

## Chapter 1 : Symptoms and Detection - Ovarian Cancer Research Alliance

*A review of clinical features of multiple patients who are part of a suspected outbreak of acute watery diarrhea can be helpful in identifying cholera because of the rapid spread of the disease.*

In lieu of an abstract, here is a brief excerpt of the content: Edward Lauterbach Pasquale Accardo. *The Medical Iconography of Sherlock Holmes*. Fairleigh Dickinson UP, Rader and Howard G. *The Sleuth and the Scholar*: And this list is by no means complete. This book contains a wealth of interesting facts and commentary, but Accardo spreads himself too thin. He brings up a topic, suggests a few examples, then frequently stops abruptly with little or no detailed discussion and leaves his reader hanging. One waits in vain for Accardo to discuss original insights that deserve in-depth analysis or tie together the multitude of ideas he tosses out. Impressive lists of authors, lists of titles of works and characters from fiction, quotations, statistical tables, and formulae are presented, but these would be more useful if Accardo discussed them more fully in his text. Most of these have been acknowledged by previous Doyle scholars, but even so Accardo needs to relate them directly to Holmes. Pages contain notes giving the sources for references and quotations as well as additional comments. Pages contain a bibliography of materials to which he seldom or never refers. Perhaps Accardo did not wish to duplicate information, but a single bibliography is customary. Occasionally, where a footnote is needed, none is present, and no source can be found in the bibliography, but the necessary information eventually appears in a footnote many pages later. The index is incomplete. Accardo calls his method "research notes. Perhaps he describes his own technique when he talks about "the shock of recognition of a mismatch between expectation and actuality, the surprised perception of the significance of this discrepancy, the resultant focusing of attention, the sparking of curiosity and the sudden insight into a simpler and more profound unity of phenomena. His ideas need further development and synthesis. Bargainnier, in his Preface to *Comic Crime*, recognizes the "uneasy relationship between mirth and murder. In an unusual reading of the Holmes stories, "The Comic in the Canon.

**Chapter 2 : Tests for Prostate Cancer**

*The standard respiratory function test for case detection of chronic obstructive pulmonary disease (COPD) is spirometry. The criterion for diagnosis defined in guidelines is based on the FEV<sub>1</sub>/FVC ratio forced expiratory ratio (FER) and its severity is based on forced expiratory volume in one.*

Combined, the multidisciplinary team should have expertise in the following areas: Expertise relevant to the development of technologies, assays or devices to ensure their suitability for use in an LMIC. Expertise in global health care delivery is required to establish collaborations with health care workers in the local sites for validation and utilization of the assay or device. Examples of suitable collaborations in the target country include hospitals, medical schools, charities, local governments, community groups, Non-Governmental Organizations NGOs, and governmental entities with expertise in the local setting. An industrial partner is required to provide expertise in fabrication, help with governmental regulatory approvals including in-country regulatory expertise, and prepare, disseminate, and sustain the technology for clinical use. Additionally, investigators should demonstrate familiarity with international regulatory requirements. Provide the overall goals for the entire application and indicate separately Specific Aims to be accomplished in the UG3 phase and in the UH3 phase. Organize the Research Strategy in the subsections identified below. UG3 exploratory phase - address each of the items listed below. Discuss its deployment potential in terms of costs and operability. Plans to test functionality with clinical specimens or patients. Potential clinical utility i. Description of the proposed LMIC site, including its clinical capabilities to treat the cancer and how use of the proposed technology comports with its cultural sensitivities. Plans to address regulatory issues at the local LMIC site s, including human subject issues. Specific performance milestones to be achieved during the UG3 phase, e. UH3 validation phase - address each of the items listed below. Plans for any additional engineering or development that might be needed to optimize the assay or device for operability in an LMIC setting, for example by adding desirable attributes; Plans to validate the use of the technology in an LMIC. Description of a preliminary business plan and industrial participant s for fabrication, distribution, sustainability, equipment maintenance, consumable supplies, and premarketing regulatory approvals. The business plan must also specifically address sustainability and propose a scenario for technology distribution mechanism. Such a scenario must address the possibility that the investigators may abandon the plans for full commercialization. Specific performance specifications and milestones to be achieved during the UH3 phase. Milestones should be well-defined in the application. For examples of appropriate milestones, see <http://> Furthermore, timelines must include metrics for assessment of progress in both the UG3 and UH3 phases, including specific milestones for progressing from the UG3 phase to the UH3 phase. At the end of the "Approach" section for the UG3 and UH3 subsections, milestones and timelines should be provided under separate headings. The following are particularly important: All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan. Do not use the Appendix to circumvent page limits. Foreign Institutions Foreign non-U. Overview Information contains information about Key Dates. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. Organizations must submit applications to Grants. Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission. Paper applications will not be accepted. Applicants must complete all required registrations before the application due date. Eligibility Information contains information about registration. For assistance with your electronic application or for more information on the electronic submission process, visit Applying Electronically. If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Guidelines for Applicants Experiencing System Issues. See more tips for avoiding common errors. Application Review Information Important Update: Criteria Only the review criteria described below will be considered in the review process. As part of the NIH mission, all applications submitted to the NIH in support of biomedical and behavioral research are evaluated for scientific and technical merit through the NIH peer review system.

This FOA is focused on new technologies or modifications of existing technologies that can have a significant impact on cancer detection, diagnosis, monitoring, and treatment in limited resource settings, such as those often encountered in low- and middle-income countries. Therefore, the potential of the proposed projects to result in a tool useful for a specific cancer-related clinical need of the targeted LMIC and suitable for an LMIC setting is essential and will be emphasized in assessing the overall merit of the applications. Priority will be given to technologies that are likely to be sustainable and projects with a high potential for fast, low-cost application in low resource settings. Overall Impact Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field s involved, in consideration of the following review criteria and additional review criteria as applicable for the project proposed. Scored Review Criteria Reviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field. Significance Does the project address an important problem or a critical barrier to progress in the field? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field? Specific for this FOA: Does the technology proposed address an appropriate cancer problem that is significant in the proposed settings of a given LMIC? What is the potential of the proposed technology to be sufficiently and broadly adopted by local healthcare providers in the proposed setting? If Early Stage Investigators or New Investigators, or in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field s? What is the likelihood that all the collaborators and partners will be able to work together to effectively complete translation of the proposed technology for clinical use in the global health setting? Innovation Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed? How innovative are the proposed approaches in terms of combining low cost at the manufacturing and operation levels with functionality and usability in the selected low-resource setting? Approach Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? What is the likelihood that the described technology will be adapted to specifications appropriate to LMIC settings with clinical performance comparable to medical delivery in high resource settings? How well thought out is the overall plan for the progression from UG3 to the UH3 validation phase? How appropriate is the design of the UH3 clinical validation trial e. Environment Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements? Is the range of proposed collaborations sufficient in terms of including appropriate organizations in the U. Are the commitments of all partnering institutions sufficient for the conduct of the proposed studies? Additional Review Criteria As applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall impact score, but will not give separate scores for these items. Are milestones provided for the UG3 and UH3 phases properly objective and quantitative whenever appropriate? Are these milestones well aligned with the specific aims of each phase? How realistic are these milestones and associated timelines? Do the proposed milestones and timelines clearly identify benchmarks for successful completion of the UG3 phase that could serve as a decision point to advance studies to the UH3 phase? Protections for Human Subjects For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46, the committee will

evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: For additional information on review of the Human Subjects section, please refer to the Guidelines for the Review of Human Subjects. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research. Vertebrate Animals The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points:

