Office-Based Laboratory Indications and Interpretation

3

Benjamin Noblitt

Part I: The Basics

Basics of Laboratory Testing

In the very early years of medicine the practitioner had to rely solely upon their physical exam to diagnose and subsequently treat disease. The physical exam has become no less important in today's day and age, but the use of the laboratory and the various tests that they can run has greatly augmented diagnostic ability and accuracy.

Physical exam findings are fundamental to every healthcare practitioner. Most diseases can be diagnosed on history and physical exam, or at the very least an appropriate differential can be obtained. Some would argue that this is the core skill set required to be an effective healthcare practitioner. While advances in medicine have made small improvements in the physical exam, there have been enormous advances in the laboratory setting. This has allowed the practitioner to gain an enormous increased ability to effectively diagnose disease.

Calibration is key. Calibrating a history and physical exam is near impossible; the way one practitioner performs an examination will be different from how another practitioner performs their exam. Additionally, the patient history is invaluable to diagnosis, but it also has the same built-in variance—there is no way to standardize physical exam and patient history. In contrast to this, the laboratory has the ability calibrate and standardize their results.

In summary, the history and physical exam are still, and should always be the foundation of diagnosis and the development of a differential. However, the laboratory can help provide additional, reliable, and repeatable information to the practitioner that they would not be otherwise able to obtain.

B. Noblitt (✉)
University of Cincinnati Oral and Maxillofacial Surgery, Cincinnati, OH, USA
e-mail: NoblitBN@ucmail.uc.edu

E. M. Ferneini, M. T. Goupil (eds.), *Office-Based Maxillofacial Surgical Procedures*, https://doi.org/10.1007/978-3-030-22371-7_3

Understanding the Laboratory: Statistics

It is vital to understand the statistical nuances of laboratory tests. No single lab test is perfect, and there will likely never be one. As such, some tests are more reliable than others, some provide greater diagnostic ability than others, and some rely on the history and physical exam of the patient before they are of any use. It is well beyond the scope of this chapter to cover the statistical world involved with the laboratory, but a few key points will be covered.

Pre-test probability is the probability that a patient will have either a positive or negative result PRIOR to having the test performed. This number is based on epidemiological data, but is more commonly determined based on the practitioner's experience.

For example, if a patient has a history of chronic kidney disease, it is reasonable to determine that the patient will likely have an elevated creatinine. This means that if they take a blood sample, and the laboratory tests the blood creatinine, there is a *high* pre-test probability of measuring an *elevated* creatinine value.

The value in this knowledge is most easily seen when an unexpected lab value is obtained. For example, let's say we see an 18-year-old, lean, muscular varsity soccer player come to the office. For some reason a blood test is drawn (ignore the reason why) which presents a hemoglobin of three. This lab value is likely false due to such a low pre-test probability based on the scenario given. Hemoglobin levels that low will translate into physical exam findings that are in opposition to how the patient presented. The patient here is a very healthy athlete that would not be able to physically perform at his level with a hemoglobin of three. The value of this knowledge is being able to see that the most likely scenario is a false lab result. This would direct the practitioner to send a new set of laboratory specimens instead of working the patient up for profound anemia.

There is little use in attempting to calculate the actual pre-test probability of a lab test. It is more important for the practitioner to simply understand the idea that common diseases are common, and that the lab values should fit the clinical presentation of the patient.

Tests can be sensitive and/or specific.

Tests that are very **sensitive** can be used to **rule out** disease when the test is negative. This is because a sensitive test is good at detecting a value when there is one present. Unfortunately, they also can tend to give false positive results. The important point is that a very sensitive test will rarely be negative when a positive value is present. This means that if a very sensitive test is negative, one can rest assured that the disease process is NOT likely to be present.

Tests that are very **specific** are used to **rule in** disease when a test is positive. This is because a specific test has high requirements for detecting a value when one is present. Unfortunately, since they are so specific they also tend to give negative results even when a positive value is present. The important point is that very specific tests will rarely give positive results when there is no positive value. This

means that if a very specific test is positive, one can rest assured that the disease process IS likely to be present.

