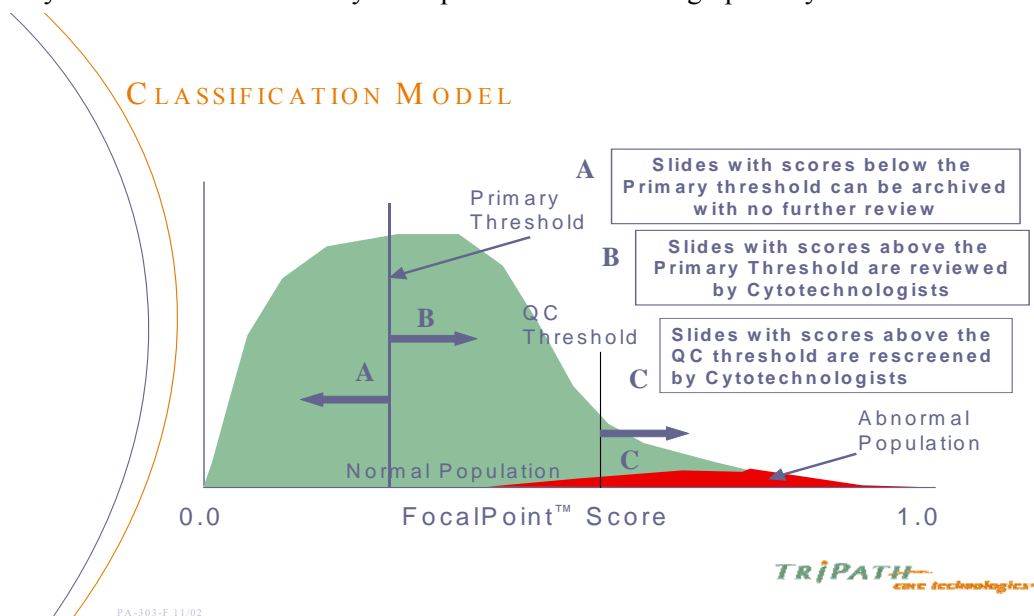


AUTOMATED PAP SMEAR SCREENING SYSTEM

The Pap smear has done an excellent job of reducing morbidity and mortality from cervical carcinoma during the last 45 years. Despite this, there are well-known sources of error involved with the collection, preparation and screening of traditional Pap smears. These errors include both false positive and false negative results. In an attempt to reduce the limitations of the conventional Pap smear, extensive research over the last 15-20 years has been directed toward automating the Pap screening process. An offshoot of this research has been the introduction of liquid-based Pap techniques such as TriPath Imaging's SurePath™ and Cytoc's ThinPrep™, both of which have improved Pap specimen collection and screening. Within the past few years, TriPath Imaging has been able to bring an FDA-approved product to the market. The FocalPoint™ technology received initial FDA approval for quality control rescreening of conventional Pap smears in 1996. In 1998 the FDA granted the device approval for the primary screening of conventional Pap smears and in 2001 FDA approval for the primary screening of SurePath™ liquid-based Pap specimens was given.

The FocalPoint™ computer-assisted Pap screening system directly addresses the problem of human error in the screening of Pap smears. Despite the advances made by utilizing liquid-based Pap specimen technology false negatives remain a problem. Automated screening minimizes potential false negatives caused by human errors including failure to identify abnormal cells because of fatigue, distraction or lack of concentration as well as due to misinterpretation. This computerized process also leads to a reduction in false positive results.

The Focal Point™ system screens each slide using a high-speed video imaging system. Each image is digitized and then analyzed through the use of proprietary interpretation algorithms, which include a massive database of abnormal cell images. The system then ranks the slides as to likelihood of containing abnormal cells. This printed, ranked review of the slides is then available to the screening cytotechnologists who can focus on the cases stratified as likely to contain an abnormality. This process is illustrated graphically below.