**Chapter 3 : Mesothelioma Diagnosis and Mesothelioma Detection - Malignant Mesothelioma Information**

*Continued Early Detection of Pancreatic Cancer. Treating pancreatic cancer is challenging when it's discovered at an advanced stage, as is usually the case.*

The acquisition process for developing and fielding a rapid infectious disease diagnostic assays system is designed around an evolutionary strategy. By leveraging commercial technologies that currently more Amplification techniques take tiny amounts of nucleic acid material and replicate them many times through enzymatic reactions, some that occur through cycles of heating and cooling. These include methods that involve target amplification e. Nucleic acid-based methods are generally specific and highly sensitive and can be used for all categories of microbes Christensen et al. Amplification methods can identify minute traces of the genetic material of an organism in a specimen, avoiding the need for culture. These techniques are particularly useful for organisms that are difficult to culture or identify using other methods e. Results can be provided more rapidly than through most conventional methods, especially culture. However, because amplification methods are so sensitive, false positives from trace contamination of the specimen or equipment can easily occur. In addition, because these techniques depend on enzymatic activity, false-negatives also occur when a sample contains contaminants that inhibit enzyme activity Hartman et al. Nucleic acid-based tests are also limited in that they do not provide information on the viability of the detected organism. Immunodiagnosics is the standard against which many agent detection, identification, and diagnostic technologies are compared. Antibody-based assays continue to serve as preliminary and confirmatory diagnostic formats for many infectious and noninfectious diseases. These assays are typically rapid, sensitive, specific, reliable, and robust. Immunodiagnostic technologies are relatively unsophisticated, making them available to nearly any laboratory. Hand-held assays HHAs are immunoassays that are based on immunochromatography or lateral flow assay format. Generally, a sample is applied to the testing unit and by flowing along a membrane, an indicator line forms where antibodies to the analyte of interest are bound. The presence of a line indicates the presence of the analyte, while the absence of a line denotes a negative result. Applying a sample solubilizes the tagged antibodies and initiates the first binding of the target by the tagged antibodies. As the sample continues migrating down the filter paper, the analyte of interest encounters a set of antibodies bound to the membrane and an antibody-analyte-antibody sandwich is formed. While early HHAs incorporated enzymes as labels to yield a visible signal, advances have done away with the multistep enzyme immunoassay format and have incorporated reporter molecules such as colloidal gold or colored latex spheres that yield a direct signal. These physical signal generators rely on the aggregation of a large number of tags to enhance signal visualization by the naked eye. Although HHAs have limitations, their overall ease of use and quickness make them useful in certain situations. Time-resolved fluorescence TRF is an immunoassay application that employs the basic immunoassay analyte sandwich capture format, but with detector antibodies that are directly labeled with a lanthanide chelate, such as europium, samarium, terbium, and dysprosium. The strengths of TRF are its increased sensitivity and the potential for multiplexing. TRF uses the differential fluorescence life span of lanthanide chelate labels compared to background fluorescence. The long-lived fluorescence signal and the difference in wavelength between absorbed and emitted light results in a very high signal-to-noise ratio and excellent sensitivity Hemmila et al. The long fluorescence decay time allows the measurement of immunoassay fluorescence after any background fluorescence has decayed. By pulsing the excitation light repeatedly, in 1 second the fluorescent material can be excited more than times with an accumulation of the generated signal that improves both the overall signal and the reduction of background signals. TRF assays are particularly useful in clinical immunoassays, but have limitations with environmental samples where europium or other lanthanides naturally occur. The contaminating compounds behave much like labeled lanthanides, prolonging the background fluorescence and lowering TRF sensitivity. Electrochemiluminescence ECL is immunoassay technology in which a detector antibody is tagged with a chemical that emits light luminescence when it is excited by an electrical stimulus. There are several electrochemiluminescent chemical moieties, but ruthenium is the most common. The technology relies on two

components: When an electrical current is applied to an electrode, both components are activated by oxidation. The oxidized TPA is transferred into a highly reducing agent, which reacts with activated Ru to create an excited-state form of Ru. This form returns to its ground state with emission of a photon at nm wavelength. An advantage of the Ru-TPA methodology is that the measurement of a single sample can be repeated multiple times because the electron-transfer photon-release reaction regenerates the Ru resulting in signal amplification. Although ECL assays are simple, rapid, and sensitive Kijek et al. The sample matrix will influence the sensitivity by varying positive cut-off values; therefore, matrix-specific positive and negative control samples are used to establish standard curves and cutoff values. Several diagnostic systems are using a technology to analyze microsphere-based multiplex protein assays. The advantage of multiplex assays is that multiple results are available from one sample without individual testing. Up to different biomolecules proteins, peptides, or nucleic acids can be analyzed in a single test. A microplate platform allows the automated analysis of a well plate in 30 minutes yielding a throughput of 1, assays in a plex system. Currently kits for simultaneous quantitative measurement of up to 25 to 30 proteins are available, including cytokines, phosphoproteins, growth factors, kinases, and transcription factors. Several investigators are using these systems to develop multiplexed assays for biological warfare agents. One system was evaluated by the U. Army with extremely good results, but the equipment is currently not rugged enough for use by the warfighters. The key to future rapid diagnostic systems is the development of a completely and fully integrated system. Previous diagnostic research efforts were only concerned with the development of an assay technique and failed to address the full spectrum of an integrated system. To fully address an integrated system, protocols, sample processing, reagents, assays, platforms, and evaluations need to be completely explored. Protocols are equivalent to an intended-use statement. Without addressing how and why the assay or system is to be used, misapplication will result in incorrect and potentially serious testing reliability issues. The single most important aspect of rapid testing is sample processing. The sample is the most important component in a system, and an inappropriate or improperly handled sample will jeopardize an otherwise robust assay. For example, detection of *Bacillus anthracis* is highly problematic. The spores of *Bacillus anthracis* are very refractile to easy and rapid sample preparation. Alternate methods are required to produce the highest quality sample, which include concentrating the sample if possible and methods to release either the nucleic acids or specific proteins from the spore. Another consideration of sample preparation, especially for many molecular methods, is the removal or neutralization of inhibitors of amplification. Systems consist of more than just assays Figure Developers need to be cognizant of all the details. While most commercial manufacturers have appropriate production systems and quality manufacturing practices in place for producing consistent, reliable, and appropriate reagents that are compliant with Food and Drug Administration FDA requirements, research-derived systems often fall short. In addition, integration of assays with various platforms is often overlooked in initial system development. While some assays perform well on multiple platforms, many assays suffer optimization issues when moved from one platform to another. Unless provisions are made for multi-platform development, and shown to be equally effective through validation, platform equivalency should not be assumed. Another consideration in system development for systems developed by professional scientists working in modern laboratory facilities is the inherent expectation that assays and systems will work in the hands of less trained personnel outside of the pristine laboratory facilities. Often, this is not the case. Field evaluation, under conditions of actual employment, is critical before assays and systems can be confidently deployed and used. Systems-based architecture needs to include the full gamut of functions from protocols through validation. Validation of the appropriateness and effectiveness of assays and systems is paramount in the development process Emanuel et al. Development of assays and systems needs to include assay validation parameters such as linearity, limits of detection, inclusivity and exclusivity testing, ruggedness, robustness, and repeatability. Validation parameters are detailed in Box The concentrations will range from pg to 1 fg of the target nucleic acid. When cloned material is required i. A critical and often overlooked issue is that diagnostic systems and tests intended to be used to test clinical samples must be approved by the U. Food and Drug Administration in order to legally be distributed and used in the United States. Many of the technologies discussed in this article are mature enough to produce clinically

