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AD Express

September 2023

On The aRight Track, For Precise Results

Editorial board

From the Editors' Desk

Dear Reader,

With September the season of festivity sets in. May the season of joy & festivity usher in positivity & hope in all that we do. We wish our readers a happy festive season & take this opportunity to thank all our patrons for the immense support we have garnered over the years.

We will continue to encourage contributors to write on their experiences & share their expertise.

In this edition of the year we share an interesting repertoire of topics ranging from the bare basics to the exclusive & esoteric. The opinion of individual practitioners also matters as much as anybody in lab medicine. Astute judgment & robust background of the branch enables lab medicine specialist to hone a set of skills that only get better with time. In a first time endeavour, we share the expertise of the lab medicine specialists from case series studies as well as experience from practice titled; "Expert opinion".

In our article section we explore the time honoured debate "whether the post prandial glucose can be lower than the fasting levels" in a rather probing write up. Apollo diagnostics is committed to the adoption of best practices in lab medicine. Our next article delves into one of a kind approach, Apollo diagnostics employs in the application of lean in laboratory medicine. We have introduced another dimension to our quizzes by introducing 'What's on the stage', which reinforces the fact that a strong background of cell morphology will augur good for any laboratory. We expect our creative tendencies to gravitate towards biochemistry ballads, serology sonnets & musings from microbiology in the forthcoming issues.

We thank Gautam Roy & Hemaal Dhar for formatting copy after copy & giving AD express shape. AD express has gained considerable impetus by the way of your contributions & we welcome more from you all. Also humbly request you to share your feedback on 'AD express' & we assure you that feedback from you will give us scope to improve.

Wishing you all a Happy Ganesh Chathurthi, a happy festive season & a great year ahead!

Best regards,

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Expert opinion

Articles

EXPERT OPINION

1. Interferences in FNAC – Dealing with hemorrhagic smears

Dr. Manju Kumari - Consultant Pathologist. Apollo Diagnostics, HLM Sheetla Hospital, Gurugram, Haryana

Foreword:

Since the phenomenal publication in 1941 by Drs.Papanicolau & H.Traut, diagnostic cytopathology has developed as parallel but distinctly separate discipline from histopathology. Procedures such as 'the PAP test' & FNAC are part of everyday pathology reporting. Cytolopatholohgy samples which are reported as unsatisfactory, many a time lead to disgruntled clinicians, who may question the competency of the reporting pathologist. Unsatisafactory smears may be due to the result of various factors ranging from improper fixation to erroneous smearing technique.

Blood is ubiquitous in the human body & some tissues are more vascular than others. Glands such as thyroid which are often aspirated have copious blood suppy & may yield only blood if the wrong equipment is used for FNAC. Thyroid FNA when done with a 23G needle yields blood more often than not. One of the most common perils that microscopist's face when reporting cytology material is 'blood'.The following write up illustrated the impediment blood poses as a interferent in reporting FNAC material & ways to overcome the same.

On the other hand some samples are deemed unsatisfactory after examination by pathologists.This may not always be attributed to poor technique or choice of material used in harvesting the sample,but because of interference due to factors that obscure cellular morphology & detail.

Cytorich fixative system- A new modality in haemorrhagic FNAC

Several methods have been explored to overcome the interference of blood in FNAC smears. The use of 2 % acetic acid along with the fixative is a time honoured method described in text books.

We evaluated 'CytoRich Red', a commercially available fixative that could lyse red blood cell lysis in liquid based cytology technique .'CytoRich Red' is quite effective in dealing with hemorrhagic cervical PAP smears.

Concise account of the study : Thirty hemorrhagic smears from breast (16) , thyroid (08), lymph node (04) and soft tissue (02) lesions were included in the study. The fine needle aspirate was divided into two parts. First part was used for conventional smears and CytoRich Red treated smears. An unstained smear was stored in cold acetone for immunocytochemistry, which was applied on relevant cases.

The second part was used for Liquid-Based cytology (LBC). All smears were compared for cytomorphological features and background material.

The smears were classified into 3 groups based on the percentage of hemorrhage that is <25%, 25-50% and >50%. Statistical analysis was done by SPSS version 24. A p value of _0.05 was considered as significant.

What we learnt from the study:

Red blood cells were significantly reduced without hindering staining with a statistically significant difference between background haemorrhage in conventional smears and CytoRich Red treated smears (p value <0.001).