The system also identifies endocervical cells, endometrial cells and microorganisms thus allowing the cytotechnologists to concentrate on the search for abnormal cells. Depending on the screening population, the system can classify up to 25% of slides as “normal”, where further (human) review is not necessary. Again, this allows the cytotechnologists to focus on the slides more likely to contain abnormal cells. (The system also selects the 15% of “normal” slides most likely to be abnormal and triages them for automatic quality control rescreening by a second cytotechnologist to enhance the CLIA88-mandated quality control rescreening procedure.)

It is estimated that even the best laboratories have an irreducible Pap smear screening false negative rate between 5-10%. The FocalPoint™ system has been shown to have a false negative rate of 1.4% and to reduce false negatives by 32% and false positives by 16%. (1-4). The system also reduces cytotechnologist fatigue and improves productivity within the laboratory.

Since utilization of the FocalPoint™ system adds expense to the process, the AMA CPT Manual recognizes new CPT codes for slides screened by this automated process:

- 88147 for automated screening of conventional Pap smears,
- 88148 for conventional Pap smears screened by both the automated instrument and by manual re-screening,
- 88174 and 88175 for liquid-based Pap smears with automated screening without and with manual re-screening respectively.

The Centers for Medicare and Medicaid Services (CMS) recognize this technology and reimburse at a higher rate for slides screened by the automated technology relative to those screened by the manual technique alone. The Rex Hospital Laboratory recognizes the advantages of automated Pap smear screening and is currently implementing the FocalPoint™ system. Beginning in March 2003 all conventional Pap smears and SurePath™ slides will be screened using this technology. Unfortunately, at this time, ThinPrep™ slides can not be screened using the FocalPoint™ system.

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DEATHS TO BE REPORTED TO THE MEDICAL EXAMINER

From time to time confusion arises as to which deaths need to be reported to the medical examiner. The county medical examiner is an officer of the State of North Carolina and is charged with the duty of investigating and certifying specified categories of human deaths in the state. A medical examiner’s authority derives from Article 16 of Section 130A of the North Carolina General Statutes. All of the pathologists at Rex are medical examiners duly appointed by the State of North Carolina. The following is a list of types of deaths that should be reported to a medical examiner:

1. Homicide
2. Suicide
3. Accident
4. Trauma
5. Disaster

6. Violence
7. Unknown, unnatural or suspicious circumstances
8. In police custody, jail or prison
9. Poisoning or suspicion of poisoning
10. Public health hazard (such as epidemic)
11. Deaths **during** surgical or anesthetic procedures
12. Sudden unexpected deaths **not reasonably related** to known previous disease
13. Deaths without medical attendance

Please note that there is **no 24-hour rule** in the State of North Carolina. In other words, deaths within 24 hours of admission to the hospital do not require medical examiner investigation unless they fall under one of the above listed criteria. On the other hand, it is the proximate cause of death that determines the manner of death and medical examiner jurisdiction. For example, an elderly lady falls and fractures her hip. While recovering from her broken hip in the hospital, she develops pneumonia and dies. This case should be referred to the medical examiner. The manner of death would be “accidental”. The cause of death would be pneumonia as a consequence of a femoral fracture.

According to North Carolina General Statute 130A-115, if a death is due to natural causes, *any physician* that has access to the medical history of the deceased and has viewed the deceased at or after death can fill out the Death Certificate. It is **not** necessary that the physician of record have definitive evidence of the exact mechanism of death in such cases. For example, an obese, hypertensive elderly individual that complained of antemortem chest pain can be classified as dying of “Ischemic Heart Disease” without documented EKG or enzyme changes. Such cases **do not** have to be reported to the medical examiner and do not fall under medical examiner jurisdiction.

If there is any question as to whether or not a given death should be investigated by a medical examiner, please contact the pathologist on call. We are happy to help you determine if this is a “medical examiner case”. If a medical examiner accepts jurisdiction in a case, it does not necessarily follow that an autopsy will be performed. An autopsy may be performed if the medical examiner deems that it is “in the public’s interest”. If a case is to be reported to the medical examiner, please **do not** seek permission for autopsy from the decedent’s family prior to consultation with the medical examiner. If the family has already been asked and has denied a request for autopsy, then the medical examiner is placed in a tenuous situation if he or she deems that an autopsy is necessary.