useful diagnostic products. However, companies that may have the capability to manufacture these diagnostic tests, and to gain FDA approval for them, typically are not interested in doing so for tests to diagnose tropical diseases or biological threat agents because the commercial demand is low. This is a chronic problem with no easy solution. To help support the deployment of rapid agent identification systems, especially those that do not have enough commercial value to be fully supported by commercial manufacturers, the Department of Defense relies on the Joint Program Executive Office's Critical Reagents Program CRP. The CRP is a national resource for the biological defense community, whose mission is production of detection reagents, standardization of procedures and training, and optimization and transition of detection technologies. Their commodity areas include the production of antigenic and genomic materials for test and evaluation purposes, antibodies, to include the manufacturing of hand-held devices, molecular detection reagents, and sampling kits. Because of the confined nature of these materials and the lack of commercialization due to the limited customer base, CRP provides a vital link to the defense community to ensure harmonization of tests and evaluations and as an avenue for advanced development. In the course of development of newer, faster, better, and cheaper rapid diagnostic devices, the Department of Defense program is looking at potential future platforms. Many characteristics of those future systems are discussed above, but one that is showing some promise is DNA microarrays. Microarrays or DNA chips are one of the latest methods for rapid infectious disease diagnostics. Microarrays are a recent adaptation of Northern blot technology Grunstein and Hogness, ; Schena et al. The ability to label nucleotide sequences with fluorescent tags, much like fluorescent antibody technology, has increased their use in diagnostics. Microarrays are small, solid supports typically glass slides on which DNA sequences are attached, or spotted, at fixed, orderly, addressable locations. The DNA is composed of short, single-stranded fragments, typically 5 to 50 nucleotides long. Microarrays can have up to tens of thousands of spots, allowing for a large amount of data collected for each sample tested. Microarrays depend on the annealing of two nucleic acid strands to function. When sample DNA is prepared, usually through polymerase-based amplification, fluorescent dyes are incorporated into the amplicon so that hybridization can be detected. The kind of information required from microarrays drive how the arrays are developed and used. Microarrays can be spotted with known sequences of a variety of oligonucleotides for basic genomic investigation. Utilizing known sequences from already sequenced organisms and hybridizing genomic material from organisms not previously sequenced, sequence differences can be determined. With more than 10, sequences and growing as automated systems improve to interrogate on a single chip, variation in genomic sequences can provide accurate species and subspecies determination. Gene expression-based measurements of mRNA levels, and the differences between these levels in various states of organism growth i. Although microarrays have the demonstrated potential for diagnostics, routine use is hampered by several considerations.

*The early detection and diagnosis of cancer usually increases the chances of successful treatment. In addition, treatments for early cancer are often less complex and less expensive than treatments for more-advanced disease, sparing patients and their families greater hardship. However, too many.*

Early cancer detection is important and accurate diagnosis is crucial to better your chance for recovery. Your doctor will discuss the best way to detect or diagnose cancer based on your health and family history, symptoms, and other factors. Your tests are unique to you and your situation. Learn about these common cancer detection and diagnosis techniques. Common Cancer Detections Biopsy. Used to take sample body tissue cells. These cells are analyzed for cancer presence. Common cancer diagnostic biopsies include: A sample is drawn from your bone marrow, the spongy tissue inside your bone. Typically used to get lung , bladder, or colon tissue. Endoscopic biopsy is guided by a tiny, lighted camera. Your doctor uses a special needle to extract cells from an area in question. Needle biopsies are usually used to test areas that are felt under the skin like breast lumps and enlarged lymph nodes. Your mammograms are used for both early breast cancer detection, as well as for diagnosis of lumps, breast pain, or unusual breast symptoms. Your doctor will recommend the frequency and type of mammogram preferred. Learn more about mammography and other breast cancer detection tests. A bone scan is a comfortable procedure used to determine if cancer has developed in or spread to your bones. It works much like a standard X-ray, but differs in that a radioactive material is injected into your body and settles into your bones. Learn about bone scans and cancer detection. Magnetic resonance imaging MRI uses radio waves and a magnetic field to gather images of various body parts. MRI is often used to assist in breast , brain, spinal cord, and liver cancer diagnosis. Know more about MRI and cancer diagnosis. Your doctor may order a CT, a series of X-ray images, for further information to locate or diagnose a tumor, or to guide surgical, biopsy, or radiological procedures. Provides more information about the tissues and presence of tumors. A small amount of radioactive material is injected, giving your doctor a highlighted view of the area under suspicion for cancer. Learn how PET scans help with my diagnosis. Creates a clearer picture of your tissue and organs. It uses sound waves and a computer to indicate the presence of tumors. Your doctor may order an ultrasound for your kidneys, liver, or other organs. Learn about ultrasound and cancer diagnosis. Often used to guide a biopsy, endoscopy uses a tiny, lighted camera to view your colon, esophagus, lungs, stomach, portions of the small intestine, and other organs. It can detect tumors and diagnose lung cancer , colon cancer , esophageal cancer, and other cancers. Know how endoscopy can detect and diagnose cancer. Except with blood cancers, blood tests are used only in conjunction with other diagnostic cancer tests. Common blood tests you may receive are:

**Chapter 5 : Diagnosis & Detection| Giardia | Parasites | CDC**

*Our authors and editors. We are a community of more than , authors and editors from 3, institutions spanning countries, including Nobel Prize winners and some of the world's most-cited researchers.*