Very few tests have both high sensitivity and specificity. It is important to know the limitations of any lab value or test before treating the results of any test as truth.

Understanding the Laboratory: Diagrams

Many common labs are presented in a shorthand format called a fishbone diagram. There are multiple variations in these diagrams, but the two common examples (Figs. 3.1 and 3.2) are presented below for the sake of familiarity:

Understanding the Laboratory: Nothing in Isolation

Tests should not be interpreted in isolation. Each lab value should be interpreted in conjunction with the clinical exam and history of the patient. For example, if a patient presents with an elevated white blood cell (WBC) count, a practitioner might have a differential diagnosis including a possible infection. The patient then reveals that that they have chronic asthma and take inhaled corticosteroids as needed. With this added history, the elevated WBC is now understood to be the result of the corticosteroids, not an infection or other such cause. If the lab test was interpreted alone, it would have led down an erroneous pathway. Laboratory tests should be ordered based on the practitioner's evaluation of the clinical exam and history, not the other way around.

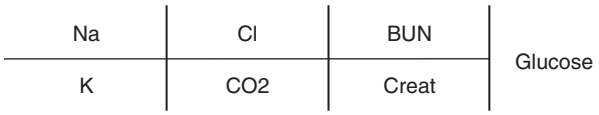

Fig. 3.1 Electrolytes: cations, anions, urine, and sugar

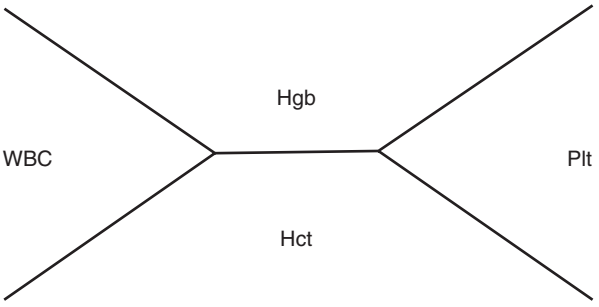

Fig. 3.2 CBC: white blood cell count, hemoglobin, hematocrit, and platelets

Understanding the Laboratory: Time Frame

Lab values can represent either a single point in time or an average over a block of time. For example, if someone has their blood glucose measured, it will show what the blood glucose is at that single moment. If the blood glucose is measured again a few hours later, it will likely be a very different number. Other tests can represent a longer period of time. For example, the hemoglobin A1c number allows the practitioner to get an idea of what the average blood glucose levels looked like for a patient over the last 60–90 days. It is important to know the timeframe of the lab tests being interpreted.

Understanding the Laboratory: Reference Ranges

Reference ranges for a lab value will vary from region to region, and even sometimes from hospital to hospital. These variations are typically not significant but are enough to create a "gray zone" for interpretation. Furthermore, reference ranges typically will be different for children and adults, men and women, etc. Note that children and pregnant women are especially prone to having different reference ranges than that of the general population.

Understanding the Laboratory: Blood Tests

The body is composed of many different tissues (bone, muscle, cartilage, etc.), fluids (blood, urine, CSF, saliva, etc.), and compartments (intracellular, extracellular, etc.). Laboratory tests can be associated with each one of these, but some are more common than others. The most common lab tests are from blood (more specifically venous blood), urine, and soft tissue. Venous blood has a different composition than that of arterial blood, so it is important to know the difference. Systemic arterial blood is coming from the heart and lungs and is fully oxygenated while venous blood is oxygen depleted. Also, venous blood is usually full of metabolic waste as it washes the waste products from the tissue bed it is coming from (with exception of the renal veins). It is the practitioner's responsibility to know and understand these differences when it comes time to interpret the laboratory results they requested.

Part II: Common Labs Drawn for Office-Based Procedures

Complete Blood Count: WBC, RBC, Hgb, Hct, and Plt

The complete blood count (CBC) is a common set of labs that are used to assess the cells in the blood. These tests are usually automated tests that physically count the number of cells per unit of volume to give a concentration of each cell type.

