Immunochemistry (Blood Bank)

Immunochemistry prepares donated blood or blood components for transfusion or other medical applications. This is also referred to as "blood banking." The tests in immunochemistry include the following:

1. Blood type and Rh - identifies a person's blood type (O, A, B or AB) and Rh which can be either positive or negative.
2. Cross match (compatibility test) - determines if a unit of blood may be used for a transfusion for a particular patient.
3. Disease testing – tests for a variety of disease

## Molecular Diagnostics

A section that may or may not be part of the main clinical laboratory is the molecular diagnostics division. It has the greatest potential for microtechnology adaptation. Molecular diagnostics determines how genes and proteins interact within a cell. Applications of molecular diagnostics include the following:

1. Studying inherited diseases such as Sickle Cell Anemia, Cystic Fibrosis, Inherited Colon Cancer
2. Studying infectious diseases such as HIV, HCV, HPV
3. Pharmacogenetics – Determining a specific drug response.

## Let's Review

Match the following clinical tests to its classification.

|  |   | <b>Classification</b> |   | <b>Clinical Test</b>                     |
|--|---|-----------------------|---|--|
|  | 1 | Blood test            | A | Types of cells in a tissue sample        |
|  | 2 | Chemistry             | B | Growing bacteria                         |
|  | 3 | Microbiology          | C | HIV test                                 |
|  | 4 | Urinalysis            | D | Platelet count                           |
|  | 5 | Cytology              | E | Checking the genes for inherited disease |
|  | 6 | Histology             | F | Testing for enzymes                      |
|  | 7 | Immunology            | G | Checking blood type                      |
|  | 8 | Immunohematology      | H | Examine cells for malignancy             |
|  | 9 | Molecular Diagnostics | I | Test for blood and bacteria in the urine |

**Table 1: Classification of Clinical Tests**

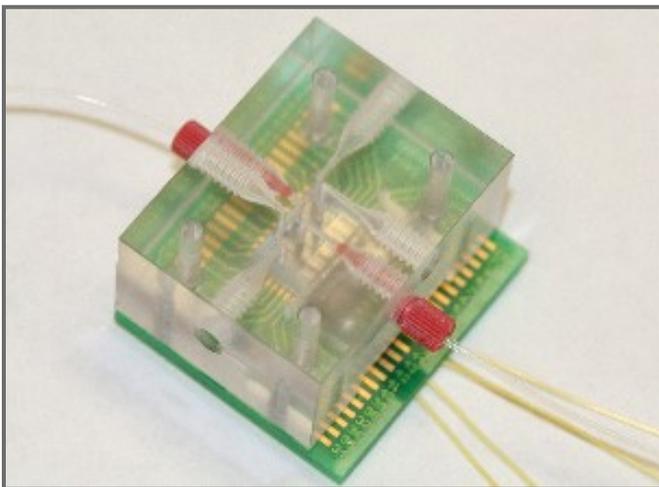
### Lab-on-a-Chip (LOC)

Some of the clinical tests described in this unit are currently converted for micro-sized testing devices. Such devices are called Lab-on-a-chip or LOC. A LOC is a device that integrates one or more clinical tests on a milli-sized or micro-sized device.

One application of a LOC is a device that performs a blood analysis using a minute sample of blood, about as much as a mosquito bite. Depending on the device, the blood can be analyzed for various blood counts (e.g. WBC, RBC, platelets), immune deficiencies, or infections.

Researchers at the California Institute of Technology, the University of California, Los Angeles, and IRIS International, Inc., are working on a hand-held device that will analyze a minute blood sample in about two minutes. One application for this device is to analyze the blood of astronauts while on space missions.

Below is a miniaturized, portable version of a blood-count machine that is being tested by astronauts. On long missions, astronauts need the ability to analyze blood samples in real-time to diagnose infection, allergies, anemia or deficiencies in the immune system. This device, about the size of a cellphone, is being designed to accomplish this task.<sup>15</sup>



*Lab-on-a-chip – Blood Analysis [Photo courtesy of Y. Tai, California Institute of Technology]*

## **What is a Lab-on-a-Chip (LOC)?**

As previously mentioned, a LOC is a device that integrates one or several laboratory functions on a single device that is millimeters or micrometers in size. LOC's are microfluidic devices, meaning that they are micro-sized devices that deal with the transportation of a precise amount of fluid (liquid or gas) in very small amounts (e.g., microliters, nanoliters, picoliters).