The Pap test does not test for ovarian cancer; it screens for cervical cancer. If a woman has the signs and symptoms of ovarian cancer, her doctor will probably perform a complete pelvic exam, a transvaginal or pelvic ultrasound, radiological tests, such as a transvaginal ultrasound or CT scan, and a CA blood test. Used individually, these tests are not definitive; they are most effective when used in combination with each other. If a woman has a strong family history or a genetic predisposition such as a BRCA mutation , doctors may use some of these tests to monitor a woman. CA is a substance in the blood that may increase when a cancerous tumor is present; this protein is produced by ovarian cancer cells and is elevated in more than 80 percent of women with advanced ovarian cancers and in 50 percent of those with early-stage cancers. CA, however, is approved by the Food and Drug Administration to monitor the effectiveness of treatment for ovarian cancer and for detecting disease recurrence after treatment. The protein CA exists in greater concentration in cancerous cells. Although the CA blood test is more accurate in postmenopausal women, it is not a reliable early detection test for ovarian cancer. In about 20 percent of advanced stage ovarian cancer cases and 50 percent of early stage cases, the CA is not elevated even though ovarian cancer is present. As a result, doctors generally use the CA blood test in combination with a transvaginal ultrasound. Because CA misses half of early cancers and can be elevated by benign conditions, the National Cancer Institute does not endorse using it to screen women for ovarian cancer who are at ordinary risk or in the general population. Read more information on CA A woman who presents with a known tumor may have this test to determine if her surgery should be done by a gynecologist or a gynecologic oncologist –” doctors who are specially trained to treat women with gynecologic cancers. The test measures the levels of five proteins in blood that change when ovarian cancer is present. However, this test has not been approved for use as an ovarian cancer screening tool, nor has it been proven to result in early detection or reduce the risk of death from this disease. Inhibin B and Inhibin A. The probe sends off sound waves which reflect off body structures. The waves are then received by a computer that turns them into a picture. An ultrasound alone is not an accurate way to screen for ovarian cancer. Ovarian cancer is rarely detected in a pelvic exam and usually in an advanced stage if it is. Recto-vaginal Pelvic Examination also called a bimanual exam This exam allows your doctor to examine the ovaries for lumps or changes in shape or size. Every woman should undergo a rectal and vaginal pelvic examination at her annual check-up with her gynecologist. A Pap test is routine in a pelvic exam but it detects cervical cancer, not ovarian cancer. Diagnosis The only definitive way to determine if a patient has ovarian cancer is through surgery and biopsy. Doctors will perform surgery after they obtain enough evidence from their exam and test results. If there is a suspicion from these tests that ovarian cancer might be present, the patient should seek a referral to a gynecologic oncologist before surgery occurs. Research shows that women treated by gynecologic oncologists live longer than those treated by other physicians. The most common preliminary tests are: CT scan or computerized tomography: CT scans employ x-rays to take multiple cross-sectional images of the tissues and bones in the body. Doctors can analyze the images individually or use software to make a three-dimensional model of the internal organs. CT scans help define the boundaries of a cancerous tumor and show the extent of tumor spread, helping a doctor determine where to operate. CT scans also are used to monitor disease recurrence. Before undergoing a CT scan, you may receive by mouth or intravenously a contrast material that allows tissues and organs to show up more readily. The need for a biopsy: None of the above tests are definitive when used on their own. They are most effective when used in combination with each other. The only way to confirm the presence of ovarian cancer suspected by the tests is through a surgical biopsy of the tumor tissue. If tests imply a likelihood of ovarian cancer, the doctor will likely perform a laparotomy or laparoscopy depending on what the CT shows. A laparotomy is a surgical procedure involving a long incision in the wall of the abdomen to remove fluid and tissue, such as the ovaries, fallopian tubes, uterus and connecting tissue, depending on how far the cancer has spread. A doctor may also

perform laparoscopic surgery to perform the biopsy and remove a small, benign cyst or early ovarian cancer and to determine the extent of spread. A laparoscope is a thin tube with a camera that allows the doctor to see and remove tissue. If a woman has fluid inside the abdomen, a doctor before surgery may inject a needle through the abdomen wall to collect the fluid for analysis. By looking at the cells in the tissue and fluid under a microscope, a pathologist describes the cancer as Grade 1, 2, or 3. Grade 1 is most like ovarian tissue while Grade 3 cells are more immature and more likely to metastasize. Get email updates about research news, action alerts and ways to get involved.

**Chapter 6 : Diagnosis and Detection | Cholera | CDC**

*Disease Detection and Diagnosis Workshop Introduction These activities teach pupils to think about how doctors and other staff diagnose illnesses and how.*

Received Jun 11; Accepted Aug Copyright Pioneer Bioscience Publishing Company. This article has been cited by other articles in PMC. Abstract The standard respiratory function test for case detection of chronic obstructive pulmonary disease COPD is spirometry. Spirometry is a safe and practical procedure, and when conducted by a trained operator using a spirometer that provides quality feedback, the majority of patients can be coached to provide acceptable and repeatable results. This allows potentially wide application of testing to improve recognition and diagnosis of COPD, such as for case finding in primary care. However, COPD remains substantially under diagnosed in primary care and a major reason for this is underuse of spirometry. The presence of symptoms is not a reliable indicator of disease and diagnosis is often delayed until more severe airflow obstruction is present. Early diagnosis is worthwhile, as it allows risk factors for COPD such as smoking to be addressed promptly and treatment optimised. Paradoxically, investigation of the patho-physiology in COPD has shown that extensive small airway disease exists before it is detectable with conventional spirometric indices, and methods to detect airway disease earlier using the flow-volume curve are discussed. Spirometry, chronic obstructive pulmonary disease COPD , case finding, flow-volume curve Pathology of chronic obstructive pulmonary disease COPD Relatively early research in the s and s into what was by then recognized as a smoking-related disease 1 focused on pathology, and especially tissue remodeling changes in the airways and lungs. It was observed that throughout the airways there was some element of inflammation, but sub-mucosal mucous gland hyperplasia, epithelial goblet cell hyperplasia and epithelial squamous metaplasia were prominent. The characteristic lung lesion was usually peri-bronchial, centri-lobular parenchymal destruction, termed emphysema 2 - 4. An important conclusion from the detailed pathological analysis of this epoch was that the airway pathological component in COPD was universal and generalized, while emphysema usually developed later, perhaps as a secondary phenomenon, and only in some individuals but by no means all. This is different from the diffuse primary pan-acinar emphysema that occurs in the younger-onset alpha-1 anti-trypsin anti-proteinase deficiency lung disease, for example 5. The next research epoch involved innovative physiological laboratory work in the late s into the s, which defined the obstructive consequences of smoking-related airway disease and the anatomical site of increased airway resistance that ultimately lead to symptoms 6 , 7. From this work, construction of a series of iso-volume pressure-flow curves gave rise to development of the now widely used flow-volume curve, but then without the sophisticated, sensitive and computerized equipment now available, and which we will be discussing later in some detail. However, even by that time and using the relatively crude bellows-based spirometer, the standard measure for defining airway obstruction had been specified as a reduction in the ratio of forced expiratory volume in one second FEV1 to forced vital capacity FVC , the forced expiratory ratio FER ; indeed in that regard little has changed over the last fifty years or so, in spite of improved understanding of physiology. Paradoxically, the seminal work of Macklem and others in clinical physiology showed that the first change in spirometry in COPD was actually a reduction in FVC due to air trapping, rather than a change in FEV1 8. Importantly, they showed that this in turn is caused by fixed small airway narrowing, in airways less than 2 mm internal diameter. To demonstrate this, they used flow-volume studies in patients and volunteers with gases of different densities, and also measured flow resistance in different parts of the airway with retrograde catheters in resected lungs. Normal small airways have low resistance to air flow but this is markedly increased in COPD 9 - In contrast, in asthma the main pattern is one of non-uniformly distributed larger airways obstruction, except in older asthmatics and those that smoke in whom a peripheral distribution of resistive change was common, similar to COPD. Notably, it was shown in this epoch of physiological research, that there could be a great deal of peripheral increase in flow resistance before there was any indication on traditional spirometric measures. Patho-physiological correlation studies followed, indicating that in small airways in COPD there is indeed narrowing due to wall thickening, fibrosis and indeed airway obliteration 10 ,

