

## Monolayer Cytology Introduction




Monolayer Cytology technologies have been proven to provide slides of superior quality. MDS conversion to liquid based collection will be completed during 2002.

MDS is in the process of converting to liquid based collection for Gynecological Cytology. The production of a monolayer slide in the laboratory results in a more consistent preparation, enhancement in slide quality and reduction in the number of slides reported as unsatisfactory or "limited by" when compared to conventional Pap Smears. We have chosen the AutoCyt® system of Tripath Imaging to prepare monolayers.

Collection in your office is simplified because the collection device is submitted to MDS in fixative along with all the cells obtained. You no longer need to prepare and fix the slide. A better and more complete sample is available to the laboratory because the new technique results in many more cells being collected with the brush

or spatula then after a conventional smear has been prepared. It is important that the attached collection instructions are followed. In particular, clockwise rotation of the device five (5) times will ensure that an optimal endo-cervical component is obtained.

Please note that we will be able to process only samples submitted in the Tripath fixative provided by MDS. Although we anticipate some improvement in turn-around-time a significant shortage of Cytotechnologists will persist into the foreseeable future. It is essential that when expedited interpretation is required for clinical reasons, you must indicate this need on the requisition. 




## The Treatment of Enteric Parasitic Infections

As clinicians continue to care for increasing numbers of immunocompromised patients and as travel becomes more common-place, the management of infections due to intestinal parasites continues to be a challenge. In this issue of LabNews, treatment regimens for common pathogenic parasites are summarized in Table 1. Factors prompting referral to specialists for further treatment advice may include: clinical and immune status of the patient, pathogenicity of the organism, and first-line therapy "failures".

In some instances, the decision to offer specific treatment may depend upon the clinical status of the patient. For example, only symptomatic patients infected with *Dientamoeba fragilis* should receive treatment.<sup>1</sup> The same principle applies to patients with giardiasis, although food handlers, the immunocompromised and those infected as a result of an outbreak should receive treatment, regardless of symptoms.<sup>2</sup> Patients with cryptosporidiosis do not usually

require treatment unless they are immunocompromised, when infections tend to be prolonged. Note that reliable curative treatment for this infection is currently not available.

Patients infected with *Entamoeba histolytica* should receive treatment regardless of symptomatology. Patients with invasive infection (ie colitis, amoebic abscess) should always receive an intraluminal agent such as iodoquinol after treatment with metronidazole.<sup>3</sup> Please note that the laboratory is not able to discriminate between pathogenic *E. histolytica* and nonpathogenic *E. dispar* by microscopic techniques. Physicians are encouraged to order specific *E. histolytica* serology testing in order to delineate which patients require treatment. 

### References

1. Can J Infect Dis, 1998; 9(2): 69-70.
2. Lee *et al.*, CID 2000; 30: 401-402.
3. The Medical Letter, January 1998; 40(1017): 1-12.

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**Table 1: Treatment Regimen for Common Pathogenic Parasites**

Etiologic Agent	Drug (in order of preference)	Adult Dosage	Paediatric Dosage
<i>Ascaris lumbricoides</i>	Mebendazole	100 mg bid x 3d or or 500 mg once	100 mg bid x 3d 500 mg once
	Pyrantel pamoate	11 mg/kg once (max. 1 gram)	11 mg/kg once (max. 1 gram)
	Albendazole*	400 mg once	400 mg once
<i>Cyclospora</i>	Trimethoprim- sulfamethoxazole	TMP 160 mg, SMX 800 mg bid x 7 days	TMP 5 mg/kg, SMX 25 mg/kg bid x 7 days
<i>Dientamoeba fragilis</i>	Iodoquinol	650 mg tid x 20d	40 mg/kg/d (max. 2 g) in 3 doses x 20d
	Paromomycin	25-35 mg/kg/d in 3 doses x 7d	25-35 mg/kg/d in 3 doses x 7d
	Tetracycline**	500 mg qid x 10d	500 mg qid x 10d
<i>Entamoeba histolytica</i> asymptomatic infection	Iodoquinol	650 mg tid x 20d	30-40 mg/kg/d (max 2g) in 3 doses x 20d
	Paromomycin	25-35 mg/kg/d in 3 doses x 7d	25-25 mg/kg/d in 3 doses in 7d
	Diloxanide furoate*	500 mg tid x 10d	20 mg/kg/d in 3 doses x 10d
<b>symptomatic infection</b>	Metronidazole followed by Iodoquinol, Paromomycin or Diloxanide furoate*	500-750 mg tid x 10d	35-50 mg/kg/d in 3 doses x 10d
<i>Enterobius vermicularis</i>	Pyrantel pamoate	11 mg/kg once (max. 1 gram); repeat in 2 weeks	11 mg/kg once (max. 1 gram); repeat in 2 weeks
	Mebendazole	100 mg once; repeat in 2 weeks	100 mg once; repeat in 2 weeks
	Albendazole*	400 mg once; repeat in 2 weeks	400 mg once; repeat in 2 weeks
<i>Giardia lamblia</i>	Metronidazole	250 mg tid x 5d	15 mg/kg/d in 3 doses x 5d
	Tinidazole*	2 grams once	50 mg/kg once (max. 2 g)
	Furazolidone	100 mg qid x 7-10d	6 mg/kg/d in 4 doses x 7-10d
	Paromomycin	25-35 mg/kg/d in 3 doses x 7d	
<i>Trichuris trichura</i>	Mebendazole	100 mg bid x 3d or 500 mg once	100 mg bid x 3d or 500 mg once
	Albendazole*	400 mg once	400 mg once