Advantages of LOCs to current clinical laboratory testing methods:<sup>16</sup>

- lower consumption of fluids (less waste and smaller sample sizes)
- faster analysis and response times
- better process control due to faster responses of the system (e.g., thermal control for exothermic chemical reactions)
- compact systems
- massive parallelization allowing for high throughput analysis
- lower fabrication costs, mass production (allowing for cost-effective disposable chips)
- safer platform for chemical, radioactive or biological studies
- point-of-care testing devices

Disadvantage of LOCs:<sup>16</sup>

- still a new technology and not fully developed
- physical and chemical effects at the smaller-scale can be more complex than macro-sized testing equipment (e.g., capillary forces, surface roughness chemical interactions of construction materials on reaction processes)
- “detection principles may not always scale down in a positive way”

Examples of LOCs Applications:<sup>16</sup>

- Used to detect bacteria, viruses and cancers
- Blood sample preparation
- Cellular LOC for single cell analysis

Many LOCs are “point-of-care” or POC devices, because they are devices that can be used outside of the clinical laboratory at remote locations and many times, at home by the primary users.

## **Training, Licensure, and Certification of Clinical Laboratory Personnel**

The people who perform these tests and procedures are specialists in their disciplines. They are trained in programs certified and licensed by government or independent agencies. Once employed, they are generally required to complete a certain amount of continuing education credits for continued employment and certification.

Traditionally, the majority of clinical laboratory testing is performed by Clinical Laboratory Scientists (Medical Technologists or MLTs) with four years of education and Clinical (Medical) Laboratory Technicians (MTs) with two years of education.

In addition, the labs in which these tests are performed are certified and regulated by governmental agencies to use standard methods and achieve quality results. This government certification is intended to ensure that, for example, test results from Austin, Texas are comparable to those from Los Angeles, California.

## Food for Thought

There are several advantages and disadvantages for applying microtechnology to clinical laboratory tests. What are a couple of advantages? What are a couple of disadvantages?

Now that you have learned about the various types of test that are performed, which areas do you think lend themselves best to microtechnology applications? Why?

## Summary

Clinical laboratories perform a variety of tests ranging from analyzing body fluids to molecular diagnostic testing. Much of this testing involves sophisticated, expensive equipment and requires trained personnel to collect the testing samples, run the tests, and evaluate the tests. As such, the personnel that work in these laboratories are trained by certified programs, must pass a certification exam, and are required to maintain their certification through continuing education or employment. Laboratories are recertified by governmental or private agencies.

The value of microtechnology to clinical lab testing is

- a decrease in cost due to miniaturization of the tests, and
- the possibility of point-of-care testing, allowing for the testing of people who do not have access to modern laboratory facilities.

## Glossary of Key Terms

Analyte - The specific substance or biomarker the test is designed to detect and, in some tests, quantify.

Biomarkers - Products of the body that can indicate a predisposition or a diseased state based on their concentration in the bodily fluids. For example, a high concentration of prostate specific antigen indicates the possibility of prostate cancer. In this case, the biomarker, prostate antigen, serves as an analyte for clinical laboratory test.

Chemical analysis - The testing for chemical analytes in bodily fluids such as sodium, drug metabolites (what is left over after a drug has been broken down by bodily processes), enzymes, or prostate antigen.

Cytotechnologists – Technologists that prepare slides of body cells and microscopically examine these cells for abnormalities that may signal the beginning of cancerous growth. They also examine chromosomes displayed in preparations specifically designed to permit analysis for normalcy in number and structure.

Descriptive physical testing - Viewing a sample, such as a biopsy, and descriptively describing or rating it for the presence of abnormal characteristics. This type of testing has traditionally required trained analysis to be considered valid.

HCV - Hepatitis C virus

HIV - Human immunodeficiency virus

Histotechnologists – Technologists that prepare human or animal tissue samples for microscopic examination.

Human Genome Project - The DNA sequencing of the entire human genome. Sequencing has been extended to several other representative species. This has been undertaken primarily to understand how DNA is expressed at the protein level. It is an ongoing project that is coordinated globally and includes the study of ethical use of this information.

Qualitative test(ing) - Detects the presence or the absence of an analyte; does not determine concentration.

Quantitative testing - Measures the exact concentration of an analyte.

Molecular diagnostics - The use of DNA sequence information and how it is expressed, to diagnose the presence of an infectious disease or even a genetic disease.

Multiplexing -The ability to test for more than one disease, biomarker or test parameter simultaneously.

Plasma - The liquid component of blood obtained when blood is spun at high speed, pelleting the cellular components.

Semiquantitative - When a test produces an approximation of the quantity or amount of an analyte; falling short of a quantitative result.

Serum - Plasma without the clotting factors.