12 , This was a new and startling insight, which is now confirmed by more sophisticated methodology 14 , that there can be extensive small airway disease, damage and obliteration before it is detectable with conventional spirometric tests. Over the years, new physiologic methods were developed to try and pick up these early small airway changes in smokers before overt COPD, defined by the FER emerged. However none was robust or practical enough at the concurrent stage of technological development to be suitable for clinical laboratory or medical office use. Such attempts continue with increasingly sophisticated techniques, and this is dealt with in a separate article in this volume; the FER remains the standard. In this article, we will review and discuss how useful in clinical practice this standard measure is, what we know about its pitfalls in clinical application and especially in primary care practice. We will also look anew at how the use of all the information available in the current standard flow-volume curve, which is now routinely obtained at the time of FER measurement but largely ignored, can potentially be harnessed and give a better overview of the status of the airways. This might contribute to recognizing early physiological impairment in smokers, perhaps as an alternative to the need to develop more expensive and complex tests. Prevalence increased with age and smoking history, but other factors were also thought to be important in explaining the variation. The Australian survey showed large variations between centres the causes of which are being investigated unpublished data. Attributable fractions are higher in industrialized countries than developing countries 18 , and other risk factors are also important, including exposure to biomass smoke, occupational exposures to dust and fumes, history of pulmonary tuberculosis, outdoor air pollution, and poor socioeconomic status 20 or chronic asthma. However smoking remains the most important cause of COPD in western countries. FEV1 normally decreases with age, and the rate of fall is an important spirometric indicator of disease progression in COPD. Thus, this may misclassify some older patients as having COPD. It has been proposed that classification should be based on a lower limit of normal LLN  $i$ . Maximum flow achieved during forced expiration decreases progressively as lung volume falls and is most evident in the expiratory flow-volume curve where flow is plotted as a function of volume. Although flow and volume are complex biological signals, the curve is highly repeatable in both healthy and obstructed individuals and the shape of the curve can be helpful as it reflects the underlying mechanics limiting maximal flow. In healthy younger adults the shape of the flow-volume curve usually approximates a straight-sided triangle with maximum flows decreasing linearly with lung volume. In people with obstructive lung disease key physiologic features of the flow-volume curve are reduced expiratory flows in proportion to disease severity and the presence of a concavity in the descending limb; the latter indicating an abnormal decrease in maximal flow as lung volume falls. More recently, only 5. Undetected COPD or asthma is common in primary care; over half those aged between years in general practices in the Netherlands had symptoms or signs. There is also consistent evidence of misclassification of COPD in general practice. This probably relates to the diagnosis not being based on objective spirometry testing criteria. However such screening has not been widely implemented; a US Preventive Services Task Force assessment of the evidence did not recommend screening with spirometry and concluded with moderate certainty that there was no net benefit. A more cost effective strategy using opportunistic case finding in primary care based on the presence of risk factors age and smoking and symptoms is recommended in the UK Update Guideline on COPD. In many health systems, primary care provides the most accessible and most frequently accessed health care and efforts to increase recognition and diagnosis of COPD have mainly focussed on general practice 43 ,. An alternative approach is to base spirometry testing on respiratory-relevant symptom screening using a questionnaire 47 , with the cut-off score for subsequent spirometry chosen to maximise sensitivity and specificity. Linking symptom screening to case finding for COPD is ideal if the intention is to commence treatment in symptomatic individuals, but this approach is less suitable if the aim is to reduce end-organ disease. However, there is substantial evidence that reported symptoms are unreliable for diagnosis, although in general the symptom burden in COPD increases with severity of airflow obstruction. There is wide variation in the degree of breathlessness, health status and exercise capacity within GOLD stages; thus even when airflow obstruction is severe in COPD, some people do not report symptoms or exercise limitation. Patients may attribute their symptoms to ageing and attribute multi-casual explanations that lessen the importance of obtaining a diagnosis. On the other hand, respiratory

symptoms typical of COPD may be noted in practice records for long periods prior to diagnosis<sup>56</sup>, with varying attitudes and degrees of vigilance among general practitioners to early diagnosis<sup>56</sup>. Thus diagnosis of COPD may be delayed and indeed often does not occur until an acute exacerbation results in admission and hospital-based diagnosis. Early diagnosis is a contentious issue, but it optimises the opportunities to prevent worsening of disease and prevention of comorbidities. Guidelines for COPD emphasise that it is a multi-system disease requiring a multidimensional approach to treatment. The increased risk with COPD is present even when allowance is made for cigarette smoking history. Similarly, the association of reduced FEV1 with increased overall mortality has been recognized in studies in non-smokers<sup>63</sup> and smokers, with the effect of reduced FEV1 independent of smoking history. The potential importance of the FVC was highlighted in a USA general population cohort without chronic respiratory diagnoses or persistent respiratory symptoms, in which survival was associated with higher FVC in both men and women after adjustment for smoking and demographic factors. Such associations underlie the need for an earlier awareness of abnormality on spirometry as a part of a general health screening approach, such as was taken in cardiovascular disease to reduce the high burden of mortality that existed 40 years ago. Value of current diagnostic tools for COPD: The test is relatively quick to perform, well tolerated by most patients and the results are immediately available to clinician. It is important to appreciate that the clinical value of spirometry is critically dependent on the correct operation and accuracy of the spirometer, performance of the correct maximal breathing manoeuvre, selection of the best test results to use and correct interpretation. Development of spirometry A spirometer is a medical device that allows measurement of how much air is expelled and how quickly the lungs can be emptied, in a maximal expiration from full inflation. It was only a few years later in that the American physiologists, Fry and Hyatt, in a landmark study of lung mechanics, replotted the data contained in the timed spirogram in the form of the flow-volume curve<sup>73</sup> which is now universally accepted as the preferred method of graphically displaying spirometric data. The flow-volume curve is now available in almost all commercially available spirometers and is displayed in real-time as the patient performs the test. Modern spirometers Almost all modern spirometers utilise a sensitive real-time flow sensor to directly measure respired flow and obtain volume by electronic or numerical integration. Manual volume-displacement spirometers are still in limited use, especially in primary care<sup>74</sup>, such as the iconic wedge bellows Vitalograph which over many decades has played a very significant role in popularising the measurement and application of spirometry beyond the expert laboratory, but this genre of spirometer usually lacks portability, is difficult to clean and disinfect, can be difficult to calibrate and requires spirometric variables to be calculated manually and does not produce the flow-volume curve. Most, if not all, modern spirometers meet minimum international performance standards and validation procedures that were developed jointly by the American Thoracic Society and European Respiratory Society. These include meeting accuracy requirements for volume, flow and time signals using specifically developed test signals, and applying the back-extrapolation technique to identify both sluggish starts to the blow and the zero time point from which timed volumes such as FEV1 are calculated. Modern spirometers also have the added advantages of infection control, automatic calculation of all lung function indices including correction for temperature, pressure and water-saturation conditions. Many will also provide immediate computer-generated feedback to the operator on the test quality and repeatability as well as real-time graphical display of the spirogram and flow-volume curve, will select the best results to report, calculate normal reference values including the lower limit of normal, and can automatically upload results to medical records. Primary care spirometry Spirometry is commonly performed outside the lung function laboratory. The high spirometer ownership was not surprising given that a large number of patients with lung disease are first seen and subsequently managed in primary care. Opinion is divided as to whether the quality of spirometry performed outside expert laboratories meets adequate minimum standards<sup>75</sup> with the potential for high rates of misclassification, especially when the results are near the lower limit of normal<sup>69, 77</sup>. The measurement of spirometry requires a motivated and enthusiastic operator to coach the patient to perform a number of very rigorous maximally forced and sustained breathing manoeuvres. It is not surprising therefore that unlike most other medical tests such as the measurement of blood pressure and the electrocardiogram, the quality of spirometry tests are crucially

