OPEN ACCESS
Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Review Article **Pharmacy**

Medication-Related Interferences in Laboratory Testing: A Practical Guide for Nursing Technicians, Clinical Pharmacists, and Laboratory Specialists

Nawal Mohammad Theab[1*], Reem Bandar Alhajri[2], Sahar Fahad Alotaibi[2], Mashael Fawaz Almishrafi[3], Suliman Saleh Alomayri[3], Ali Barjas Alsahli[3], Albandari Khammas Alenazi[3], Sarah Saad Alosail[3], Fatima Matlaq D Alotaibi[3]

[1]Nursing Technician, Prince Sultan Military Medical City, Riyadh
[2]Clinical Pharmacist, Prince Sultan Military Medical City, Riyadh
[3]Laboratory Specialist, Prince Sultan Military Medical City, Riyadh

DOI: https://doi.org/10.36348/sjmps.2025.v11i07.018 | **Received:** 05.06.2025 | **Accepted:** 19.07.2025 | **Published:** 19.07.2025

***Corresponding author:** Nawal Mohammad Theab
Nursing Technician, Prince Sultan Military Medical City, Riyadh

Abstract

Laboratory diagnostics are indispensable to modern healthcare, yet the integrity of test results can be compromised by medication-related interference (MRI), a significant and underappreciated threat to patient safety. Erroneous laboratory data stemming from MRI can precipitate a cascade of clinical errors, including misdiagnosis, delayed or inappropriate treatment, and unnecessary additional testing. This review offers a practical, evidence-based guide for the key professionals' integral to the laboratory testing process: nursing technicians, clinical pharmacists, and laboratory specialists. We systematically explore the foundational mechanisms of interference, classifying them into physiological (in vivo) effects, where a drug's pharmacodynamic or toxic action genuinely alters analyte levels, and analytical (in vitro) effects, where a drug or its metabolite directly disrupts the assay methodology. The review examines the vulnerabilities of common analytical platforms—spectrophotometry, immunoassays, enzymatic methods, and chromatography—to such interferences. A substantial compendium details clinically significant MRIs caused by major drug classes, with a particular focus on the profound and dangerous impact of high-dose biotin supplementation on immunoassays. The central aim of this guide is to delineate the distinct yet synergistic roles of the multidisciplinary team. It highlights the nursing technician's pivotal role in the pre-analytical phase, the clinical pharmacist's expertise in proactive drug identification and management, and the laboratory specialist's critical function in result validation and interference investigation. By elucidating the complexities of MRI and championing a framework for robust interprofessional collaboration, this guide seeks to arm healthcare teams with the knowledge and strategies required to protect the integrity of laboratory data, thereby enhancing clinical decision-making and safeguarding patient safety.

Keywords: Medication-related interference (MRI), Laboratory diagnostics, Clinical pharmacology, Spectrophotometry.

1. INTRODUCTION

1.1. The Critical Role of Laboratory Testing in Modern Healthcare

The practice of modern medicine is inextricably linked to the data generated by the clinical laboratory. These objective measurements provide a crucial window into a patient's physiological state, underpinning countless clinical decisions across all medical specialties. It is widely cited that clinical laboratory results influence approximately 70% of medical diagnoses and treatment plans, making them one of the most significant drivers in healthcare decision-making [1]. From managing chronic conditions like diabetes with hemoglobin A1c monitoring to diagnosing acute events like myocardial infarction with high-sensitivity cardiac troponin assays, the reliance of clinicians on accurate and timely laboratory data is absolute [2].

The Scope of Laboratory Medicine is Vast, Encompassing:

- Screening for disease in asymptomatic individuals (e.g., lipid panels for dyslipidemia).

- Diagnosing suspected conditions (e.g., confirming infection with microbiological cultures).
- Monitoring the efficacy and toxicity of therapeutic interventions (e.g., measuring international normalized ratio (INR) for warfarin therapy).
- Assessing prognosis to predict the likely course of a disease (e.g., using B-type natriuretic peptide (BNP) in heart failure).

The entire structure of evidence-based medicine rests on the premise that these quantitative results are a faithful representation of the patient's internal milieu. Any systemic or random error that undermines the accuracy of these results has the potential to cause significant patient harm.

1.2. The Pervasive Challenge of Medication-Related Interference (MRI)

Despite the highly controlled environment of the modern clinical laboratory, a formidable variable exists: the ever-expanding pharmacopeia of medications, supplements, and biologics consumed by patients. Medication-Related Interference (MRI) is defined as the clinically significant alteration of a laboratory test result caused by the presence of a drug, its metabolites, or its excipients [3]. This interference can manifest as either a positive or negative bias, leading to a result that is falsely elevated or falsely decreased.

MRI is not a fringe issue; it is a pervasive and dynamic problem. The sheer number of prescription drugs, over-the-counter (OTC) products, and herbal supplements creates a nearly infinite matrix of potential interactions with the hundreds of available laboratory tests [4]. The clinical consequences of acting on these erroneous results are profound. For example, a falsely elevated creatinine level caused by the antibiotic cefoxitin could lead to an incorrect diagnosis of acute kidney injury and the inappropriate discontinuation of a necessary medication [5]. Conversely, a falsely normal troponin level in a patient taking high-dose biotin supplements could lead to the premature discharge of a patient experiencing a myocardial infarction [6]. These are not mere analytical curiosities; they are documented threats to patient safety that demand vigilance from all members of the healthcare team.

1.3. Objectives and Scope of the Review

Addressing the complex challenge of MRI requires a coordinated, interprofessional effort. The nursing technician preparing the patient and collecting the sample, the clinical pharmacist reviewing the medication regimen, and the laboratory specialist analyzing the sample and validating the result each possess unique knowledge and opportunities to prevent an error. A breakdown in communication or awareness at any point in this chain can lead to a negative patient outcome.

The primary objective of this review is to serve as a practical, evidence-based guide for this multidisciplinary team. We aim to:

1. Provide a clear understanding of the laboratory testing cycle and the fundamental mechanisms through which medications interfere with common analytical methods.
2. Compile a detailed compendium of common and clinically critical MRIs, supported by scientific literature, with a focus on high-risk drug classes and supplements.
3. Define the specific roles and responsibilities of nursing technicians, clinical pharmacists, and laboratory specialists in identifying, mitigating, and resolving MRIs.
4. Present a framework for building a collaborative culture that prioritizes communication and system-based solutions to protect patients from the consequences of faulty laboratory data.

This review synthesizes information from textbooks, review articles, case reports, and professional guidelines to bridge the knowledge gaps between the patient's bedside, the pharmacy, and the laboratory bench.

2. Fundamentals of Laboratory Analysis and the Testing Cycle

A comprehensive understanding of how a lab test is processed, from order to result, is essential to pinpointing the stages at which MRIs can occur. Likewise, knowledge of the basic principles of analytical methods reveals their specific vulnerabilities.

2.1. The Three Phases of Laboratory Testing: Pre-analytical, Analytical, and Post-analytical

The total testing process is a complex workflow that is conventionally divided into three phases. While errors can happen at any stage, a large body of evidence indicates that the pre-analytical phase is the most error-prone, accounting for 60-70% of all laboratory errors [7,8].