CBC	
WBC	9.1
RBC	4.50
Hemoglobin	13.7
Hematocrit	41.7
Platelets	254

Fig. 3.3 A common example presentation of the CBC with normal range values. Note that many labs auto populate these panels with other readings such as the mean corpuscular volume (MCV), red cell distribution width (RDW), mean corpuscular hemoglobin concentration (MCHC), etc. Also note that units are implied if not given

The CBC is one of the most common lab panels ordered because the lab values it utilizes can be used as proxies for the body's immune status, hemodynamics, and hemostasis. If the practitioner has reason to suspect any issue with these, a CBC would be warranted.

The CBC can come in many different formats, but the essentials of a CBC are noted below (Fig. 3.3).

White Blood Cells (WBC) Count

Common reference range: 3.8–10.8 × 10^3 cells/μL [1]

This test looks at the concentration of circulating white blood cells in the blood. WBCs are the immune system's work horses and are used in the immune response to facilitate the body's immune function. Elevated numbers (leukocytosis) can be indicative of many things such as infection, a response to medications, or a disorder of the bone marrow. Depressed numbers (leukopenia) can indicate a viral infection, cancers of the bone marrow, autoimmune disorders, a response to a medication, or even severe infections. In the setting of clinical swelling, an elevated WBC is often a diagnostic sign of infection.

Red Blood Cells Count (RBC)

Common reference range for males: 4.2–5.8 × 10^6 cells/μL [1]

Common reference range for females: 3.8–5.1 × 10^6 cells/μL [1]

This test looks at the concentration of circulating red blood cells in the blood. RBCs are used to carry oxygen from the lungs to the tissues of the body. This test is often paired with other tests such as the hemoglobin and hematocrit mentioned later in this chapter because the RBC count alone is not very diagnostic. On its own, elevated numbers can indicate bone marrow disease, heart disease, lung disease, dehydration, or a response to medications. Similarly, decreased numbers can indicate anemia, nutrient deficiency, kidney injury, bone marrow disease, or even a response to medications.

Hemoglobin (Hgb)

Common reference range for males: 13.2–17.1 g/dL [1]

Common reference range for females: 11.7–15.5 g/dL [1]

This test looks at the amount of hemoglobin in the blood. Hemoglobin is carried inside the RBCs and is the substrate to which oxygen is carried in the blood. As mentioned earlier, this is one of the tests that is commonly paired with the RBCs to give a better idea of the oxygen carrying capacity of the blood. Elevated hemoglobin values have similar causes to that of elevated RBC counts; bone marrow disease, heart disease, lung disease, dehydration, or a response to medications. Decreased levels of hemoglobin can have many causes including various anemias, chronic bleeding, heavy menstrual cycles, cancer, nutrient deficiency, kidney injury, bone marrow disease, hypothyroid, or even a response to medications. A sedated patient with a low hemoglobin will likely have a low oxygen reserve and will desaturate quickly and easily.

Hematocrit (Hct)

Common reference range for males: 38–50% [1]

Common reference range for females: 35–45% [1]

The hematocrit is the ratio of total RBC volume to total blood volume after centrifugation. For this reason, some people refer to this as the packed-cell volume (PCV) test. In general, elevated Hct counts can be caused by dehydration, or any other cause of elevated RBCs. Decreased hematocrit counts can be from any cause of decreased RBCs or increased blood volume such as the administration of IV fluids.

Platelets (Plt)

Common reference range: 140–400 × 10^3/μL [1]

This test looks at the concentration of platelets in the blood. Platelets are the first responders to an injury and are essential in hemostasis. They form a platelet plug during primary hemostasis and subsequently initiate secondary hemostasis. Elevated platelet counts (thrombocytosis) can be caused by acute bleeding, splenectomy, cancer, or infections. Decreased platelet counts (thrombocytopenia) can be caused by sequestration of platelets in the spleen, bone marrow disease, certain immune related diseases, or even a response to medications. Low platelet counts are often associated with easy bruising, prolonged bleeding, mucosal bleeding, and petechia.