dependent on the operator and cooperation of the patient and thus spirometry performed in primary care is often of poor quality. Although the key to obtaining quality spirometry is attending a comprehensive training course, the importance of testing experience cannot be overstated and may well be the most important factor. The concave pattern on flow-volume curve. Current guideline criteria for airway obstruction and its severity essentially rely on just two variables FEV<sub>1</sub> and FVC, and their ratio the FER. Although these variables have played an important role in developing our understanding of the mechanisms and functional effects of COPD, we have emphasised that they are relatively insensitive to early obstructive small airway pathology, because these cause FVC to fall first with initial preservation of the FER. Spirometry has thus been of limited use as a screening tool for early disease; this is disappointing as it is the most practical and widely performed test of lung health and should therefore be ideal to screen for early disease. We present a case that relying solely on the FEV<sub>1</sub> and FER potentially misses information contained in the whole flow-volume curve, particularly the concave pattern, which may provide greater sensitivity in detecting and monitoring early disease. The development of concavity in the descending limb of the maximum expiratory flow-volume curve is a recognised feature of airflow obstruction, with greater concavity reflecting increased obstruction, and the first indication of a concavity is frequently seen in the tail of the curve<sup>30</sup>. The functional information provided by the FEV<sub>1</sub> is necessarily limited to the first second of the forced expiratory manoeuvre when the lung is relatively fully inflated and the small airways exposed to significant distending forces. In contrast, the concave pattern seen in people with airflow obstruction is not limited to the first second but often extends over most of the curve, reflecting a global pattern of airway dysfunction. In early airflow obstruction, when the FEV<sub>1</sub> is normal, a concavity is often present and may well be mostly confined to the terminal portion of the curve where lung volume is relatively low and the distending forces on the small airways are significantly reduced, resulting in a higher peripheral airway resistance and non-uniform emptying in peripheral lung regions. It is notable that the latter may well be the major spirometric defect signalling early disease, and requires better quantitative assessment. It is not surprising, therefore, that even though the underlying mechanics determining FEV<sub>1</sub> and the concave pattern overlap, they are not necessarily equivalently strong physiological signals at different disease stages. They may however be quite complementary, not only in assessing airflow obstruction overall but especially in detecting early obstructive small airway disease. It seems reasonable that to detect and assess early disease we need a method that is sensitive to inhomogeneous airway emptying because this almost certainly precedes the development of the more advanced obstruction for which we use currently the standard FER. Highly sophisticated technology is currently being developed to measure this inhomogeneous lung emptying, but it could well be that much of this information is already available in the expiratory flow-volume curve if only it can be harnessed. Strong evidence that a concavity confined in the terminal portion of the curve is most likely to be associated with small airways dysfunction came from further studies that compared flow-volume curves obtained breathing gases of widely differing gas density which showed that maximal flows near the terminal portion of the flow-volume curve predominantly reflect small airway function. This is also consistent with studies using wave speed mechanics<sup>86</sup> and the equal pressure point theory<sup>72</sup> which predicts that the flow-limiting segment developed during forced expiration moves peripherally into progressively smaller airways as lung volume falls and especially when peripheral airway resistance increases. The clinical value of quantifying concavity has been under-appreciated although demonstrated spirometrically in different populations<sup>84, 87</sup> - The study by Kraan et al. Another study showed the degree of concavity was greater in those with a smoking history and people with breathlessness and wheezes.

**Chapter 7 : Cancer Detection and Diagnosis | Promedica**

*Diagnosis and Detection, an exploration of Doyle's medical and literary sources, covers a wide variety of topics, only some of which are pertinent to the understanding of Sherlock Holmes.*

Most prostate cancers are first found during screening with a prostate-specific antigen PSA blood test or a digital rectal exam DRE. If cancer is suspected based on results of screening tests or symptoms, tests will be needed to confirm the diagnosis. The actual diagnosis of prostate cancer can only be made with a prostate biopsy. Medical history and physical exam If your doctor suspects you might have prostate cancer, he or she will ask you about any symptoms you are having, such as any urinary or sexual problems, and how long you have had them. You might also be asked about possible risk factors, including your family history. Your doctor will also examine you. Your doctor may also examine other areas of your body. He or she might then order some tests. The chance of having prostate cancer goes up as the PSA level goes up. When prostate cancer develops, the PSA level usually goes above 4. Men with a PSA level between 4 and 10 have about a 1 in 4 chance of having prostate cancer. When considering whether to do a prostate biopsy to look for cancer, not all doctors use the same PSA cutoff point. Some may advise it if the PSA is 4 or higher, while others might recommend it starting at a lower level, such as 2. Other factors, such as your age, race, and family history, may affect this decision. The PSA test can also be useful if you have already been diagnosed with prostate cancer. In men just diagnosed with prostate cancer, the PSA test can be used together with physical exam results and tumor grade determined on the biopsy, described further on to help decide if other tests such as CT scans or bone scans are needed. The PSA test is a part of staging determining the stage of your cancer and can help tell if your cancer is likely to still be confined to the prostate gland. If your PSA level is very high, your cancer is more likely to have spread beyond the prostate. This may affect your treatment options , since some forms of therapy such as surgery and radiation are not likely to be helpful if the cancer has spread to the lymph nodes , bones, or other organs. Transrectal ultrasound TRUS For this test, a small probe about the width of a finger is lubricated and placed in your rectum. The probe gives off sound waves that enter the prostate and create echoes. The probe picks up the echoes, and a computer turns them into a black and white image of the prostate. You will feel some pressure when the probe is inserted, but it is usually not painful. The area may be numbed before the procedure. It is also used during a prostate biopsy to guide the needles into the correct area of the prostate. TRUS is useful in other situations as well. It can be used to measure the size of the prostate gland, which can help determine the PSA density described in Prostate Cancer Prevention and Early Detection and may also affect which treatment options a man has. TRUS is also used as a guide during some forms of treatment such as brachytherapy internal radiation therapy or cryotherapy. Prostate biopsy If certain symptoms or the results of tests such as a PSA blood test or DRE suggest that you might have prostate cancer, your doctor will do a prostate biopsy. A biopsy is a procedure in which small samples of the prostate are removed and then looked at under a microscope. A core needle biopsy is the main method used to diagnose prostate cancer. It is usually done by a urologist, a surgeon who treats cancers of the genital and urinary tract, which includes the prostate gland. When the needle is pulled out it removes a small cylinder core of prostate tissue. This is repeated several times. Most urologists will take about 12 core samples from different parts of the prostate. Though the procedure sounds painful, each biopsy usually causes only a brief uncomfortable sensation because it is done with a special spring-loaded biopsy instrument. The device inserts and removes the needle in a fraction of a second. Most doctors who do the biopsy will numb the area first by injecting a local anesthetic alongside the prostate. You might want to ask your doctor if he or she plans to do this. You will likely be given antibiotics to take before the biopsy and possibly for a day or 2 after to reduce the risk of infection. For a few days after the procedure, you may feel some soreness in the area and will probably notice blood in your urine. You may also have some light bleeding from your rectum, especially if you have hemorrhoids. Many men notice blood in their semen or have rust colored semen, which can last for several weeks after the biopsy, depending on how often you ejaculate. Your biopsy samples will be sent to a lab, where they will be looked at a microscope to see if they contain cancer cells. If cancer is seen, it will also be