## **References**

1. "Second Grant to Allow Faster Sequencing." Seema Kumar, Whitehead Institute. MIT. March 17, 1999. <http://web.mit.edu/newsoffice/1999/grant-0317.html>
2. "Automated Analyzers for Clinical Laboratories". Patent US8222048 B2. Abbott Laboratories. 2012. <http://www.google.com/patents/US8222048> ]
3. Medmira, Inc. (<http://medmira.com/products/multiple>)
4. "First Rapid Home-Use HIV Kit Approved for Self-Testing". Consumer Updates. FDA. July 3, 2012. <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm310545.htm>
5. "Microtechnology in the Clinical Laboratory". Clinical Chemistry Podcast. An interview with Dr. Peter Wilding, an Advisory member of the Center for Biomedical Micro and Nanotechnology. 2010.

6. "Quality Control Testing Employs OraSure's Intercept® Drug Testing for Quick, Efficient and Accurate Student Drug Testing at Schools". Stories from the Field. OraSure Technologies, Inc. 2013.
7. DNA Analysis Training-Silica Beads, NFSTC (National Forensic Science Technology Center). <http://projects.nfstc.org/bsw/index.htm>
8. Step-Tactin® Magnetic Nanobeads for MHC 1 Streptamers. IBC Solutions for Life Sciences. <http://bit.ly/2FwNu4d>
9. Life Technologies. Dynabeads® Types and Uses. <http://www.lifetechnologies.com/us/en/home/brands/product-brand/dynal/dynabeads-types-and-uses.html>
10. "Magnetic 'nanobeads' help detect chemical and biological agents". Oregon State University. News Medical. April 27, 2011. <http://www.news-medical.net/news/20110427/Magnetic-nanobeads-help-detect-chemical-and-biological-agents.aspx>
11. "High-throughput magnetic flow sorting of human cells selected on the basis of magnetophoretic mobility". Reece, Sanders, Kenney, Guernsey, Todd, Leary. Proc. SPIE 7568, Imaging, Manipulation, and Analysis of Biomolecules, Cells, and Tissues VIII, 75680P (February 24, 2010); doi:10.1117/12.842956 <http://proceedings.spiedigitallibrary.org/proceeding.aspx?articleid=780592>
12. Sedimentation Rate (Erythrocyte Sedimentation Rate). MedicineNet.com. [http://www.medicinenet.com/sedimentation\\_rate/article.htm](http://www.medicinenet.com/sedimentation_rate/article.htm)
13. "Three-Dimensional Cell Culture: Making Cells Feel Right at Home". UnderstandingNano.com. (Source of article: National Cancer Institute; News Release April 2010) <http://www.understandingnano.com/magnetic-nanobeads-levitate-cells.htm>
14. "Prostate Cancer". Wikipedia, a free encyclopedia.
15. "Building a hand-held lab-on-a-chip to simplify blood tests." National Space Biomedical Research Institute. April 11, 2006. <http://nsbri.org/2006/04/building-a-hand-held-lab-on-a-chip-to-simplify-blood-tests/>
16. Fundamentals of Molecular Diagnostics by David E Bruns, Edward, R. Ashwood, and Carl A. Burtis. Saunders Elsevier Publishers 2007.
17. U.S. Department of Labor Bureau of Labor Statistics Occupational Outlook Handbook. [www.bls.gov](http://www.bls.gov)
18. "Microtechnology in the Clinical Laboratory: Will It Solve Analytical problems, and when Will it Make an Impact?: Peter Wilding. Clinical Chemistry 56:4. 508-514 (2010). <http://www.clinchem.org/content/56/4/508.full.pdf>

19. “Microfluidics and Lab-on-a-chip for Biomedical Applications”, Chapter 5: Lab-on-a-Chip & applications. Stanislas. CNRS. Universite de Lyon, France. Stansan International Group.
20. “Blood tests at your fingertips”. Louisa Dalton, Special to C&EN. C&EN. Vol 95 Issue 1 (pp. 16-19). January 2, 2017. <https://cen.acs.org/articles/95/i1/Blood-tests-fingertips.html>

### **Disclaimer**

The information contained herein is considered to be true and accurate; however the Southwest Center for Microsystems Education (SCME) makes no guarantees concerning the authenticity of any statement. SCME accepts no liability for the content of this unit, or for the consequences of any actions taken on the basis of the information provided.

*Support for this work was provided by the National Science Foundation's Advanced Technological Education (ATE) Program through Grants. For more learning modules related to microtechnology, visit the SCME website (<http://scme-support.org/>).*

*This Learning Module was developed in conjunction with Bio-Link, a National Science Foundation Advanced Technological Education (ATE) Center for Biotechnology @ [www.bio-link.org](http://www.bio-link.org).*