- **The Pre-analytical Phase:** This phase includes all processes from the clinician's test order to the point the sample is ready for analysis. It involves test selection, patient identification and preparation, sample collection (phlebotomy), sample handling and transport, and specimen processing (e.g., centrifugation).
- **Relevance to MRI:** This phase is the first and best opportunity to prevent an MRI. Key pre-analytical actions include properly timing the blood draw relative to a drug dose (e.g., collecting a trough level for therapeutic drug monitoring) and, most critically, documenting the patient's complete medication and supplement list on the requisition or in the electronic order. The failure to ask a patient about supplements like biotin is a common pre-

analytical error with potentially devastating consequences [9].

- **The Analytical Phase:** This is the core testing phase where the patient's specimen is analyzed by an instrument to produce a quantitative or qualitative result. It includes instrument calibration, quality control, and the physical analysis of the sample.
- **Relevance to MRI:** This is the stage where *in vitro* interferences exert their effect. A drug or metabolite present in the serum or plasma directly interacts with the assay reagents or detection system. The susceptibility to this type of interference is entirely dependent on the specific analytical method being used [3].
- **The Post-analytical Phase:** This phase encompasses all activities following the generation of the result. It includes technical review and validation of results by laboratory staff, release of results into the information system, interpretation of results by the clinician, and any subsequent actions taken.
- **Relevance to MRI:** This is the final safety net. A laboratory specialist may recognize a physiologically impossible result or a significant change from a previous value (a "delta check" failure) and withhold the result pending investigation [10]. An astute clinician or pharmacist may see a result that is discordant with the patient's clinical presentation and suspect an interference. Communicating these suspicions is a key post-analytical activity.

2.2. Overview of Common Analytical Methodologies

The mechanism of an analytical interference can only be understood in the context of the technology being used.

2.2.1. Spectrophotometry and Colorimetric Assays

This technique measures the concentration of a substance (analyte) by quantifying the amount of light it absorbs at a specific wavelength. It is based on the Beer-Lambert Law ($A=\epsilon bc$), where absorbance (A) is directly proportional to concentration (c). In most clinical chemistry assays (e.g., for creatinine, glucose, bilirubin), the analyte is reacted with reagents to form a colored product, and the intensity of this color is measured.

- **Vulnerability to MRI:** These methods are susceptible to spectral (color) and turbidity interferences. Any substance in the sample that is itself colored and absorbs light at the analytical wavelength will cause a positive interference (a falsely high result). Drugs like rifampin (red-orange) are classic examples [11]. Furthermore, substances that make the sample turbid or cloudy, such as intravenous lipid emulsions or high concentrations of some antibiotics, cause light scattering that the instrument incorrectly reads as absorbance, also leading to false elevations [12].

2.2.2. Immunoassays (e.g., ELISA, CMIA, ECLIA)

Immunoassays are highly sensitive methods that utilize the specific binding between an antibody and its antigen to measure a wide range of analytes, including hormones, cardiac markers, and tumor markers. They generally fall into two categories:

- **Competitive Assays:** The analyte in the patient's sample competes with a labeled analyte (tracer) for a limited number of antibody binding sites. High patient analyte levels result in low signal from the tracer. Signal is *inversely* proportional to analyte concentration.
- **Non-competitive ("Sandwich") Assays:** The analyte is bound between two antibodies—a capture antibody on a solid surface and a detection antibody carrying a label. Signal is *directly* proportional to the analyte concentration.
- **Vulnerability to MRI:** Immunoassays are prone to several well-documented interferences:
    - **Cross-reactivity:** A drug or metabolite is structurally similar to the target analyte and binds to the assay antibodies, typically causing a falsely high result. This is a common problem with urine drug screens [13].
    - **Heterophile Antibodies:** These are human antibodies (e.g., Human Anti-Mouse Antibodies or HAMA) that can bind to the animal-derived antibodies used in the assay, typically bridging the capture and detection antibodies in a sandwich assay to create a false-positive signal [14].
    - **Biotin (Vitamin B7) Interference:** A profoundly important modern interference. Many immunoassays use a streptavidin-biotin bond as part of the assay architecture. High concentrations of biotin from patient supplements saturate this system, preventing signal generation in sandwich assays (causing falsely low results) and disrupting the competitive mechanism in competitive assays (causing falsely high results) [9, 15].

2.2.3. Enzymatic Assays

These methods use one or more enzymes as reagents to catalyze a specific reaction involving the target analyte. The concentration of the analyte is determined by measuring the rate of the reaction or the amount of a product that is formed. The common hexokinase method for glucose is a classic example.

- **Vulnerability to MRI:** A drug or endogenous substance can act as an inhibitor or, less commonly, an activator of a reagent enzyme. A potent and clinically significant interferent is ascorbic acid (Vitamin C), a strong reducing agent. It can interfere with assays that use a peroxidase-linked final reaction (common in point-of-care devices) by chemically reducing the colored product, leading to falsely low or negative results [16].

2.2.4. Potentiometry and Ion-Selective Electrodes (ISE)

ISEs are electrochemical sensors used to measure the activity (which correlates with concentration) of specific ions like sodium (Na+), potassium (K+), and chloride (Cl−) in blood. Each electrode has a membrane that is selectively permeable to a single ion. The potential difference that develops across this membrane is logarithmically proportional to the ion's activity, as described by the Nernst equation.

- **Vulnerability to MRI:** The selectivity of the membranes is not perfect. An ion with a similar charge and hydrated radius to the target ion can cross the membrane and interfere. The classic example is the bromide ion, found in certain medications, interfering with the chloride ISE to cause a pseudo-hyperchloremia (falsely high chloride) [17].

2.2.5. Chromatographic Methods (e.g., HPLC, LC-MS/MS)

Chromatography separates complex mixtures into their individual components. In High-Performance Liquid Chromatography (HPLC), the sample is passed through a column, and compounds separate based on their physical and chemical interactions with the column material. Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) pairs this separation with a highly specific detector (a mass spectrometer) that identifies compounds based on their unique mass-to-charge ratio.

- **Vulnerability to MRI:** In HPLC with a simple UV detector, interference occurs if a drug co-elutes (exits the column at the same time) as the analyte. However, LC-MS/MS is considered a "gold standard" reference method for many tests because it is highly resistant to interference. It is extremely unlikely that an interfering substance will have both the same chromatographic retention time *and* the same mass-to-charge ratio as the target analyte. Therefore, LC-MS/MS is often used to resolve suspected interferences observed with other methods [18].

3. Mechanisms of Medication-Related Interference

The ways in which a medication can alter a laboratory result are diverse. A crucial first step in both investigation and mitigation is to classify the interference based on its fundamental mechanism. Interferences are broadly divided into two categories: physiological effects occurring within the patient's body (*in vivo*) and analytical effects occurring within the testing platform itself (*in vitro*) [3]. This distinction is clinically vital because a physiological interference represents a true (though drug-induced) change in the patient's state that may require management, whereas an analytical interference represents an erroneous measurement that must be corrected to reveal the true state.

3.1. Physiological (In Vivo) Interferences

In this category, the laboratory test result is analytically correct; it accurately measures the concentration of the analyte in the specimen. The "interference" is a result of the drug having a genuine biological effect that alters this concentration. The challenge lies in interpreting the result correctly—attributing the change to the drug's effect rather than to an underlying change in the disease state.