Coagulation Studies: PT, INR, aPTT

If a surgeon has reason to suspect a disorder in hemostasis, it is likely that they will order a coagulation panel. Assessment of the coagulation process can alter the treatment planning and surgical process used by the practitioner, making this another very common panel (Fig. 3.4).

Most coagulation panels consist of the following:

Coagulation Panel	
PT	24.2
INR	2.40
aPTT	41.8

Fig. 3.4 A common example of the coagulation panel. Note that this example shows a patient who is on warfarin with a prolonged PT, elevated INR, and prolonged aPTT. Also note that units are implied if not given

Prothrombin time (PT)

Common reference range: 11.6–14.4 s [1]

Prothrombin is a coagulation factor that is used in the extrinsic pathway (tissue factor pathway) of the coagulation cascade (as opposed to the PTT which uses the intrinsic pathway). The PT looks at the time it takes to clot after clotting is initiated. The test is timed and is reported in seconds. The more seconds means a lower ability to clot, while fewer seconds means a higher ability to clot. This test is commonly used to assess the coagulation of a patient with liver damage (prothrombin in made in the liver) or for someone who is on blood thinners such as warfarin. If a patient has liver disease or is on such a blood thinner, one would expect longer durations to clot.

International Normalized Ratio (INR)

Common reference range: 0.9–1.1 [1]

Normal therapeutic range: 2.0–3.0 [2]

High-risk therapeutic range: 2.5–3.5 [2]

The INR is the more common presentation of the PT time. The reason is that small variations in the materials used in the lab can provide substantial differences in the duration of clotting and thus can greatly affect the PT duration. To remove this variation, the lab can run a reference test to act as a baseline time to clot specific to that lab's materials. The ratio of the sample clot time to the reference clot time is reported as the INR. The INR can then be consistently compared from patient to patient regardless of where the INR was performed. If a surgery patient presents with an elevated INR, practitioners will sometimes often request a reduction of the INR by the patient's physician prior to surgery. Note that the risks (such as an embolism) and benefits of lowering the INR have to be taken into consideration prior to altering the patient's regimen. The upper INR limit before surgery is held is typically provider specific, but an INR of 2.8 is a common ballpark figure. Note that the INR can change in as little as 24–48 h, so an INR the day before surgery can sometimes be prudent.

Activated Partial Thromboplastin Time (aPTT)

Common reference range: 24.3–33.1 s [1]

The aPTT is used to measure the intrinsic pathway of the coagulation cascade, as opposed to the PT (which uses the extrinsic pathway). This test is similar to the

PT in that it is timed in seconds. The "activated" portion comes from an activator being added to a regular PTT test to reduce the overall time of the test (roughly takes half as along). Additionally, this test is often paired with the PT in order to assess the full coagulation cascade. Prolonged aPTT can be the result of hemophilia, von Willebrand disease, liver disease, lupus anticoagulant, or even a response to medications. Similar to a prolonged PT and elevated INR, a prolonged aPTT will indicate prolonged bleeding from surgical intervention.

Glucose Assessment: Blood Glucose and Glycosylated Hemoglobin

Blood Glucose (BG)

Common reference range for fasting blood glucose: 70–100 mg/Dl [1]

Blood glucose levels are probably the most common in office lab measured. Blood glucose is most commonly measured with a finger stick test chairside. This is done quickly with a high rate of accuracy and is usually tolerated well by the patient. Additionally, it can often be added onto other blood tests (such as the CBC) after they are drawn to avoid a finger stick.

Both high and low blood sugars are of concern. Elevated blood sugars are associated with chronic issues such as neuropathy, retinopathy, macroangiopathy, etc. One such concern that is very relevant to the surgeon is the immunosuppression and impaired wound healing. Chronically elevated blood sugars impede circulation as well as the immune response. Because of this, diabetics can take longer to heal and recover from surgical insult than those with more normalized blood sugar levels. The more elevated the blood sugar, generally the greater the impairments [3].