assigned a grade see the next section. Getting the results in the form of a pathology report usually takes at least 1 to 3 days, but it can sometimes take longer. Even when taking many samples, biopsies can still sometimes miss a cancer if none of the biopsy needles pass through it. This is known as a false-negative result. If your doctor still strongly suspects you have prostate cancer because your PSA level is very high, for example a repeat biopsy might be needed to help be sure.

**Grade of prostate cancer Gleason score or Grade Group** The grade of the cancer is based on how abnormal the cancer looks under the microscope. Higher grade cancers look more abnormal, and are more likely to grow and spread quickly. There are 2 main ways to measure the grade of a prostate cancer.

**Gleason score** The Gleason system assigns grades based on how much the cancer looks like normal prostate tissue. If the cancer looks a lot like normal prostate tissue, a grade of 1 is assigned. If the cancer looks very abnormal, it is given a grade of 5. Grades 2 through 4 have features in between these extremes. Almost all cancers are grade 3 or higher; grades 1 and 2 are not often used. Since prostate cancers often have areas with different grades, a grade is assigned to the 2 areas that make up most of the cancer. These 2 grades are added to yield the Gleason score also called the Gleason sum. The first number assigned is the grade that is most common in the tumor. Although most often the Gleason score is based on the 2 areas that make up most of the cancer, there are some exceptions when a biopsy sample has either a lot of high-grade cancer or there are 3 grades including high-grade cancer. In these cases, the way the Gleason score is determined is modified to reflect the aggressive fast-growing nature of the cancer. In theory, the Gleason score can be between 2 and 10, but scores below 6 are rarely used. Prostate cancers are often divided into 3 groups, based on the Gleason score: Cancers with a Gleason score of 6 or less may be called well-differentiated or low-grade. Cancers with a Gleason score of 7 may be called moderately-differentiated or intermediate-grade. Cancers with Gleason scores of 8 to 10 may be called poorly-differentiated or high-grade.

**Grade Groups** In recent years, doctors have come to realize that prostate cancer can be divided into more than just these 3 groups. Likewise, men with a Gleason score 8 cancer tend to do better than those with a Gleason score of 9 or 10. Because of this, doctors have developed Grade Groups, ranging from 1 most likely to grow and spread slowly to 5 most likely to grow and spread quickly:

**Other information in a pathology report** Along with the grade of the cancer if it is present, the pathology report often contains other information about the cancer, such as:

**Prostatic intraepithelial neoplasia PIN:** PIN is often divided into 2 groups: The importance of low-grade PIN in relation to prostate cancer is still unclear. If low-grade PIN is reported on a prostate biopsy, the follow-up for patients is usually the same as if nothing abnormal was seen. If high-grade PIN is found on a biopsy, there is about a 1 in 5 chance that cancer may already be present somewhere else in the prostate gland. This is why doctors often watch men with high-grade PIN carefully and may advise a repeat prostate biopsy, especially if the original biopsy did not take samples from all parts of the prostate.

**Atypical small acinar proliferation ASAP:** This might also be called glandular atypia or atypical glandular proliferation.

**Proliferative inflammatory atrophy PIA:** In PIA, the prostate cells look smaller than normal, and there are signs of inflammation in the area. For more information about how prostate biopsy results are reported, see the Prostate Pathology section of our website.

**Imaging tests to look for prostate cancer spread** Imaging tests use x-rays, magnetic fields, sound waves, or radioactive substances to create pictures of the inside of your body. If you are found to have prostate cancer, your doctor will use your digital rectal exam DRE results, prostate-specific antigen PSA level, and Gleason score from the biopsy results to figure out how likely it is that the cancer has spread outside your prostate. This information is used to decide if any imaging tests need to be done to look for possible cancer spread. Men with a normal DRE result, a low PSA, and a low Gleason score may not need any other tests because the chance that the cancer has spread is so low. The imaging tests used most often to look for prostate cancer spread include:

**Bone scan** If prostate cancer spreads to distant sites, it often goes to the bones first. A bone scan can help show whether cancer has reached the bones. For this test, you are injected with a small amount of low-level radioactive material, which settles in damaged areas of bone throughout the body. A special camera detects the radioactivity and creates a picture of your skeleton. A bone scan may suggest cancer in the bone, but to make an accurate diagnosis, other tests such as plain x-rays, CT or MRI scans, or even a bone biopsy might be needed.

**Computed tomography CT scan** A CT scan uses x-rays to make detailed, cross-sectional images of your body. Still, it can sometimes help tell if prostate cancer has

spread into nearby lymph nodes. If your prostate cancer has come back after treatment, the CT scan can often tell if it is growing into other organs or structures in your pelvis. CT scans are not as useful as magnetic resonance imaging MRI for looking at the prostate gland itself. But MRI scans use radio waves and strong magnets instead of x-rays. A contrast material called gadolinium may be injected into a vein before the scan to better see details. MRI scans can give a very clear picture of the prostate and show if the cancer has spread outside the prostate into the seminal vesicles or other nearby structures.