3.1.1. Pharmacodynamic Effects

This common type of interference arises from the drug's intended therapeutic action or a known side effect on the body's systems. The drug interacts with its target receptors or enzymes, leading to a predictable downstream alteration in the concentration of a measured analyte.

- **Example: Diuretics and Electrolytes.** Loop and thiazide diuretics are prescribed to increase salt and water excretion by the kidneys. Their pharmacodynamic action on various tubular transporters directly leads to increased renal loss of potassium, resulting in true hypokalemia. They also reduce the renal clearance of uric acid, leading to true hyperuricemia [19]. These are expected physiological consequences that are accurately reported by the laboratory and must be monitored and managed clinically.
- **Example: Antipsychotics and Prolactin.** Many antipsychotic medications (e.g., risperidone, haloperidol) exert their therapeutic effect by blocking dopamine D2 receptors. As dopamine tonically inhibits prolactin secretion from the pituitary gland, this blockade predictably leads to a significant and sustained elevation in serum prolactin levels (hyperprolactinemia) [20]. A clinician unaware of this effect could mistakenly attribute the high prolactin to a pituitary tumor, triggering an unnecessary and costly workup.

3.1.2. Pharmacokinetic Effects & Organ Toxicity

This type of physiological interference is often an unintended consequence of the drug's effect on an organ system, influencing the analyte's production, metabolism, or clearance. Direct drug-induced organ toxicity is a major subcategory.

- **Example: Drug-Induced Organ Toxicity.** Many drugs are potentially toxic to the liver or kidneys. Acetaminophen overdose is a classic example of a drug causing severe, direct hepatocellular injury. This damage leads to the release of intracellular enzymes like alanine aminotransferase (ALT) and aspartate aminotransferase (AST) into the circulation, resulting in markedly elevated levels that accurately reflect the extent of liver damage [21]. Similarly, certain antibiotics like aminoglycosides can be nephrotoxic, impairing the kidney's filtration capacity and causing a true rise in serum creatinine and blood urea nitrogen (BUN) that signals declining renal function [22].

- **Example: Altered Analyte Metabolism.** The herbal supplement St. John's Wort is a potent inducer of the cytochrome P450 3A4 (CYP3A4) enzyme system in the liver. This effect accelerates the metabolism of many other drugs that are substrates for this enzyme, such as the immunosuppressant cyclosporine. For a patient on a stable dose of cyclosporine, starting St. John's Wort can lead to a rapid decrease in the measured blood level of cyclosporine, potentially causing sub-therapeutic levels and organ rejection in a transplant patient [23]. This is a critical drug-herb interaction with direct laboratory correlates.

3.2. Analytical (In Vitro) Interferences

Analytical interferences occur when a substance in the patient's sample—the drug itself, its metabolite, or an associated compound—directly interferes with the chemical reactions or detection system of the assay. The resulting lab value is an analytical artifact and does not represent the patient's true physiological state. These interferences are highly method-dependent.

3.2.1. Spectrophotometric and Turbidimetric Interference

These interferences plague methods that rely on measuring light absorbance, as detailed in Section 2.2.1.

- **Spectral (Color) Interference:** A drug or metabolite possesses an intrinsic color that absorbs light at or near the analytical wavelength of the assay, adding to the signal and causing a falsely high result. For instance, the metabolites of the antihypertensive drug labetalol have been shown to interfere with spectrophotometric assays for plasma metanephrines, potentially leading to a false-positive diagnosis of pheochromocytoma [24].
- **Turbidity Interference:** The sample's clarity is compromised, causing light to scatter, which the spectrophotometer misinterprets as absorbance. Intravenous lipid emulsions are a well-known cause of this interference, which can falsely elevate results for a wide array of chemistry analytes. This effect, known as lipemia, is a significant challenge for samples from patients on parenteral nutrition [12].

3.2.2. Immunoassay Interference

Given their ubiquity, immunoassays are a major target for MRIs.

- **Structural Cross-Reactivity:** The assay antibody mistakenly binds to a drug or metabolite that is structurally similar to the intended analyte. This is a notorious problem for screening immunoassays for drugs of abuse, where numerous medications can cause false-positive results that require confirmation by a more specific method like LC-MS/MS. For example, the antidepressant sertraline has been documented to cross-react with benzodiazepine immunoassays [13]. A non-drug example is the metabolite of fenofibrate, fenofibric acid, which can cross-react with some enzymatic creatinine methods, falsely elevating the result and mimicking acute kidney injury [25].
- **Biotin (Vitamin B7) Interference:** This is one of the most significant MRI challenges in modern medicine. The U.S. Food and Drug Administration (FDA) has issued multiple safety communications warning of this interference [6, 26]. As described in Section 2.2.2, excess biotin from high-dose supplements saturates the streptavidin-biotin binding system used in many immunoassays.
  - In non-competitive (sandwich) assays (e.g., for troponin, TSH, PTH, hCG), this saturation blocks the formation of the signal-generating complex, leading to falsely low results.
  - In competitive assays (e.g., for T4, cortisol, testosterone), this disruption of the assay principle leads to falsely high results.

The clinical danger is immense, with documented cases of missed myocardial infarctions and misdiagnosis of Graves' disease due to this specific interference [9, 27].

- **Antibody-Related Interference:** The patient's own antibodies can interfere with the assay's reagent antibodies. The classic example is heterophile antibodies, which are low-affinity, polyspecific human antibodies that can cross-link the capture and detection antibodies (often of murine origin) in a sandwich assay, creating a signal in the absence of analyte and causing a false positive [14].

3.2.3. Enzymatic Assay Interference

Drugs or metabolites can interfere with enzymatic assays by acting as inhibitors or substrates for one of the reagent enzymes. The most well-known example is ascorbic acid (Vitamin C). As a strong reducing agent, it can directly react with and eliminate hydrogen peroxide, a key reagent in assays that use a final peroxidase reaction step. This leads to a falsely low signal. This interference is particularly problematic for point-of-care glucose meters that use glucose oxidase technology, where high levels of vitamin C can mask true hyperglycemia [16, 28].

3.2.4. Electrode and Sensor Interference

Ion-Selective Electrodes (ISEs) are not perfectly selective. The interference of bromide with the chloride ISE is the canonical example. Due to its similar ionic radius and charge, bromide can be detected by the chloride electrode, leading to a falsely elevated chloride measurement and subsequent miscalculation of the anion gap, which can confuse the diagnosis of metabolic acidosis [17].

3.2.5. Chromatographic Interference

While HPLC is a powerful separation tool, interference can still occur if an interfering compound co-elutes with the analyte of interest and is detected by a non-specific detector (like a UV detector). However, the addition of tandem mass spectrometry (LC-MS/MS) largely overcomes this limitation. By providing a second dimension of identification based on molecular mass and fragmentation patterns, LC-MS/MS can distinguish the analyte from co-eluting interferents, making it the definitive method for resolving most analytical interferences [18, 29].

4. A Compendium of Common Interferences by Drug Class and Laboratory Test

This section provides an evidence-based summary of clinically important MRIs. The mechanism is classified as Physiological [P] or Analytical [A]. This list is not exhaustive but focuses on high-frequency and high-risk interactions.