Low blood sugars are more of an acute concern. Hypoglycemia starves tissue of essential nutrients and can be fatal. Because of this, hypoglycemia must be treated if it is suspected. Common symptoms of hypoglycemia include tachycardia, pallor, shakiness, confusion, blurred vision, etc. [3].

Many diabetic patients know what it feels like to be hypoglycemic. It is always prudent to ask the patient if they know how their body reacts to being hypoglycemic and to let the provider know if they feel they are becoming hypoglycemic. Note that a patient can still be hypoglycemic even if they show no symptoms.

The use of 10–15 mg of carbohydrates is a good starting point for glucose levels below 70 [3]. Orange juice or soda is a good source of these sugars. If an IV has already been placed, the provider can consider crystalloid solution with 5% dextrose as well. 10–25 g of IV dextrose is usually a good dose (20–50 mL of 50% dextrose solution or 200–500 mL of a 5% solution) [4].

Glycosylated Hemoglobin (A1c)

Common reference range chart (Fig. 3.5) [5]:

Glycosylated hemoglobin also known as hemoglobin A1C, HbA1c, or just A1c help give an estimate of the average blood glucose level over the last 60–90 days.

HbA1c	Associated Blood Glucose
5%	97 mg/dL
6%	126 mg/dL
7%	154 mg/dL
8%	183 mg/dL
9%	212 mg/dL
10%	240 mg/dL
11%	269 mg/dL
12%	298 mg/dL
13%	326 mg/dL
14%	355 mg/dL

Fig. 3.5 This chart shows the hemoglobin A1c with its associated blood glucose levels. Note that these are the average blood glucose level over the past 60–90 days

The basic premise is that glucose will bind to the hemoglobin in the blood at different rates based on its concentration. Since the average life span of the red blood cell is about 90–120 days, the A1c can give an estimate of the average blood glucose over about 60–90 days [3].

Note that the blood glucose variability is not covered by the A1c, only the average value. This means that someone with relatively consistent blood glucose and someone with highly variable blood glucose can average the same A1c number despite these differences.

Assessment of Pathology: Culture and Sensitivity, Biopsy with Permanent Stain, and Immunofluorescence

Culture and Sensitivity

Cultures can be separated from most laboratory tests because most tests look at molecular values whereas cultures are attempting to harvest living organisms. Many lab tests can be completed in a matter of minutes or hours, but this is not the case for cultures. Cultures are analogous to a farmer growing livestock. Because of this, cultures tend to take more time to produce results that that of most other lab tests. These results are on the order of days to weeks.

Another important aspect is that some bacteria require very specific environments to grow. Unfortunately, the environment of the culture is often quite different than the environment of the sample, so not all bacteria/fungi are able to be cultured.

The second part is the sensitivity portion of the test. Sensitivity is based on the culture specimen. If the organism is able to be cultured the lab can then test to see which antibiotics the organism is susceptible to. This is most useful when the offending organism has developed resistance to certain medications. This can allow for better understanding of the treatment options available to the practitioner.

Note that the culture process usually can take several days, so empiric treatment should be started before the results of the study comes back.

Not all infections necessitate a culture and sensitivity. Many localized infections can be treated with minor interventions. However, larger and more aggressive infections should cause the practitioner to think about the utility of a culture and sensitivity.

If a culture and sensitivity are to be obtained, it is recommended to have the patient swish with chlorhexidine mouthwash for 30 s prior to obtaining an oral sample. Additionally, it is best to limit contamination and all attempts at obtaining purulent discharge only should be made.

Biopsy with Permanent Stain

Biopsies are another very common procedure in the office. This is covered in greater depth in sect. History and Physical, Chap. 8. Biopsies are sent when clinical history and physical exam are not sufficient to provide a diagnosis. When the biopsy is sent, it should be sent with a clinical history, either radiographs or radiographic read of the lesion, and a differential diagnosis. This will help the pathologist interpret the histopathology.

