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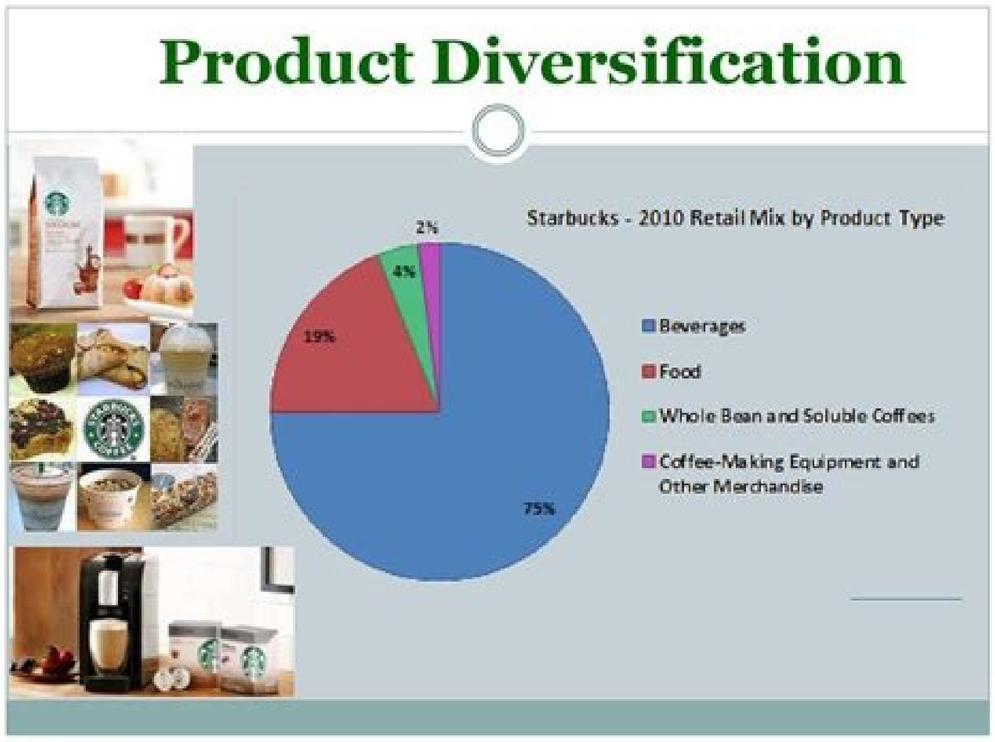

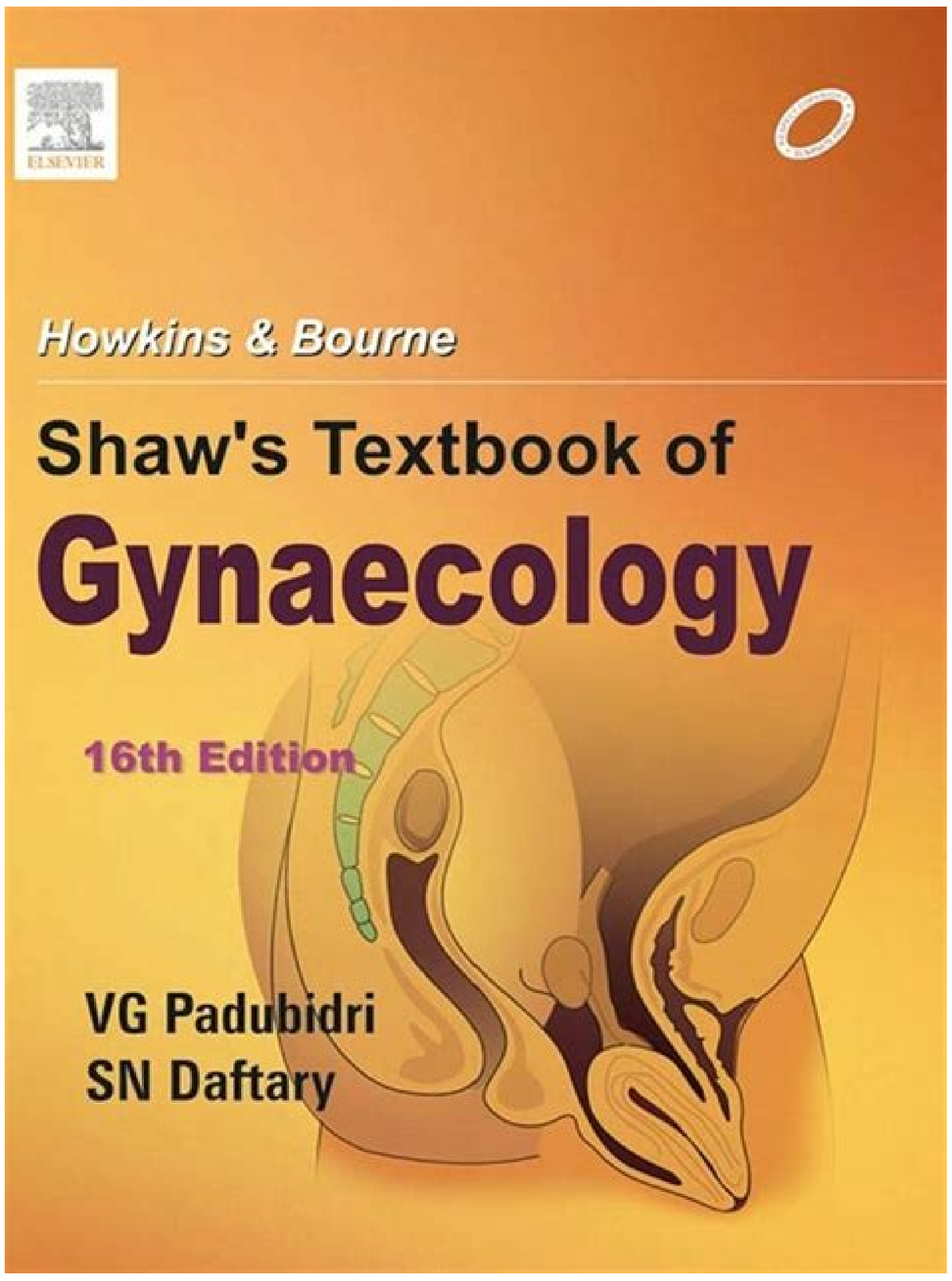

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Graves’ DiseaseLG is a 34-year-old woman who presented to her primary care physician (PCP) 6 months ago with symptoms of palpitations, heat intolerance, anxiety, and tremor. She was diagnosed with hyperthyroidism as a result of Graves’ disease and was started on propylthiouracil (PTU) 100 mg by mouth 3 times daily. After several months, LG was successfully managed to a euthyroid state and her PTU dose was gradually tapered to her current maintenance dose of PTU 150 mg daily. During her most recent follow-up with her PCP, LG was given a prescription for methimazole (MMI) 10 mg daily and was told to begin this therapy in place of PTU. Somewhat concerned, LG brings the prescription to the pharmacy and asks the pharmacist, “Why does my medication need to be changed? The other pill was working for me.” How should the pharmacist respond? Craig I. Coleman, PharmD Dr. Coleman is an assistant professor of pharmacy practice and director of the pharmacoeconomics and outcomes studies group at the University of Connecticut School of Pharmacy.CASE TWO Is It Too Late? CV, a 52-year-old woman, presents to the emergency department at a highly regarded stroke treatment facility. The neurologist on call rules out intracerebral hemorrhage and determines that CV is having an ischemic stroke due to an embolus in the middle cerebral artery. He also determines, with the help of CV’s family, that her stroke symptoms began just over 3 hours ago. At present, CV has a National Institutes of Health Stroke Scale (NIHSS) score of 19 of a maximum of 42 (higher score signifies a worse stroke severity). CV’s medical history was significant only for hypertension, which was treated with hydrochlorothiazide 25 mg once daily. The neurologist quickly dials the telephone to request intravenous (IV) recombinant tissue plasminogen activator (rtPA) (or alteplase) from the pharmacy. A pharmacist, new to the hospital setting, answers the call and collects the information regarding CV’s status, but is unsure what to do. The pharmacist recalls learning in school that IV rtPA had to be initiated within the first 3 hours. Should the pharmacist send the IV rtPA? ANSWERS Case 1: The pharmacist should assure LG that she is receiving an appropriate alternative to PTU, as MMI is considered a safer option in certain patient populations due to the risk of PTU-related acute liver failure. Both belonging to the thionamide class, PTU and MMI carry FDA approval for the treatment of hyperthyroidism and until recently both agents have been considered first-line in adult patients. In April 2009, the FDA and the American Thyroid Association recommended (see Bahn RS. Thyroid. 