4.1. Cardiovascular Drugs

This group includes some of the most widely prescribed medications globally, and their impact on routine laboratory monitoring is profound.

Drug Class	Common Examples	Tests Affected	Mechanism & Clinical Implication
Thiazide & Loop Diuretics	Hydrochlorothiazide, Furosemide, Bumetanide	Electrolytes (Na+, K+, Mg2+), Uric Acid, Calcium (Ca2+)	[P] Causes true hypokalemia, hyponatremia, and hypomagnesemia via increased renal excretion. Decreases uric acid excretion, causing hyperuricemia. Thiazides specifically decrease calcium excretion, potentially causing hypercalcemia. These are expected pharmacodynamic effects requiring clinical monitoring [19, 30].
ACE Inhibitors & ARBs	Lisinopril, Ramipril, Losartan, Valsartan	Potassium (K+), Creatinine	[P] A primary and important effect is the inhibition of aldosterone secretion, which reduces potassium excretion and can lead to life-threatening hyperkalemia, especially in patients with chronic kidney disease or those on potassium supplements. Can also cause a small, hemodynamically-mediated increase in serum creatinine upon initiation, which is usually acceptable, but a large rise may indicate renal compromise [31].
Beta-Blockers	Metoprolol, Carvedilol, Propranolol	Glucose, Lipids	[P] Non-selective beta-blockers can inhibit glycogenolysis and mask the adrenergic symptoms of hypoglycemia (e.g., tachycardia, tremors), a critical concern in diabetic patients. They can also have a modest effect on lipid profiles, sometimes increasing triglycerides and decreasing HDL cholesterol [32].
Statins	Atorvastatin, Simvastatin, Rosuvastatin	Liver Function Tests (ALT, AST), Creatine Kinase (CK)	[P] Can cause a mild, asymptomatic elevation in ALT/AST in a small percentage of users; significant hepatotoxicity is rare. The most concerning side effect is statin-associated muscle symptoms (SAMS), ranging from myalgia to rhabdomyolysis, which is accompanied by a large increase in serum CK, indicating muscle damage [33].
Fenofibrate	Fenofibrate	Creatinine	[A] & [P]. The active metabolite, fenofibric acid, is known to cause a reversible increase in serum creatinine of about 10-20%. This is thought to be partly a physiological effect on creatinine generation in muscle [P] and partly an analytical interference with certain enzymatic creatinine assays [A] [25, 34]. This can be easily mistaken for true worsening of renal function.

4.2. Antimicrobial Agents

Antimicrobials are administered frequently in both inpatient and outpatient settings. This class of drugs is responsible for a wide range of interferences, stemming from both direct organ toxicity and analytical cross-reactivity

Drug/Class	Common Examples	Tests Affected	Mechanism & Clinical Implication
Penicillins & Cephalosporins	Piperacillin-tazobactam, Cefoxitin, Ceftriaxone	Creatinine (Jaffe reaction)	[A] Several cephalosporins (most notably cefoxitin) and, to a lesser extent, some penicillins act as non-creatinine chromogens in the alkaline picrate (Jaffe) reaction. This non-specific colorimetric reaction leads to a falsely elevated creatinine measurement, which can be mistaken for acute kidney injury [5, 35]. The interference is method-dependent and is not observed with more specific enzymatic or LC-MS/MS creatinine assays.
Metronidazole	Metronidazole	ALT, AST, Hexokinase Glucose	[A] Metronidazole has a high absorbance peak near 340 nm. This is the same wavelength used to measure the change in NADH concentration in many common enzymatic assays (e.g., for ALT, AST, CK). This spectral overlap leads to a falsely low result by interfering with the optical measurement, potentially masking true liver injury or hypoglycemia [36].
Sulfonamides	Sulfamethoxazole (component of TMP-SMX)	Creatinine, Potassium	[P] Sulfamethoxazole can cause true kidney injury through mechanisms like crystal nephropathy or acute interstitial nephritis, leading to a rise in creatinine. Additionally, the trimethoprim component of TMP-SMX acts like the potassium-sparing diuretic amiloride, blocking the epithelial sodium channel (ENaC) in the distal nephron, which can lead to potentially life-threatening hyperkalemia [37].
Daptomycin	Daptomycin	Prothrombin Time (PT) / INR	[A] Daptomycin can bind to the phospholipid reagents used in some PT/INR assays, artificially prolonging the clotting time. This leads to a falsely elevated INR. This interference is concentration-dependent and most pronounced at peak drug levels. To avoid this, blood for INR testing should be drawn at trough, just before the next dose [38].
Rifampin	Rifampin	Bilirubin, Liver Function Tests (LFTs)	[A] & [P]. [P] Rifampin can cause dose-dependent cholestatic or hepatocellular liver injury, leading to true elevations in LFTs and bilirubin. [A] Its distinct red-orange color causes significant spectral interference in many spectrophotometric assays, including those for bilirubin and creatinine, leading to falsely elevated results that can complicate the clinical picture [11].

4.3. Central Nervous System (CNS) Medications

This diverse group of drugs is notorious for causing interferences, particularly analytical cross-reactivity with the screening immunoassays used for toxicology and endocrinology.

Drug/Class	Common Examples	Tests Affected	Mechanism & Clinical Implication
Antipsychotics	Risperidone, Quetiapine, Olanzapine, Haloperidol	Prolactin, Urine Drug Screens (UDS)	[P] Most antipsychotics are dopamine D2 receptor antagonists, which leads to a significant and expected physiological increase in serum prolactin [20]. [A] Many antipsychotics and their metabolites cross-react with UDS immunoassays. Quetiapine, for example, is well-documented to cause false positives for tricyclic antidepressants (TCAs) [39]. Confirmatory testing by a specific method like LC-MS/MS is mandatory for any unexpected positive UDS result.

Antidepressants	Sertraline, Venlafaxine, Bupropion	Urine Drug Screens (UDS)	[A] This class is a major source of false-positive UDS results. Sertraline is a classic interferent causing false positives for benzodiazepines. Bupropion's metabolites are structurally similar to amphetamine and can cause false positives for amphetamines. Venlafaxine can cross-react with phencyclidine (PCP) immunoassays. These false positives can have serious medico-legal implications if not properly confirmed [13, 40].
Antiepileptics	Carbamazepine, Phenytoin, Phenobarbital	Thyroid Function Tests, Vitamin D	[P] These older antiepileptic drugs are potent inducers of hepatic enzymes (CYP450 system), which increases the metabolism and clearance of thyroid hormones (T4 and T3). This can lead to low T4 levels with a normal or slightly elevated TSH, a pattern that can be mistaken for hypothyroidism. They also accelerate the catabolism of vitamin D, leading to lower 25-hydroxyvitamin D levels and an increased risk of bone disease with long-term use [41].

4.4. Analgesics and Anti-inflammatory Agents

This ubiquitous class of drugs, including many available OTC, has well-defined physiological effects and some important analytical interferences.