However, this difference was not significant between the Cytorich Red fixed smears and LBC. The Diagnostic utility of CytoRich Red treated smears was more than that of LBC alone (p value < 0.05). Also, there was no significant loss of desired material on CytoRich Red fixed smears.

Concluding remarks : Cytorich red fixative system can be used in case of hemorrhagic fine needle aspiration slide which provides a clear background without compromising the cellularity of the smears.

Hemorrhagic smears obscure cell morphology & hence compromise reporting.

Smears reported as unsatisfactory warrant repeat examination & sampling. This amounts to significant cost burden & loss of precious time to the health care professional. In addition unnecessary acrimony exists between the lab medicine practitioner & the clinician.

Exchange of information between the clinician & the pathologist & studied on exploring new reagents that will help pathologist's discern cell morphology better will help towards positive patient outcomes.

The complete study can be accesed at https://www.jdpo.org/journal-article-file/10814

1. Toxicology testing; dark art of lab medicine.

An interview with Dr.Ramesh Kinha – GM, Technical, Apollo Diagnostics.

Interviwer : Mr.Gautam Roy, DGM, Product development & speciality testing

Prologue:

Rapid industrialization and the increasing use of chemicals in various sectors have raised concerns about their potential health hazards. Adoption of modern agricultural practices with a resultant rise in pesticide usage too have contributed to these concerns. There has also been a surge in pharmaceutical manufacturing and consumption in India in the last 15 to 20 years. All of these are contributing to an increasing need for toxicology testing in India. The following exchange between our technical leadership focuses on the growth of toxicology tests in India, the tools and technologies used, and their future scope.

1. **Why is toxicology testing gaining importance in India?**

   The pharmaceutical industry in India is worth 65 Billion dollars and is expected to grow at a CAGR of over 10 % Drug trials & drug testing is bound to increase in the next decade & hence toxicology testing is gaining importance in India.

   Also occupational health has gained considerable traction & the exposure of employees to toxic substances is being monitored rigorously. This is often regulated by labour authorities & this is another angle to toxicology testing.

2. **What are the different types of toxicology tests prevalent today and what specific objectives do they serve?**

   Toxicology testing can be broadly classified into three types:

   (i) Testing of employees working in an industry or agricultural setting wherein they are exposed to potentially harmful chemicals, heavy metals or radiation.

   (ii) Testing of human subjects in phase 3 drug trials wherein the trial group is tested for pharmacological effects of the drug in question.

   (iii) Therapeutic monitoring of patients for drug levels. In certain instances, the drug levels in serum has to be maintained within a narrow range & hence the quantity of drug present in the circulation has to be closely monitored.

3. **What tools and techniques are used for toxicology testing today and what are the emerging innovations and advancements in toxicology tests?**

   Several techniques that fall under the realm of clinical chemistry are being used in toxicology testing. While spectrophotometry is a widely available tool for estimation of analytes in serum, techniques such as ELISA, ECLIA & CLIA use labelled antibodies for targeted quantification.

4. **Are these new techniques and technologies widely adopted by diagnostic laboratories in India? What has been their adoption rate in the rural India?**

   These techniques are widely available in urban India, however in rural India these techniques may not be widely available.

5. **What are the regulations related to toxicology tests in India and worldwide?**

   Testing for drug levels related to drug trails requires specific licensing in India as well as in several countries. The rules & regulations are dictated by the 'drug & clinical trial rules, 2019' & also the 'Drug & cosmetic act, 1945.'Accreditation is not mandatory in India for testing toxic analytes such as heavy metals, alcohol or benzo diazepam, however statutory guidelines could vary from country to country. For instance the

FDA regulated the pharmaceutical as well as the in vitro diagnostic industry in the US.

6. **What business challenges do diagnostic laboratories in India and worldwide face when it comes to toxicology tests?**

   Toxicology tests are esoteric & expensive. Novel antibodies have to manufactured for new drugs & it may be effected only if significant volumes of testing are facilitated. This involves considerable R & D as well as expertise. Validation & vetting of the data generated involves scientific personnel as well as the approval of statutory authorities.

7. **What does the future look like for toxicology testing in India?**

   Though challenges are there when it comes to toxicology testing, there is an increasing demand for the same with new drug trials overlooking the horizon & occupational health taking center stage. There is considerable onus on research & development in this area to make testing technology accessible.

Take Home Message :

Toxicology testing in India is bound to grow in the coming years.

The expertise of the leaders in the IVD manufacturing has to be scaled up to meet the demands of the industry.