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Fetal Fibronectin

Beginning in early March, the Laboratory will offer on-site fetal fibronectin testing as an adjunct to the management of patients with possible preterm labor or at high risk for preterm delivery. Fetal fibronectin (fFN) is a glycoprotein, which is postulated to play a role in anchoring chorioamniotic membranes to the uterine mucosa. Fetal fibronectin is normally present in cervicovaginal secretions during the first half of pregnancy and again near term. Between 22 and 37 weeks, fFN is typically not detectable in samples from these sites. Several studies have determined that the presence of fFN (at a concentration ≥ 50 ng/mL in cervicovaginal fluids during this time frame is associated with an increased risk of premature delivery within 7-14 days and prior to 37 weeks.¹⁻⁴ Depending upon the population of women being studied, the positive predictive value is relatively low (16.7 – 46.3%), but the negative predictive value is high (93.9 – 99.2%).²⁻⁴ As a result, the test can be quite useful in triaging women who require further evaluation and/or treatment from those who can be followed less aggressively. In one study, the vast majority (80%) of women presenting with signs or symptoms of preterm labor had a negative fFN. In this study, 124 of 125 women with a negative result (99.2%) did NOT deliver within the ensuing 14 days.² When used in conjunction with clinical findings on pelvic exam, the test can reduce unnecessary hospitalizations and the cost of additional (? unnecessary) treatment. Several algorithms have been developed to assist in the management

of patients with possible preterm labor or at risk for preterm delivery. (Contact your local Adeza sales representative or the authors below if you would like one.)

Rex will use the Adeza Biomedical Rapid fFN assay, a qualitative immunoassay calibrated to detect fFN concentrations ≥ 50 ng/mL. The expected turnaround time is 1 hour from receipt of the specimen. As with any lab test, ***proper specimen collection is essential to obtaining accurate results!!!!*** Stated another way, most problems with this test result from improper specimen collection or specimen handling. The only acceptable specimen is one collected with the Adeza specimen collection kit (see the sales rep. again). Specimens should be obtained from the posterior vaginal fornix during a speculum exam ***prior to digital cervical exam.*** The Dacron swab in the kit should be inserted into the vagina and rotated across the posterior fornix for approximately 10 sec. The swab should be carefully removed and placed into the tube of buffer provided in the kit. Break the shaft at the scored area and carefully insert it into the hole inside the tube cap. Push the cap tightly over the shaft, to assure a tight seal. (A leaking tube will result in an unacceptable specimen.) Label with patient's name and send with a completed lab requisition for "fetal fibronectin" testing. The specimen is stable at room temperature for 8 hours, but should be kept cool. If testing is going to be delayed, a refrigerated specimen (2-8° C) is stable for 3 days. Either digital cervical exam or vaginal probe ultrasound will invalidate results [both false (+) and false (-)]. If these procedures are performed prior to collecting a sample, specimen collection should be delayed for 24 hours. Soaps, lubricants, disinfectants or creams will also interfere. fFN specimens should be collected prior to obtaining specimens for microbiologic culture, as abraded tissue may interfere with sample preparation. Finally, sexual intercourse within 24 hours preceding specimen collection can result in false (+) results. Negative results are believed to be valid.¹

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2002 Antibiogram

We are pleased to present the antibiogram prepared from isolates recovered in the Rex Microbiology Laboratory during the past year as an insert in this issue of the *Bulletin*. Thanks to Sheila McMahon, Susan Tricas, DuWayne Engman, and Ashley Hooks for collecting the data and preparing the spreadsheet.

For further information, call the Laboratory (784-3040). Telephone extensions are: Pathologists' Direct Line (3201), Sharon Logue (Lab Director 2400), Robin Ivosic (Outreach and Microbiology Lab Manager 3053), Elaine Patterson (Core Lab Manager 3054), Jackie Okoth (Core Lab PM Manager 4248), Diane Young (Anatomic Pathology Manager 3888), Nga Moore (Customer Service Manager 3396), Diane Stephenson (Blood Bank Manager 4767), Justin Hodges (Blood Plan Manager 4750)