2009;19:673-674) that PTU not be prescribed as first-line therapy in most adults or children based on reports of PTU-related serious liver injury from both the FDA Adverse Event Reporting System and liver transplantation monitoring programs. It is estimated that 1 in 10,000 adults taking PTU develop PTU-related acute liver failure, which may occur at any point in therapy with a sudden onset and rapid progression to liver failure. Instances where PTU is recommended over MMI include the initiation of therapy in the first trimester of pregnancy or in the setting of life-threatening thyrotoxicosis or thyroid storm. Given LG is of child-bearing age, the pharmacist should also counsel LG on the teratogenic risk (category D) of MMI and the importance of using effective birth control while on therapy. Case 2: Absolutely, and as quickly as possible. Time is brain function! IV rtPA has been approved by the FDA for the treatment of acute ischemic stroke within the first 3 hours of symptom onset. However, based upon the positive results of the European Cooperative Acute Stroke Study (ECASS III), which evaluated the benefits of IV rtPA administered between 3 and 4.5 hours after symptom onset, the American Heart Association Stroke Council has recently expanded their maximum time cut-off for IV rtPA to 4.5 hours (Class Ib recommendation for most patients). ECASS III found that when compared with placebo, patients receiving IV rtPA in the 3- to 4.5-hour window had significantly higher odds (34%) of a more favorable outcome, with no differences in mortality, but a higher incidence of intracranial hemorrhage (P = .001). However, ECASS III did not enroll patients older than 80 years, or those taking oral anticoagulants, with a baseline NIHSS score >25, or with both a history of stroke and diabetes. So, while the 3- to 4.5-hour extended window is still recommended in patients with these characteristics, it carries a weaker recommendation (Class IIb C). Since CV is reporting within 4.5 hours of stroke symptom onset, the pharmacist should send 0.9 mg/kg (maximum of 90 mg) of IV alteplase, with instructions to give the first 10% as a bolus dose and the remainder as a 1-hour infusion. Read the answersfunction showAnswer() {document.getElementById("answer").style.display = 'block';document.getElementById("link").style.display = 'none';} This year has been a roller coaster for investors. As a result, it provides a great case study on market timing (more specifically, why timing the market doesn’t work and should be avoided). I realize we have a lot of aspiring and beginner-level investors here, so for those not aware of what market timing is, Wikipedia aptly defines market timing as: “The strategy of making buy or sell decisions of financial assets (often stocks) by attempting to predict future market price movements. The prediction may be based on an outlook of market or economic conditions resulting from technical or fundamental analysis. This is an investment strategy based on the outlook for an aggregate market, rather than for a particular