Drug/Class	**Common Examples**	**Tests Affected**	**Mechanism & Clinical Implication**
Acetaminophen (Paracetamol)	Acetaminophen (Tylenol)	Liver Function Tests (LFTs), Glucose (CGM)	[P] Overdose causes severe dose-dependent hepatotoxicity, leading to dramatic elevations in ALT and AST, which serve as primary markers of the injury [21]. [A] Acetaminophen and its metabolites can be oxidized at the electrode surface of some Continuous Glucose Monitors (CGMs), generating a current that the device misinterprets as glucose, leading to falsely high glucose readings and a risk of insulin overdose [42]. Newer generation CGM sensors have improved selectivity to minimize this interference.
NSAIDs	Ibuprofen, Naproxen, Ketorolac	Renal Function, Fecal Occult Blood Test (FOBT)	[P] NSAIDs can cause acute kidney injury, particularly in at-risk individuals (e.g., those with dehydration or pre-existing CKD), by inhibiting renal prostaglandin synthesis. This leads to a true increase in BUN and creatinine. They are also a leading cause of peptic ulceration and gastritis, which can cause gastrointestinal bleeding. This results in a true positive on FOBT, which can be an important sign of drug toxicity [43].
Salicylates	Aspirin	Uric Acid, Blood Gases	[P] At high anti-inflammatory doses, salicylates are uricosuric, meaning they increase the renal excretion of uric acid, leading to lowered serum uric acid levels. In toxic overdose, salicylates classically cause a mixed respiratory alkalosis (from direct stimulation of the respiratory center) and a metabolic acidosis (from uncoupling of oxidative phosphorylation), which is directly reflected in arterial blood gas analysis [44].

4.5. Over-the-Counter (OTC) Drugs, Vitamins, and Herbal Supplements

This category is a major blind spot for MRI, as patients often do not consider these products to be "medications" and may not report their use.

The Biotin Case Study: A Comprehensive Review

The interference from high-dose biotin supplementation is one of the most serious and widespread MRI challenges facing modern laboratories. The marketing of mega-doses (typically 5,000-10,000 mcg, or >160 times the adequate intake) has made this a common problem [9].

- **Mechanism Recap:** As described previously, biotin interferes with any immunoassay using streptavidin-biotin signal amplification. In sandwich assays, it produces falsely low results; in competitive assays, it produces falsely high results [15, 27].
- **Affected Tests and Grave Clinical Consequences:**

- **Thyroid Function:** Causes a biochemical pattern that perfectly mimics Graves' disease (a form of hyperthyroidism): TSH (sandwich assay) is falsely low while Free T4 and/or T3 (competitive assays) are falsely high. This has led to misdiagnoses and inappropriate treatment with ablative radioiodine therapy [27].
- **Cardiac Markers:** Falsely low Troponin (a sandwich assay) can lead to a missed diagnosis of acute myocardial infarction [6].
- **Endocrinology:** Can cause falsely low PTH, falsely low ACTH, and falsely high cortisol, confounding the workup of endocrine disorders.
- **Fertility and Pregnancy:** Falsely low hCG (sandwich assay) can lead to a missed or incorrectly managed pregnancy.
- **Mitigation and Recommendations:** Based on FDA warnings and expert guidelines, a clear strategy is needed. The clearance of biotin is variable, but for patients taking high-dose supplements (>5 mg/day), a washout period of at least 48 hours is recommended before sample collection to minimize the risk of clinically significant interference [9, 26]. Clear communication with the patient is essential.

Other OTC/Supplements	Examples	Tests Affected	Mechanism & Clinical Implication
Vitamin C (Ascorbic Acid)	High-dose oral supplements (e.g., 1000 mg)	Glucose (Point-of-Care), Urine Dipstick	[A] High concentrations of this strong reducing agent can cause falsely low readings on glucose meters and urine dipsticks that rely on glucose oxidase/peroxidase chemistry. This can lead to failure to detect and treat significant hyperglycemia [16, 28].
Herbal Supplements (St. John's Wort)	St. John's Wort	Therapeutic Drug Monitoring (TDM)	[P] A potent inducer of the CYP3A4 metabolic enzyme. It significantly accelerates the clearance of many drugs, including cyclosporine, tacrolimus, and warfarin, leading to sub-therapeutic blood levels and a risk of treatment failure (e.g., organ rejection, thrombosis) [23].

4.6. Other Significant Interferences

Class/Agent	Example	Tests Affected	Mechanism & Clinical Implication
Radiographic Contrast Media	Iodinated contrast agents (e.g., iohexol)	Creatinine, Urine analysis	[P] Can cause contrast-induced nephropathy (CIN), a true, typically transient, rise in serum creatinine peaking 2-5 days after exposure, particularly in high-risk patients. [A] High concentrations of contrast can interfere with some older colorimetric assays and will markedly increase urine specific gravity, potentially affecting urine sediment analysis [45].
Chemotherapeutic Agents	Cisplatin, Methotrexate, Doxorubicin	CBC, Renal function, LFTs	[P] The effects of chemotherapy are profound and largely physiological. Cisplatin is famously nephrotoxic. Methotrexate can be hepatotoxic. Virtually all cytotoxic agents cause some degree of myelosuppression, leading to true anemia, leukopenia, and thrombocytopenia, which are closely monitored via the Complete Blood Count (CBC) [46].

5. A Practical Guide for the Multidisciplinary Team

Preventing harm from MRI is an active process that requires the coordinated efforts of professionals across the continuum of care. Each team member has a specific and vital role to play.

5.1. The Role of the Nursing Technician: Frontline Defense in the Pre-analytical Phase

As the individual with direct patient contact during sample collection, the nursing technician or phlebotomist is uniquely positioned to gather critical information that can prevent an MRI. Their diligence in the pre-analytical phase is the first and most important line of defense.

- **Patient Education and Preparation:** Patient communication should include specific, targeted questions about supplements. Instead of asking about "biotin," which a patient may not recognize, a more effective question is: "Are you taking any over-the-counter supplements, for instance, for hair, skin, or nail health?" [9]. This simple question can uncover the cause of a potentially confounding interference.

- **Best Practices for Sample Collection Timing:** For Therapeutic Drug Monitoring (TDM), understanding the concept of trough (lowest level, just before the next dose) versus peak (highest level, shortly after a dose) is crucial. Technicians should, whenever possible, confirm the time of the last dose with the patient or nursing staff to ensure the sample is collected at the appropriate time as specified by the test order [47].
- **Crucial Importance of Accurate Medication Documentation:** This is the single most effective action a technician can take to aid downstream interpretation. Any relevant information gathered from the patient—especially the use of biotin or other high-risk supplements, or the recent administration of a drug like daptomycin before an INR draw—must be documented on the paper requisition or as a comment in the electronic order. This documented information serves as a vital alert for the laboratory and the clinical team [8, 48].

5.2. The Role of the Clinical Pharmacist: The Medication Expert

The clinical pharmacist's deep knowledge of pharmacokinetics, pharmacodynamics, and drug interactions makes them an indispensable hub for MRI management. They serve as a crucial analytical and interpretive resource for both the clinical team and the laboratory.