**Footnotes:**

\* These drugs must be obtained through the Special Access Programme by calling 613-941-2108.

\*\* Contraindicated in pregnancy and children under the age of 8.

By: A. Sarabia, MD, FRCPC, Director, Medical Microbiology

Treatment regimens for infections due to *E. histolytica* should always include intraluminal agents such as iodoquinol.



The laboratory diagnosis of parasitic enteric infections is enhanced when clinically relevant information is communicated to the lab.

### When to Measure Folic Acid?

Folic acid is an essential nutrient in the prevention of neural tube defects (NTD). In November 1998, Canada implemented a program to ensure folic acid supplementation of all pasta, flour and grain products.

Following implementation of this program, a retrospective review of population data collected in Ontario by MDS indicates that significantly fewer individuals are at risk for folate deficiency. Defined as a decrease in RBC folate concentration (< 215 nM), the number of folate deficient cases noted prior to fortification was 57 of 3200 patients reviewed (1.8%). Post-implementation, this number decreased to 17 of 4102 (0.4%) of requests reviewed.<sup>1</sup> In addition, the mean concentration (95 % CI) of RBC folate increased from 680 (669-692 nM) to 852 (841-862 nM) during the same periods of time.

Considering this data and that presented by QMP-LS, measurement of this analyte will be required much less frequently.<sup>2</sup> Patients suspected of having any of the following conditions may still benefit from folate testing: malnutrition, alcoholism, anemia, gastrointestinal malabsorption.

#### References

1. Ray JG, Vermeulen MJ, Boss SC and Cole DEC. Clin. Biochem. 2000; 33(5): 337-343.
2. QMP-LS Endocrinology Committee Comments, Folate patterns of practice survey R-9908-PP, Endocrinology 2000; 3(2.2): 49-56.

### Reference Range Changes:

#### C-Peptide

Due to a manufacturers change in the calibration of the C-peptide kit, physicians may observe a significant decrease of up to 40% in reported serum C-peptide concentrations. A review and validation of the manufacturers stated reference range is in progress. Implementation of the reformulated kit is scheduled for March 4, 2002.

#### Parathyroid Hormone (PTH)

The PTH assay utilized by MDS has been reformulated to include the use of a new pair of monoclonal and polyclonal antibodies. This change in format has resulted in an assay of increased sensitivity and specificity to the intact PTH molecule. Note that reported concentrations of serum PTH may be up to 28% lower than previous values.

A review of the MDS reference range was completed prior to implementation on December 13, 2001. The revised PTH reference interval is 1.5-6.5 pmol/L. Due to the important physiological relationship between PTH and calcium, it is always important to interpret PTH results in conjunction with circulating levels of serum total and ionized calcium concentrations.


### Diagnosis of Hypoglycemia

Utilization of the 4 hour or 5 hour glucose tolerance test (GTT) for diagnosis of hypoglycemia is no longer recommended. The preferred test for initial investigation of suspected postprandial hypoglycemia is measurement of a single blood glucose, collected 2-5 hours after a standardized mixed meal or carbohydrate load. The most accurate assessment includes repeated blood glucose measurements at times when the patient is experiencing symptoms.

For the investigation of postprandial hypoglycemia, order a 2-5 hour post meal blood glucose level. The time of meal ingestion must be provided to the laboratory to permit correct interpretation of the results.

A post meal glucose level of less than 2.5 mmol/L, on more than one occasion, is suggestive of reactive hypoglycemia. To rule out true fasting hypoglycemia, individuals should, subsequently, be evaluated using a supervised 72 hour fasting test. For further assistance, please consult the MDS Clinical Biochemist at extension 2363.

### Collection for Liquid Based Cytology in Pregnancy

Deep insertion of a collection device into the cervical canal is inadvisable in pregnancy. In order to obtain a sample in pregnant women, the Cervex<sup>®</sup> broom provided by MDS can be used in a manner similar to the spatula which was included in the kits for conventional smears. The central bristles of the Cervex<sup>®</sup> brush should not be inserted deep into the canal but by firm pressure and rotation in a clockwise direction, the device may be used to sample the external os and ectocervix. A vaginal pool sample may also be obtained. 