Advances in toxicology testing will

3. The Tao of sugar testing.

Dr. Srivatsan.R, Consultant Biochemist, Department of clinical chemistry and immunoassay, Apollo Diagnostics RRL, Chennai.

"When you have eliminated the impossible, whatever remains, however improbable, must be the truth." – Arthur Conan Doyle

Insulin & glucagon homeostasis take a cue from the yin yang concept. The delicate balance of these two hormones dicates glucose metabolism in health & disease. While it is familiar knowledge that insulin deficiency, either absolute or relative can cause diabetes mellitus,the interplay of hormones such as adipokines,the autonomous nervous system & a number of molecules in the plasma that exhibit insulin like activity is far from simple. It can be concluded that glucose metabolism depends on a plethora of factors that are far reaching and complex.

In laboratory practice it is quite common to hear from patients & clinicians alike that the fasting & post prandial blood glucose levels are not correlating. While it is quite logical to surmise that the post prandial blood sugar level will be higher than that of the fasting state ,the human body does conjure up surprises.

Many a time, in practice we do observe the phenomenon of PPBS being lower than the FBS. Queries contradicting this normal phenomenon are handled by lab medicine practitioners on a daily basis. The notion that PPBS always has to be higher than FBS has crept into the common man psyche as well as the occasional practitioner's whim. This is because reports issued by the unorganised lab sector by large are with PPBS values always being higher than FBS values. These unorganised labs release reports that satisfy expectation rather than trying to explain science to the clinician or the patient.

GLP always teaches us to apply principles of quality & science in the pre-examination,examination & post-examination stages of the testing process.

These excerpts from literature which substantiate the claim that fasting & post prandial blood sugar values need not follow a expected pattern:

1. Insulin is an anabolic hormone is secreted from the beta cells within 30 seconds as blood laden with glucose traverses the pancreas.
2. A healthy population on beta cells secretes enough insulin to push all the glucose into cells and maintain around 70-99 mg/dL at any time. This glucose is taken up for all the functions of the body.
3. Though enough amount of insulin or sometimes high amounts of insulin may be present in the blood but glucose is not pushed into the cell.This is known as insulin resistance.
4. It's only the amount of insulin resistance the cells develop that leads to delay in this glucose being pushed into the cells and thereby leading to higher levels of glucose in the blood stream after a meal.
5. Sugar levels are also immensely dependent on activity,stress,hormonal status & food fads as well.The "Dawn & Somyogi phenomenon" described in literature are also testimony to the relationship between sugar levels & insulin deficiency or excess.

6. There are newer bio molecules like leptins,incretins,GLP Etc which are also implicated.
7. Post prandial reactive hypoglycemia (PRH) & high insulin sensitivity also could lead to the phenomenon of PPBS being lower than the FBS.

Fasting and Post Prandial glucose values are ideally interpreted within their respective biological reference ranges and should not be compared with each other. Fasting glucose values may be higher than post prandial in conditions such as: High insulin sensitivity, Post prandial reactive hypoglycemia.

4. Lean cuts for the lab

Dr. Marquess Raj – ZTC - Tamilnadu & Pondicherry

Foreword:

Lean management is centered on making obvious what adds value & reducing process waste. Laboratory management should include principles of lean along with time tested management principles such as TPS, which aim at reducing process waste, improving outcomes & in the process optimizing cost.

Practitioners of lab medicine should embrace & include the principles of lean in the laboratory workflow. Apollo diagnostics laboratories employ 'five' such processes that effectively minimize 'muda' in the workplace. The same are described in the following lines.

1. Making each tube count

The lab management should look at utilizing testing products and materials to deliver results in the most efficient way in terms of cost or speed or both. Blood collection tubes are perhaps the most common consumable used in the total testing process. A process for sharing of samples in the laboratory improves workflow & also reduces confusion.

Example: The blood collection tube with red top contains no anticoagulant & can be used for both biochemical analysis & serology. A simple mechanism such as a colour coding system by which blood collection tubes are shared across biochemistry & departments will ensure that there is a reduction in the cost incurred on tubes & thereby eliminates waste.

2. Pen free lab

With the healthcare industry embracing environment friendly measures, paperless processes are being welcomed in the IVD industry. Paper occupies space & contributes to burden in the lab work process. When robust software systems are in place, the use of worksheets unless warranted is eliminated. Reduction in the printing of worksheets definitely reduces cost & also streamlines work flow process. As many a time in systems which emphasize on printing a worksheet for sample processing, the process may get delayed because of the absence of the worksheet. The laboratories of Apollo diagnostics have processes which minimize the use of paper in the lab. This is effected by a robust LIS & computer peripherals.