The foundation of histopathology is the permanent stain. The most common stains are hematoxylin and eosin (H&E). There are many other stains available and most of them are lesion or cell specific.

Note that frozen sections can also be sent but are not as common in the office-based setting. The general reason for this is that frozen sections are mainly used to assess surgical margins. It can often take some duration of time for the results of the frozen section to return with results, and in that time the surgeon can continue to operate or wait for the results. Most surgeries of this nature are often done in the operating room, though not always.

Immunofluorescence

Many pathologies of the oral and maxillofacial region are immune modulated. Immunohistochemistry has largely been based on the application of antibodies with florescent markers on them that can bind to certain tissues. Very similar to permanent stain, this allows the practitioner to know where the lesion in question is having an immune-mediated reaction within the tissue layers. This location is diagnostically important.

The most common form of immunohistochemistry is the immunofluorescence stain. These stains should not be employed alone, but in conjunction with standard H&E preparations.

The most common pathologies on the differential that would warrant immunofluorescence staining would be the immune-mediated diseases (such as pemphigus vulgaris or pemphigoid).

Two main methods exist, direct and indirect immunofluorescence. The direct method uses antibodies labeled with fluorescein that came from another source (usually rabbits) that directly bind to the tissue in question. The indirect method uses the patient's serum antibodies and binds them to a test tissue with known substrates. These bound antibodies are then washed with fluorescein-labeled antihuman immunoglobulins. The direct method is more sensitive and more diagnostic [6].

Gender Specific Assessment: Urine Pregnancy

Urine Pregnancy (u preg)

One group of patients that is distinct from all others is pregnant women. Medications and treatments can have different effects on them when compared to nonpregnant patients. Pharmacodynamics and pharmacokinetics are different as well due to altered volumes of distribution, blood enzymes, etc. Additionally, physical manipulation is different because of the mass effect of the fetus in the abdomen.

Due to delicate state of the fetus, they are prone to injury from medications. For this reason, most medications have distinct classifications based on their safety to the fetus.

Many women will not show their pregnancy on clinical exam. Additionally, some women would not know they are pregnant until a few weeks into their pregnancy. This means that many women who do not appear to be pregnant could be.

For all of these reasons, the urine pregnancy test should be performed before any invasive procedure or administration of medications on all women of childbearing age.

If this is not feasible, any women of childbearing age should sign a waiver indicating there is no possibility of being pregnant. The risks of the procedure while being pregnant should also be reviewed with the patient.

The urine pregnancy tests look for human chorionic gonadotropin (hCG) in the maternal urine. HCG can be detected as early as 6 days after ovulation following implantation on some ultrasensitive tests. Most urine pregnancy tests are very accurate depending on the timing of the test [7].

Any woman with a positive pregnancy test should be worked up and treated as though she is pregnant.

References

1. Clinical Laboratory Reference Ranges. http://laboratory.uchealth.com/tests/reference-ranges-pdf/. 2015. Accessed 1 Sept 2018.
2. Padilla O. Normal Laboratory Values. Merck Manual. 2018. https://www.merckmanuals.com/professional/appendixes/normal-laboratory-values/blood-tests-normal-values#v8508814. Accessed 1 Sept 2018.
3. Abubaker AO, Lam D, Benson KJ. Oral and maxillofacial secrets. 3rd ed. Amsterdam: Elsevier; 2016.
4. Medscape dextrose (Rx). Medscape, LLC, New York. 2018. https://reference.medscape.com/drug/d50w-dglucose-dextrose-342705. Accessed 1 Sept 2018.
5. Nathan D, et al. Translating the A1C assay into estimated average glucose values. Diabetes Care. 2008; 31:1473–1478. http://care.diabetesjournals.org/content/31/8/1473. Accessed 1 Sept 2018.
6. Marx RE, Stern D. Oral and maxillofacial pathology: a rationale for diagnosis and treatment. 2nd ed. Berlin: Quintessence Pub; 2012.
7. Cole L, Ladner D, Byrn F. The normal variabilities of the menstrual cycle. Fertil Steril. 2009;91:522–7.