## CK Isoenzymes or CK MB – which test to order and when?

Creatine Kinase, CK, exists in five molecular forms with three isoenzymes and two variants. The three CK isoenzymes are CK-BB, CK-MB and CK-MM, also called CK1, CK2 and CK3.<sup>1</sup> The isoenzymes are derived from brain, myocardial and skeletal muscle, respectively, while CK variants are either immunoglobulin bound CK-BB or mitochondrium derived CK. While only CK-MM is present in normal serum the other isoenzymes or fractions appear as a result of various pathologies. Type 1 CK variants are commonly seen in apparently healthy older women, often associated with normal or slightly elevated total CK but are of no known clinical significance.<sup>2</sup>

### CK Isoenzymes

Complete CK isoenzyme analysis or fractionation is used to investigate patients with unexplained total CK results or presence of CK variants which may be seen in patients receiving animal derived therapies.<sup>3</sup>

This type of analysis may also be useful in the investigation of patients with isoenzyme secreting tumours, heterophilic antibodies or persistent asymptomatic elevated total CK activities. Analysis is not automated and is labour intensive, hence prolonged turnaround times for CK isoenzymes analysis precludes its use as a routine test for investigating acute myocardial infarction. CK isoenzyme analysis or fractionation does not provide added value in patients suspected of muscle disorders. These patients may be most effectively monitored with quantitation of total CK.

### CK-MB

Measurement of CK-MB mass or activity (U/L) is used in the investigation of suspected myocardial injury. Compared to CK-MB activity methods, CK-MB mass assays are preferred due to improved precision, rapid analysis capabilities, enhanced sensitivity and specificity. Results of CK-MB assays are usually expressed in absolute concentration (ug/L) and as the “relative

index” or percent CK-MB mass to total CK activity. A relative index greater than 4% is suggestive of an acute myocardial infarction, (AMI), while, indices between 2-4% are “borderline high” and warrant further clinical correlation.

As a community based laboratory service, MDS does not perform urgent requests for CK-MB analysis. If AMI is suspected, the appropriate medical response is to direct the patient to a near-by hospital with emergency services so that immediate care can be provided.

If further assistance is required, please consult laboratory personnel. 

### References

1. Moss DW et al. *Enzymes: In Tietz Textbook of Clinical Chemistry*, 2nd ed., Burtis C. A. & Ashwood E. R. eds., W. B. Saunders Co. 1994, 797 – 809.
2. Lee KN, Csako G, Bernhardt P and Elin RJ. *Clin Chem* 1994; 40: 1278 – 1283.
3. Thompson RJ, Jackson AP and Langlois N. *Clin Chem* 1986; 32: 476 – 481.



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# AutoCyte PREP

## Thin-Layer Pap Preparation

### FOUR SIMPLE STEPS



**1. Cervical Sample Collection**  
Insert the Rovers Cervex-Brush® into the endo-cervical canal. Apply gentle pressure until the bristles form against the cervix. Maintaining gentle pressure, hold the stem between the thumb and forefinger and rotate the brush five times in a clockwise direction.



**2. Preserve the entire sample**  
Placing your thumb against the back of the brush pad, simply disconnect the entire brush from the stem into the CytoRich® preservative vial.



**3. Cap and label vial**  
Place the cap on the vial and tighten. Label the vial and lab requisition form with patient name and/or number, physician name and date if desired.



**4. Send vial to your lab**  
Place the vial and requisition into a specimen bag and send to the laboratory.

### ONE CLEAR RESULT

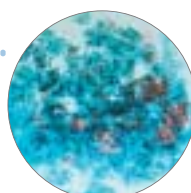
In clinical trial studies, cervical samples were taken and first smeared onto slides. Residual cells from the conventional smear were used in the AutoCyte PREP process. *In each case, the same patient sample, with very different results.*

1.

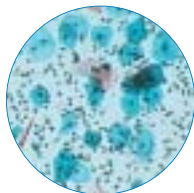


**Conventional**  
Conventional smear, dense with blood, mucus, and inflammation is diagnosed as an unsatisfactory specimen, and the patient is called back in for another sample.

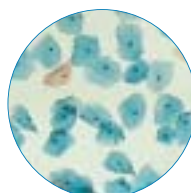
2.



**Conventional**  
The conventional smear, although diagnosed as "within normal limits" can be considered "limited" with the cells hidden by excessive cell clumping.



**AutoCyte PREP**  
The same sample was processed by AutoCyte PREP, which eliminated the obscuring material for a sample easily diagnosed as "within normal limits."



**AutoCyte PREP**  
The same sample, using residual material from the smear and processed by the AutoCyte PREP allows for diagnosis with no questions or concern.



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