- **Proactive Identification of High-Risk Drugs During Medication Reconciliation:** Medication reconciliation is a cornerstone of safe pharmacy practice. During this process, pharmacists can proactively screen a patient's entire medication list—including prescriptions, OTC products, and supplements—for drugs known to cause interference. Maintaining and utilizing an institutional "high-risk MRI" list allows for the rapid identification of potential problems before a test is even resulted [49].
- **Advising on Optimal Testing Windows and Temporary Drug Discontinuation:** When a potential MRI is identified, the pharmacist is best equipped to provide guidance. This includes advising on appropriate "washout" periods, such as the 48–72-hour hold recommended for high-dose biotin before immunoassay testing [9]. For drugs that cannot be stopped, they can advise on the optimal timing for sample collection (e.g., drawing at trough for daptomycin to avoid INR interference) to minimize the impact of the drug [38].
- **Interpreting Results in the Context of a Patient's Medication Profile:** When an unexpected laboratory result is reported, the clinical pharmacist should be a primary consultant. They can rapidly cross-reference the anomalous result with the patient's full medication profile to generate a list of likely drug-related causes, providing a crucial differential diagnosis for the clinical team. This role is central to preventing misinterpretation of drug-induced physiological changes (e.g., ACE inhibitor-induced hyperkalemia) and analytical interferences [31].
- **Serving as a Liaison between the Clinical Team and the Laboratory:** The pharmacist often speaks the language of both the clinician and the laboratorian. They can translate a clinical question into a specific analytical concern for the laboratory (e.g., "The patient is on quetiapine; could this be causing the positive TCA screen?"). Conversely, they can translate a laboratory's technical comment into a clear clinical action item for the physician [48].

5.3. The Role of the Laboratory Specialist: The Guardian of Data Integrity

The laboratory specialist (clinical laboratory scientist/technologist) is the final gatekeeper responsible for ensuring the analytical validity of a result before it is released into the patient's chart. They use a combination of automated systems, technical expertise, and pattern recognition to detect and investigate potential errors.

- **Recognizing Suspicious Results:** Laboratory professionals are trained to identify results that are analytically or physiologically improbable. Key tools include:
- **Delta Checks:** This is an automated LIS function that compares a patient's current result to their most recent previous result for the same analyte. A large, unexpected change that exceeds a predefined limit triggers a "delta check" flag, halting result release and prompting a manual investigation [10].
- **Result Plausibility and Discordance:** Specialists assess if results are biologically possible and internally consistent. A classic discordant pattern suspicious for biotin interference is a very low TSH with a very high free T4 [27]. Such patterns should trigger immediate suspicion.
- **Instrument Flags:** Analyzers automatically flag specimens for interfering substances like hemolysis (H), icterus (I), and lipemia (L), alerting the operator to potential spectral interferences [12].
- **Implementing Mitigation Strategies:** When an interference is suspected, the laboratory has a toolkit of investigative procedures:
- **Serial Dilutions:** The sample is diluted with a neutral matrix and re-analyzed. The result should decrease linearly with the dilution factor. A non-linear response is highly suggestive of an interference, as the interferent's effect often does not dilute predictably [50].

- **Alternative Methods:** If an interference is suspected with one method (e.g., Jaffe creatinine), the laboratory can re-analyze the sample using a different method known to be unaffected by the suspected interferent (e.g., enzymatic creatinine) [5].
- **Interference Removal Protocols:** For some interferents, specific removal steps can be taken. For example, treating a sample with polyethylene glycol (PEG) can precipitate large molecules like heterophile antibodies, allowing for re-analysis of the supernatant [51].
- **Adding Interpretive Comments to Reports:** This is a critical post-analytical action. Instead of simply releasing a number that is known to be suspect, the laboratory specialist should add a standardized or free-text interpretive comment. A comment such as, *"Result may be falsely elevated due to daptomycin interference with the PT reagent. Suggest re-collection at trough level to minimize effect,"* provides essential context and actionable guidance for the clinician [38, 48].

6. Fostering Interprofessional Collaboration to Mitigate Risk

While individual excellence is important, the most resilient defense against MRI is a system built on robust interprofessional collaboration. Errors thrive in silos and are defeated by communication.

6.1. Establishing Clear Communication Pathways

A collaborative culture depends on easy and direct communication. Institutions should work to break down barriers between departments by establishing direct consultation phone numbers for the laboratory and pharmacy, implementing secure clinical messaging platforms, and encouraging face-to-face discussions to resolve complex cases. Integrating clinical pharmacists into patient care rounds has been shown to reduce adverse drug events, and by extension, can help resolve MRIs in real-time [52].

6.2. Developing Institutional Protocols and Clinical Decision Support Tools

System-level solutions provide a safety net where individual vigilance may fail. This includes developing institutional protocols for investigating common interferences (e.g., a "Biotin Interference Protocol"). Furthermore, leveraging the power of the Electronic Health Record (EHR) is key. Well-designed Clinical Decision Support (CDS) can provide alerts at the point of care. For example, a CDS alert could fire when a troponin is ordered for a patient with high-dose biotin on their medication list, prompting the ordering provider to consider the risk of interference before the sample is even collected [53].

6.3. Case Studies in Successful Collaboration

Case: A 45-year-old male with a history of a kidney transplant ten years prior presents for a routine follow-up. He is on a stable regimen of tacrolimus. He mentions to the nurse that he has been feeling "unwell" and taking a new herbal supplement for "energy."

The Data:

- Tacrolimus Trough Level: 1.5 ng/mL (Target Range: 5-10 ng/mL) - *Critically Low*
- Serum Creatinine: 2.8 mg/dL (Patient's Baseline: 1.5 mg/dL) - *Acutely Elevated*

The Collaborative Resolution:

1. **The Laboratory Specialist:** The specialist running the tacrolimus assay (an immunoassay) notes the critically low level and the simultaneous request for a creatinine. When the creatinine result shows a significant increase, she recognizes the dangerous combination of a potential acute rejection (signaled by the rising creatinine) and a sub-therapeutic immunosuppressant level. She immediately calls the transplant pharmacist.
2. **The Clinical Pharmacist:** The transplant pharmacist receives the call and reviews the patient's full profile. The critically low tacrolimus level is alarming. Recalling the patient's mention of a new "herbal supplement," she suspects a drug-herb interaction. She calls the patient directly, who identifies the supplement as St. John's Wort. The pharmacist immediately recognizes this as a potent inducer of CYP3A4, the enzyme that metabolizes tacrolimus [23]. The low tacrolimus level is real, caused by rapid metabolic clearance induced by the supplement. The rising creatinine is a true physiological consequence of this sub-therapeutic level, signaling the onset of acute organ rejection.
3. **The Nursing Team and Clinician:** The pharmacist urgently pages the transplant nephrologist and communicates the findings. The physician instructs the patient to stop the St. John's Wort immediately and come to the hospital for admission. The nursing staff facilitate the admission and prepare to administer adjusted doses of immunosuppressants based on the pharmacist's recommendations.

Outcome:

Rapid communication between the laboratory and the pharmacy identified the root cause of a life-threatening situation. This allowed the clinical team to intervene immediately, preventing irreversible graft loss. This case highlights how a physiological interference, when correctly identified through collaboration, directs appropriate and urgent clinical action.

7. Future Directions and Emerging Challenges

The field of laboratory medicine is in constant flux, with new therapies and technologies presenting both new challenges and new solutions for MRI.

7.1. Interference Profiles of Novel Therapeutics and Biologics

The rise of biologic drugs, particularly monoclonal antibodies (mAbs), presents a new frontier for MRIs. Therapeutic mAbs can directly interfere with immunoassays, especially those that measure the drug's target or related proteins. For example, a therapeutic mAb targeting a specific hormone could be recognized by the reagent antibodies in an assay for that hormone, making it difficult to measure the patient's true endogenous levels [54]. Developing drug-tolerant assays and understanding the specific interference profile of each new biologic will be a major ongoing challenge.

7.2. Technological Advances to Minimize Interferences

As discussed, Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) remains the gold standard for specificity and is the ultimate tool for resolving most analytical interferences [18, 29]. As this technology becomes more automated and cost-effective, its role in the routine clinical lab is expanding beyond toxicology and endocrinology. The migration of frequently-interfered-with tests from immunoassays to LC-MS/MS platforms represents a powerful technological solution to many of the problems outlined in this review.

7.3. The Potential of Artificial Intelligence (AI) and Machine Learning in Predicting and Flagging MRIs

Artificial intelligence and machine learning may offer a paradigm shift in MRI detection from a reactive to a predictive model. AI algorithms could be trained on massive, integrated datasets from EHRs, capable of recognizing complex patterns between medications, patient demographics, comorbidities, and laboratory results. Such a system could potentially generate a real-time "MRI risk score" for any given test order, flagging high-risk scenarios for pharmacist or laboratory review before an error can occur [54].

7.4. The Need for Standardized Reporting and Global Databases for Drug Interferences

A significant barrier to managing MRI is that the relevant information is highly fragmented, hidden in case reports, package inserts, and disparate manufacturer publications. There is a pressing need for the development of centralized, curated, and easily searchable global databases for drug-laboratory test interferences. A standardized reporting framework for new MRIs would facilitate the population of such databases, creating an invaluable, up-to-date resource for clinicians, pharmacists, and laboratory professionals worldwide [4, 48].

8. CONCLUSION

8.1. Summary of Key Takeaways for Each Professional Role

- For the Nursing Technician: You are the crucial starting point of the testing process. Your role is to be the frontline investigator at the patient's side. Key Action: Ask specifically about supplements, especially for hair, skin, and nails, and meticulously document all medications and the time of collection.
- For the Clinical Pharmacist: You are the medication expert and central communication hub. Your role is to anticipate and interpret. Key Action: Perform thorough medication reconciliation, proactively identify high-risk drugs, advise the team on management, and serve as the liaison to the laboratory.
- For the Laboratory Specialist: You are the final guardian of data integrity. Your role is to detect and investigate. Key Action: Maintain a high index of suspicion for discordant or implausible results, use all available tools to investigate, and communicate findings clearly with interpretive comments.

8.2. A Final Call for Vigilance and a Collaborative Culture to Enhance Patient Safety

Medication-related interference in laboratory testing is a complex and persistent threat to patient safety. It is a problem that resides in the seams of our healthcare system—in the handoffs between professions and the gaps in communication. It cannot be solved by any single group alone. The ultimate mitigation strategy lies in dissolving professional silos and fostering a deeply ingrained culture of collaboration, mutual respect, and shared responsibility. By committing to this interprofessional approach, we can better protect the integrity of our data and, in doing so, protect the patients who depend on us.

REFERENCES

1. Forsman, R. W. (1996). Why is the laboratory an afterthought for managed care organizations? *Clinical Chemistry, 42*(5), 813–816.
2. Chapman, A. R., & Newby, D. E. (2020). High-sensitivity cardiac troponin and the universal definition of myocardial infarction. *The Lancet, 396*(10244), 83-84.
3. Kroll, M. H. (2021). Differentiating In Vivo and In Vitro Test Interferences. *Clinical Chemistry, 67*(9), 1183–1185.
4. Lippi, G., & Plebani, M. (2018). Drug-related interferences in laboratory testing: a new kind of "iatrogenic" disease? *Journal of Medical Biochemistry, 37*(2), 115–123.
5. Saenger, A. K., Laha, T. J., & Jaffe, A. S. (2007). Cefoxitin interference with the Jaffe creatinine assay: a tale of two institutions. *Clinical Chemistry, 53*(11), 2016-2018.

6. U.S. Food and Drug Administration. (2017, November 28). *The FDA Warns that Biotin May Interfere with Lab Tests: FDA Safety Communication*. Retrieved from https://www.fda.gov/medical-devices/safety-communications/fda-warns-biotin-may-interfere-lab-tests-fda-safety-communication
7. Plebani, M. (2010). The quality of the preanalytical phase: the newest frontier for quality improvement in clinical laboratory medicine. *Accreditation and Quality Assurance, 15*(11), 603-605.
8. Lippi, G., Salvagno, G. L., Montagnana, M., Franchini, M., & Guidi, G. C. (2006). The preanalytical phase in the era of quality. *Clinica Chimica Acta, 374*(1-2), 1-2.
9. Lam, L., & Gounden, V. (2019). A practical approach to the investigation of common endocrine-related immunoassay interferences. *Journal of Clinical Medicine, 8*(9), 1434.
10. Lippi, G., & Plebani, M. (2011). The delta check: a reappraisal. *Clinical Chemistry and Laboratory Medicine, 49*(10), 1613-1615.
11. Agrawal, A., & Gendler, S. (2013). Rifampin and jaundice. *Journal of Clinical Gastroenterology, 47*(7), 653-654.
12. Glick, M. R., Ryder, K. W., & Jackson, S. A. (1986). Graphical comparisons of interferences in clinical chemistry instrumentation. *Clinical Chemistry, 32*(3), 470–475.
13. Saitman, A., Park, H. D., & Fitzgerald, R. L. (2014). False-positive interferences of common urine drug screen immunoassays: a review. *Journal of Analytical Toxicology, 38*(7), 387–396.
14. Boscato, L. M., & Stuart, M. C. (1988). Heterophilic antibodies: a problem for all immunoassays. *Clinical Chemistry, 34*(1), 27–33.
15. Li, D., Radulescu, A., Shrestha, R. T., Root, M., Karger, A. B., Killeen, A. A., ... & Al-Dulaimi, R. (2017). Association of biotin ingestion with performance of hormone and nonhormone assays in healthy adults. *JAMA, 318*(12), 1150-1160.
16. National Committee for Clinical Laboratory Standards. (2002). *Interference testing in clinical chemistry; Approved Guideline—Second Edition. NCCLS document EP7-A2*. NCCLS.
17. Dimeski, G., & Badrick, T. (2010). A case of bromide interference in a chloride assay. *Clinical Chemistry and Laboratory Medicine, 48*(4), 565-566.
18. Clarke, W., & Hoke, C. (2012). The new kid on the block: the role of mass spectrometry in the clinical laboratory. *Clinical Chemistry, 58*(3), 503-504.
19. Sica, D. A. (2004). Diuretic-related side effects: development and treatment. *The Journal of Clinical Hypertension, 6*(9), 532-540.
20. Meltzer, H. Y. (2013). Update on typical and atypical antipsychotic drugs. *Annual Review of Medicine, 64*, 393-406.
21. Jaeschke, H., McGill, M. R., & Ramachandran, A. (2012). Oxidant stress, mitochondria, and cell death in drug-induced liver injury: lessons from acetaminophen hepatotoxicity. *Drug Metabolism Reviews, 44*(1), 88-106.
22. Lopez-Novoa, J. M., Quiros, Y., Vicente, L., Morales, A. I., & Lopez-Hernandez, F. J. (2011). New insights into the mechanism of aminoglycoside nephrotoxicity: an integrative point of view. *Kidney International, 79*(1), 33-45.
23. Izzo, A. A. (2004). Drug interactions with St. John's Wort (Hypericum perforatum): a review of the clinical evidence. *International Journal of Clinical Pharmacology and Therapeutics, 42*(3), 139-148.
24. Unger, N., Pitt, C., Schmidt, I. L., Walz, M. K., & Schmid, K. W. (2008). Diagnostic pitfalls in the diagnosis of pheochromocytoma. *European Journal of Endocrinology, 159*(5), 623-631.
25. Tsimihodimos, V., Miltiadous, G., & Bairaktari, E. (2018). Fenofibrate: a new cause of drug-induced increase in serum creatinine? *European Journal of Clinical Pharmacology, 74*(5), 677-678.
26. U.S. Food and Drug Administration. (2019, November 5). *Update: The FDA Warns that Biotin May Interfere with Lab Tests: FDA Safety Communication*. Retrieved from https://www.fda.gov/medical-devices/safety-communications/update-fda-warns-biotin-may-interfere-lab-tests-fda-safety-communication
27. Barbesino, G. (2019). The pesky problem of biotin interference. *Endocrine Practice, 25*(3), 295-299.
28. Tang, Z., Du, X., Louie, R. F., & Kost, G. J. (2000). Effects of drugs on glucose measurements with handheld glucose meters and a portable glucose analyzer. *American Journal of Clinical Pathology, 113*(1), 75-86.
29. Taylor, P. J. (2014). The role of liquid chromatography-tandem mass spectrometry in the clinical laboratory. *The Clinical Biochemist Reviews, 35*(2), 67.
30. Ellison, D. H., & Loffing, J. (2009). Thiazide-sensitive Na-Cl cotransporter in the distal convoluted tubule: a new paradigm for the pathogenesis of thiazide-induced hypokalemia. *American Journal of Physiology-Renal Physiology, 296*(6), F1239-F1242.
31. Raebel, M. A. (2012). Hyperkalemia associated with use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. *Cardiovascular Therapeutics, 30*(3), e156-e166.
32. Deedwania, P. C. (2004). Beta-blockers and the treatment of hypertension in patients with diabetes mellitus. *Cardiology Clinics, 22*(4), 543-556.
33. Stroes, E. S., Thompson, P. D., Corsini, A., Vladutiu, G. D., Raal, F. J., Ray, K. K., ... & European Atherosclerosis Society Consensus Panel. (2015). Statin-associated muscle symptoms: impact on statin therapy—European Atherosclerosis Society Consensus Panel Statement on Assessment, Aetiology and Management. *European Heart Journal, 36*(17), 1012-1022.

34. Balis, D., & Koulouridis, E. (2016). Fenofibrate-induced nephrotoxicity. *Hippokratia, 20*(1), 79.
35. Dimeski, G., & Jones, B. W. (2011). Cefepime and ceftriaxone interference in Jaffe creatinine assays is reagent and temperature dependent. *Clinical Chemistry and Laboratory Medicine, 49*(10), 1735-1736.
36. Berdai, M. A., Labib, S., & Harandou, M. (2016). Metronidazole-induced encephalopathy: a systematic review of the literature. *Reviews in Neurological Diseases, 13*(1), 1.
37. Fralick, M., Macdonald, E. M., & Gomes, T. (2019). Co-trimoxazole and sudden death in patients receiving inhibitors of renin-angiotensin system: a population-based study. *BMJ, 365*, l1432.
38. Bookstaver, P. B., Bland, C. M., & Griffin, B. (2013). Daptomycin: an evidence-based review of its role in the treatment of Gram-positive infections. *Core Evidence, 8*, 77.
39. Rengarajan, A., & Mullins, M. E. (2013). How often do false-positive urine drug screens occur with quetiapine? *Clinical Toxicology, 51*(6), 493-496.
40. Moeller, K. E., Lee, K. C., & Kissack, J. C. (2008). Urine drug screening: practical guide for clinicians. *Mayo Clinic Proceedings, 83*(1), 66-76.
41. Verrotti, A., Scardapane, A., & Mohn, A. (2009). Effects of antiepileptic drugs on thyroid hormones in children. *Acta Neurologica Scandinavica, 120*(1), 1-6.
42. Rebello, S. A., & Yip, W. L. (2019). Acetaminophen interference with continuous glucose monitoring systems: what an endocrinologist should know. *Journal of the ASEAN Federation of Endocrine Societies, 34*(1), 13.
43. Laine, L., Smith, R., & Min, K. (2006). Systematic review: the impact of NSAID-associated adverse events. *Alimentary Pharmacology & Therapeutics, 24*(6), 833-848.
44. O'Malley, G. F. (2007). Emergency department management of the salicylate-poisoned patient. *Emergency Medicine Clinics, 25*(2), 333-346.
45. Mehran, R., & Nikolsky, E. (2006). Contrast-induced nephropathy: definition, epidemiology, and patients at risk. *Cardiology Clinics, 24*(3), 305-316.
46. De Vita, V. T., Lawrence, T. S., & Rosenberg, S. A. (2019). *DeVita, Hellman, and Rosenberg's Cancer: Principles & Practice of Oncology* (11th ed.). Wolters Kluwer.
47. Kang, J. S., & Lee, M. H. (2009). Overview of therapeutic drug monitoring. *The Korean Journal of Internal Medicine, 24*(1), 1-10.
48. Ismail, A. A. (2017). On the interpretation of discordant endocrine test results: a plea for a change in the way we practice laboratory medicine. *Clinical Chemistry and Laboratory Medicine, 55*(6), 785-794.
49. Gleason, K. M., Groszek, J. M., Sullivan, C., Rooney, D., & Barnard, C. (2013). Reconciliation of discrepancies in medication profiles. *American Journal of Health-System Pharmacy, 70*(6), 502-509.
50. Kroll, M. H., & Elin, R. J. (1994). Interference with clinical laboratory analyses. *Clinical Chemistry, 40*(11), 1996-2005.
51. Ismail, A. A., Walker, P. L., & Cawood, M. L. (2002). Interference in immunoassay is an understated problem. *Annals of Clinical Biochemistry, 39*(4), 366-373.
52. Kaboli, P. J., Hoth, A. B., McClimon, B. J., & Schnipper, J. L. (2006). Clinical pharmacists and inpatient medical care: a systematic review. *Archives of Internal Medicine, 166*(9), 955-964.
53. Schiff, G. D., & Bates, D. W. (2010). Can electronic clinical documentation help prevent diagnostic errors? *The New England Journal of Medicine, 362*(12), 1066-1069.
54. Schwickart, M., Stubenrauch, K., & Fiedler, M. (2017). Challenges in the development of drug-tolerant immunoassays for therapeutic antibodies. *Bioanalysis, 9*(1), 81-94.