3. Interfacing

Errors can creep into the best of systems even with transcription checks when imposed with a burgeoning sample load. Interfacing of patient results without manual transcription, ensures that error of the human hand is eliminated. This ensures that patient safety is assured in the post- analytical phase. This apart from being a seamless system that saves time & energy builds confidence in the end user.

4. Patient portals

An LIS which supports a virtual patient laboratory record database is the way forward in managing patient records. There could be a portal or a mobile application to which data

can be uploaded for patient access. Apart from ease of access, there is a likelihood that the client will utilize the services of the laboratory depending on how interactive or even creative the portal is. The portal could also have added features for uploading raw data.

Example: Graphs of HbA1C or CBC histograms can be uploaded for the patient's reference. This ensures that all the efforts put in ensuring quality results are documented.

5. eArchival of tubes

Archival of sample containers is a cumbersome chore in the laboratory. Ensuring that a scanning mechanism & defined process exists in the laboratory ensures easy retrieval of samples. Labs should invest in such a process which facilitates the easy retrieval of sample tubes. This ensures that time is spent on productive work in the laboratory.

Afterword:

Elimination of waste in the laboratory can be achieved by improving on existing processes & applying the principles of lean right from the grassroots level. By reducing cost, time & by directing work hours towards more productive outcomes laboratories can become beacons of lean management. Apollo diagnostics laboratories employ all of the methodologies describes above, striving diligenty towards patient care & positive outcomes.

5. Quiz : A multitude of methods

Dr. Marquess Raj & Dr. Shalini Singh - Co-editor AD express

The medical testing laboratory is a place wherein multiple technologies can be found. Relatively commonplace technologies with complex monikers such as immunochromatography & spectrophotometry coexist with manual methods in the realm of medical testing.

Practitioners of lab medicine understand the subtle differences in the testing methods with time & experience. Though automation has simplified much of the testing process in state of the art labs, manual methods cannot be completely supplanted in certain scenarios. Automation though might sound as superior technology, the same has to validated after rigorous scrutiny. The whole purpose of automation is to reduce 'error', add value by reducing burden in & also hasten the testing process to meet the demands of the end users.

Match the preferred methodology for the given tests (Same option can be used multiple times)

1. HbA1C	A. Spectrophotometry
2. Serum creatinine	B. HPLC
3. Hemoglobin estimation	C. Calorimetry
4. Blood culture	D. Nephelometry
5. C3	E. Automation

Answers to the pervious quiz in the August 23 issue:

The appropriate 'riddles' are matched with their respective epithelium

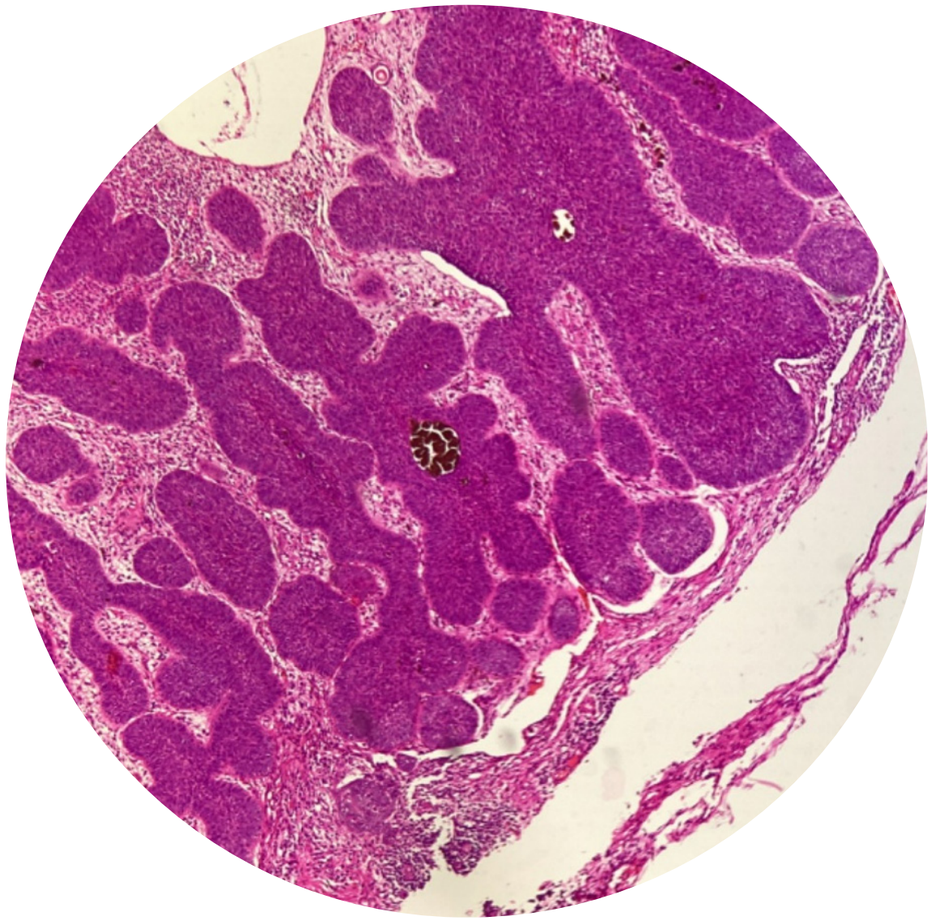
The following riddles are matched to the correct epithelium