*Detection means the existence of whatever do you want detecting but diagnosis is that the analysis in depth of existing thing For example in an image Detection is that image contains the person or not if have the person then recognize that is mal.*

But once detected, mesothelioma diagnosis is difficult for a number of reasons. First, there is a very extended time period between the exposure to asbestos and the onset of the disease, sometimes as long as 50 to 60 years. Second, the typical symptoms of mesothelioma, shortness of breath and coughing, are also symptoms of many other types of lung problems, both cancerous and non-cancerous. Thus, just because a person has these symptoms, it does not in any way provide a mesothelioma diagnosis. Third, many types of tumors can exist in the serous cavities that are not mesothelioma. These other types of tumors can be non cancerous, or benign, that originate in the tissues of the serous membranes, other than the mesothelium. Or they can be tumors that have migrated from other organs with cancerous growths due to metastases. Mesothelioma and Imaging Technologies X-rays and other types of imaging technologies can be used to detect tumors or effusion build up of fluid in the body, including mesothelioma detection. A growth in the chest cavity will show up in an X-ray or MRI analysis. But these devices cannot directly determine the type of cancer or provide a mesothelioma diagnosis. They cannot determine whether the tumor is mesothelioma or originates from some other source. Positron emission tomography PET is a type of diagnostic imaging scan that is used for malignant mesothelioma detection. PET scans use the emission of positrons tiny particles that are emitted from radioactive substances for the purpose of radiation detection. Some medical professionals are of the impression that PET scans are the most effective method through which to definitively verify a case of mesothelioma. While they believe that standard imaging techniques like x-rays and MRIs should continue to play a role in diagnosing the disease, it is felt that positron emission tomography is becoming an increasingly valuable tool in the staging and typing of the latent asbestos cancer. Diagnostic Surgery - Biopsy To provide a mesothelioma diagnosis, a biopsy is needed. This biopsy then undergoes what is called diagnostic histopathology. Histopathology is a technique where the cells from the tumor are viewed under a high-powered microscope, or electron microscopy. Electron microscopy is considered the gold standard for evaluating tumor material from a biopsy. It is a highly advanced microscope that allows viewing of the tiniest elements of cell tissue. For mesothelioma diagnosis, a pathologist a doctor who specializes in disease detection places the tumor cells under the electron microscope and then views the structure of the individual cells. The mesothelioma cells have a specific shape and pattern. Even with the electron microscope, the different types of mesothelioma cells can be hard to recognize. The three types of cells are epithelioid mesothelioma cancer cells, which are tubular in shape, sarcomatoid mesothelioma cancer cells, which are oval and irregularly shaped, and biphasic mesothelioma cancer cells, which are a combination of shapes. These cells can be confused with other types of cancer cells. New Methods For Mesothelioma Detection Due to this diagnostic confusion, much research is underway to find new methods for diagnosis. One method is to evaluate the types of compounds generated by the mesothelioma cancer cells. This is called histochemistry. Histochemical reactions have long been used to distinguish between mesothelial and other types of tumor cells. For example, mesothelial cells are known to produce specific types of carbohydrate compounds. Unfortunately, other types of cells in the body also produce these compounds. Immunochemistry is also being used to detect mesothelioma. This area of study evaluates the presence of antibodies in the body. Certain types of antibodies are known to be associated with certain types of cancer. But mesothelial cells have no specific types of antibodies that can provide a "positive" marker. Consequently, immunochemistry allows the doctor to "eliminate" the other cancers, but does not indicate the presence of mesothelioma. These techniques offer insight into the disease and may help eliminate other diseases, but none can directly detect mesothelioma. Recently, because of the difficulty in diagnosing malignant mesothelioma, research has concentrated on finding new ways to detect the presence of the disease. Researchers in Australia have found that a certain protein, called SMR or Soluble Mesothelin Related protein, is elevated in patients with mesothelioma. These

researchers have suggested that a test for the presence of SMR in the blood could represent a useful marker for the diagnosis and disease progression. They feel that such a diagnosis tool could lead to earlier detection, and thus more effective treatment. One of the most striking findings of their research was that several asbestos-exposed persons who tested positive for SMR were diagnosed with mesothelioma within three years. They suggested that evaluation of SMR may help to identify persons at risk for this deadly disease. Also, they found that SMR levels increase as mesothelioma progresses, suggesting that SMR evaluation could be used to track the progression of the disease and the effectiveness of treatment. In an effort to produce the first early-detection test to screen for malignant mesothelioma, researchers at Wayne State University have been studying the possible link between mesothelioma development and levels of a glycoprotein called osteopontin. Early clinical study findings of patients have demonstrated a link between high levels of osteopontin and the development of malignant pleural mesothelioma. Although the results are being viewed as preliminary, there is a great deal of excitement surrounding the potential of a blood test capable of screening for mesothelioma in its earliest stages. While there is no known cure for malignant mesothelioma, research is ongoing and certain successes have already been realized in terms of extending survival time beyond the one to two year post-diagnosis average. It is hoped that if mesothelioma specialists have more time to conduct treatment on a lesser developed form of the asbestos cancer, patients will have a greater chance of survival. Despite the fact that the preliminary results of the osteopontin blood test clinical trial have been met with some controversy, the National Cancer Institute NCI continues to sponsor additional study. Tell Your Doctor About Asbestos Exposure If you or a loved one has been exposed to asbestos, even if it was in the distant past, it is very important that you inform your doctor. One reason why mesothelioma is such a deadly disease is that it is detected late in the disease process. If your doctor knows of the exposure, he or she may be more aware of your symptoms or other health issues that could be used for early detection and a more optimistic mesothelioma prognosis.

## Chapter 9 : Diagnosis and Detection

*Sessile serrated adenomas and polyps (SSA/Ps), especially those in the proximal colon, are recognized as precursors to colorectal cancer, yet their detection, diagnosis and resection can still pose a challenge and are not widely known.1 Herein, we summarize the current knowledge on the endoscopic approach to detect, diagnose, and treat SSA/Ps.*

When a test is performed to detect a disease, there are four possible outcomes: True positive - test indicates that a patient has a disease that the patient does indeed have False positive - test indicates that a patient has a disease when they do not True negative - test indicates the patient is disease-free, and this is indeed the case False negative - test indicates the patient is healthy when in fact the patient has the disease Sensitivity and Specificity Medical tests are characterized by two features, sensitivity and specificity. Sensitivity refers to how accurately a test identifies people who have the disease. Specificity refers to how accurately a test identifies people who do not have the disease. The best medical tests have high sensitivity and high specificity. General Techniques A wide variety of techniques are used for cancer detection, including: Non-invasive Techniques Ultrasound uses reflection of sound waves to create an image of a part of the body MRI uses magnetic fields and radio waves to produce images of the body. PET scans use radioactive molecules to create a dynamic image of internal tissues and organs. PET scans are able to measure the metabolic activity of cells, not just their structure. CT scans use x-rays to take multiple image slices in order to create a 3D image. X-rays utilized high energy beams to create an image. Invasive Techniques Fine needle aspiration FNA uses a small needle to collect small samples of a lesion. Core needle biopsy BPA uses a larger needle to collect samples of a lesion. Fluorescence in situ hybridization FISH measures genetic changes i. Cancer Specific Techniques Some detection techniques are used to detect specific cancer types. Mammography uses low dose x-ray to create an image of a breast. Sigmoidoscopy uses a small tube containing viewing equipment to view the colon. Pap smears use a sample of cells from the cervix to detect cervical cancer. Pap smears may also detect ovarian and uterine cancers that have migrated to the cervix. Prostate specific antigen PSA test measures levels of a glycoprotein in the blood. Elevated levels of PSA may be associated with prostate cancer.