financial asset.” Kind of alluring, isn’t it? So let’s take a walk through this year’s market timing lessons together to make it not so alluring… The Allure of Market Timing The stock market started out pretty calm this year, building on a long ascent over time, as markets entered their 7th year of an aging bull market. When bull markets are this long in the tooth, it’s almost like investors are just waiting for bad news to happen to tear it all down. And they got what they wished for with a series of unforeseen events… Russia/Ukraine happened. And Greece. And more Middle East unrest. And the Shanghai Composite index (Chinese stock market) collapse. And fears over the Fed raising interest rates in the United States as the economy picked up steam. All of this market tension and volatility built into the perfect storm until finally, investors flipped the F out. And this happened… Forget roller coaster, that’s more like the Demon Drop (Cedar Point reference… anyone?). Within a matter of 2 days, the Dow index had dropped from 17,500 to 15,500 (-12%). And it was 16% off from a high of 18,400 earlier in the year. The drop was dubbed the “Flash Crash”, and it resulted in the following exchange with a colleague: colleague: “Hey, I saw that I lost $3,000 in my 401K the other day. I thought those returns were guaranteed with the 401K match.” me: “No. 401K matching does not guarantee market returns. Investing returns are never guaranteed.” (I wisely substituted this for: “Is that it? Consider yourself damn lucky, YOU

PUNK!”) colleague: “Bummer. I am freaking out.” me: “Don’t panic. You’re young, what happens today won’t matter 50 years from now. Besides, you’re probably still better off than from where you started, right?” My colleague wasn’t alone. Deep down inside, I was freaking out a bit myself, as were most investors. Earlier in the year, I had moved almost all of my assets into stock investments. My colleague was concerned about $3,000 in losses, but in just those two days, I had lost more money than I have made in annual earnings in many of my post-grad years of employment. That’s some scary stuff. The thought of a 30-40% drop as we had in 2008? Absolutely frightening. And yes, the thought did enter my mind. At this moment of panic, your emotions are screaming at you to “Sell! Sell! Sell!” in order to avoid further losses. Then, get back and enjoy the ride back up when the chaos has subsided. That’s the allure of market timing. But, it’s a trap. The reality of this case study is that you would have locked in 12% losses. Every Prognosticator is Right… Eventually Every doomsday market prognosticator just knew a market correction was going to happen. And they were finally right. Of course, there were some important details they didn’t accurately predict: When the market correction was going to happen – both in market value and in timing (many had been predicting it each of the last 5 years and when the Dow hit 