1.	Pavement like, flat as pancakes	A. Squamous
2.	Tall in stature possess fine hairs	B. Columnar
3.	Top layer cells are rounded	C. Transitional
4.	Like a stack of boxes	D. Cuboidal
5.	Nuclei not in a regular row	E. Pseudostratified

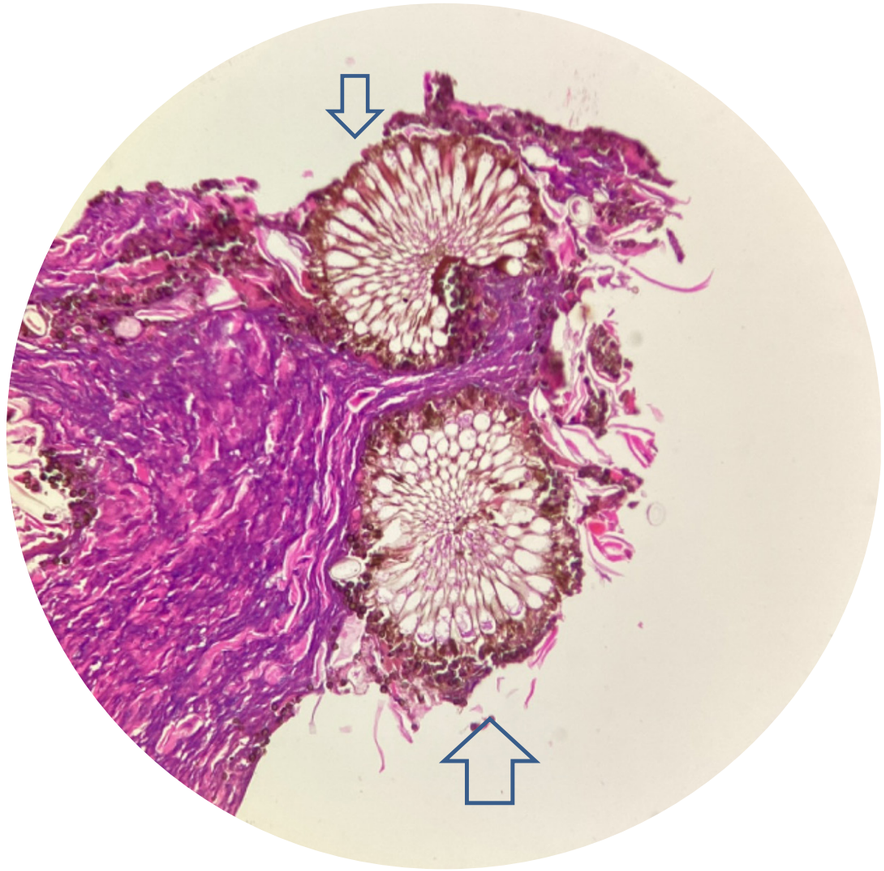
6. Quiz : What's on the stage ?

Dr.Chidambharam. C , Department of histopathology, RRL, Chennai

A. The pathognomic histopathology of a skin biopsy is given below. A brief of the same shall be given in the next issue.



B. Answer to the photomicrograph in the previous issue: Phaeohypomycosis



Clinical Significance:

The arrow in the above photomicrograph point towards a mould. The sample was from the auditory canal. The fungus possesses a distinct brown pigment & exotic morphology. A diagnosis of phaehypomycosis was given. The patient was a diabetic with chronic otomycosis. After a definite diagnosis was given, the patient was treated & responded to the same.

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