10,000, 12,000, 15,000, and 18,000). What was going to cause it (interest rates were the speculation, but nobody knew the exact cocktail of crises that would send investors into a panic). How long before it recovered its losses. Why Market Timing Doesn’t Work Predicting when the market would rebound was just as unlikely as predicting when it would drop. The market (shockingly) recovered more than 50% of its losses in just 2 days. Today, just 3 months later, it has recouped 100% of its losses, and is actually in positive territory for the year. The Greece and Chinese panic seems to have at least temporarily subsided. And market reaction to interest rate hikes has gone from a downward fear to an upward positive (I still can’t figure that one out). The biggest lesson here is as I highlighted back in my lessons from the flash crash post while this was all going down: “You. Just. Can’t. Time. The. F’ing. Market.” Timing the market, in theory, could work. But you’d have to accurately predict a lot of unpredictable things – which makes succeeding at it pure luck – a game of chance (no different than rolling the dice really). Anyone who says they accurately predicted exactly when the correction was going to happen, at what level, and how quickly it would turn around is blowing smoke up your nether regions (go ahead, try to find one person who accurately predicted all of this, I challenge you). Here is why market timing doesn’t work: Investors behave irrationally, and therefore, the market can be priced irrationally. You cannot accurately predict when the market will go up and when it will decline. Or, by how much. When you have the strongest emotional urges to buy and sell are often precisely when you should do the opposite. You never know what unexpected events are going to happen that could immediately flip market trending. You aren’t smarter than the market. Expanding on that last point, we like to think that we are smarter than everyone else at valuing the market. We are not. Even professionals with sophisticated algorithms and valuing software and years of professional expertise typically under-perform the market as a whole. Passive investing beats active investing for many of the same reasons why you can’t accurately time the market. Nobody really knows when it is going to go up, when it is going to go down, and by how much. The same is just as true for individual stocks as it is for the market as a whole. Plain and simple, market timing does not work. So don’t do it! A Better Investment Strategy than Market Timing Instead of trying to time the market, the investment strategy that is mostly likely to succeed for you is to: Passively invest in low-cost ETF’s and index funds. Consistently add to your investment positions over time and re-balance periodically. Do not panic sell. Buy when others are selling. It takes a little patience and discipline, but wealth will come to those who can muster it. Related Posts: