Part I – Annual Consultation

Jorge Alvarez had come to the doctor’s office for his annual consultation. About ten years ago, when he was 45 years old, he was officially diagnosed with Type II diabetes mellitus (TIIDM) and assigned to the care of Dr. Neha Gupta, an endocrinologist. Dr. Gupta had been working with Jorge to manage his disease. Over the past ten years, Jorge had made exercise a priority and had also worked with a dietician to help him make healthy eating choices. After implementing his new diet and exercise regimen, Jorge had even lost several pounds. Jorge worked a desk job with deadlines that at certain times of the year demanded long hours and caused considerable stress. Until now, Jorge and his health care team had been able to control his TIIDM using lifestyle modifications (e.g., diet and exercise) without the need of medication.

During Jorge’s current visit, he complained about a sore on the side of his right foot that wouldn’t heal. He explained that the injury occurred four weeks ago while doing some yard work; he had accidently hit his foot with a shovel. Oddly, despite the sore being red, swollen, and puffy, Jorge reported that it didn’t really hurt and he hadn’t even noticed the injury until he saw blood in his sock. Dr. Gupta asked Jorge if he had experienced any symptoms such as numbness, tingling, or burning sensation in his hands or feet. Jorge confirmed that in fact he had, especially in his feet, and it was worse at night when he was lying down. Dr. Gupta asked Jorge if these tingling and burning pains caused problems with his day to day life. Jorge thought over and said that sometimes he woke in the middle of the night because of cold-like pain and pins and needles sensation in his feet. Jorge said he had also experienced off-and-on general pain and tenderness in both feet over the last four months. Jorge also reported that he had not felt like himself lately; he felt tired, thirsty, and sluggish. He added that recently it had become exceptionally difficult to eat healthy and exercise because his work and his family life were increasingly busy and stressful. Dr. Gupta nodded with an expression of concern. She looked at her laptop to review Jorge’s current vital signs.

Table 1. Jorge Alvarez – Vital Signs

<table>
<thead>
<tr>
<th>Measure</th>
<th>Healthy Range</th>
<th>Jorge Alvarez - 12 Months Ago</th>
<th>Jorge Alvarez - Current Results</th>
<th>Interpretation</th>
<th>Change from Previous Visit?</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (Body Mass Index)</td>
<td>18.5–24.9</td>
<td>29.6</td>
<td>35.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (lbs.)</td>
<td>--</td>
<td>195</td>
<td>235</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (feet)</td>
<td>--</td>
<td>5’8”</td>
<td>5’8”</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature (ºF)</td>
<td>97.7–99.5</td>
<td>98.6</td>
<td>99.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>90–120/60–80</td>
<td>142/85</td>
<td>159/92</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting Heart Rate (bpm)</td>
<td>60–100</td>
<td>86</td>
<td>96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random (Non-fasting) Blood Glucose (mg/dL)</td>
<td>&lt; 140</td>
<td>155</td>
<td>305</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Noura Farih, Lauren Lund, and Sara Morgan contributed equally to the creation of the case study and are undergraduate students at Texas Tech University. Johnny Turner is a certified physician assistant with Texas Physician’s Group, Lubbock, TX. Breanna Harris is a research assistant professor in the Department of Biological Sciences at Texas Tech University.
Questions

1. Using the information in Table 1, compare Jorge’s current results with the normal ranges and fill in the interpretation column with either “high,” “low,” or “okay.” Use the last column to indicate whether the values have changed (“yes” or “no”) and, if so, in what direction (“increase” or “decrease”) from the previous year.

2. List all of the new symptoms that Jorge is experiencing. What system in his body is affected the most by these new symptoms?

3. Based on the information that Jorge has provided and the current results listed in Table 1, what does this tell you about the management of Jorge’s TIIDM? Is it still under control?

4. If you were Jorge’s doctor, which of his symptoms would you be most concerned with and why?
Part II – Blood Work

After reviewing Jorge's records, Dr. Gupta looked up from her laptop. She paused for a moment and then said, “Jorge, I’m concerned about your new neurological symptoms and the return of symptoms typical of TIIDM, namely the increased thirst, tiredness, sluggish, weight gain, increased blood pressure. Have you been monitoring your blood glucose at home like I instructed?”

“Yes I have, but not as consistently as I should.” Jorge looked down at the floor. “I hate to make excuses, Doc, but almost a year ago, my wife, Cecilia, had to quit her job so she could care for her sick and elderly parents full time. We wanted to hire someone, but the cost of the in-home care service was too high. Additionally, my insurance changed and with my new plan the co-pay for the test strips increased a lot. With the loss of income and having three daughters in college, money has been tight in our household. I just couldn’t afford the strips. I can tell you that our financial troubles have added a lot of stress.”

Dr. Gupta nodded sympathetically. In order to get a better idea of Jorge’s condition she decided to order some additional blood work (Table 2).

Table 2. Jorge Alvarez – Lab Results

<table>
<thead>
<tr>
<th>Test</th>
<th>Normal Range</th>
<th>Jorge Alvarez - 12 Months Ago</th>
<th>Jorge Alvarez - Current Results</th>
<th>Interpretation</th>
<th>Change from Previous Visit?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>&lt;150</td>
<td>215</td>
<td>253</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting Blood Glucose (mg/dL)</td>
<td>75-105</td>
<td>115</td>
<td>162</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GTT Glucose at 2hr</td>
<td>&lt;200</td>
<td>195</td>
<td>230</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary Glucose (ug/dL)</td>
<td>0-15</td>
<td>5</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary Ketones (mg/dL)</td>
<td>&lt;20</td>
<td>20</td>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-peptide test (ng/ml)</td>
<td>0.5-2</td>
<td>2.0</td>
<td>0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td>&lt; 6.5</td>
<td>6.2</td>
<td>7.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Questions

5. Using the information in Table 2, compare Jorge’s current results with the normal ranges and fill in the interpretation column with either “high,” “low,” or “okay.” Use the last column to indicate whether the values have changed (“yes” or “no”) and, if so, in what direction (“increase” or “decrease”) from the previous year.

6. Based on the additional results listed above, does it seem like Jorge’s current plan is working to manage his TIIDM? Explain your answer and include test results in the explanation.
Part III – The Nervous System Connection

Jorge had returned to the office to learn the results of his blood work. Dr. Gupta was increasingly concerned. She cleared her throat before sharing the news. “As you know, Jorge, TIIDM is defined as the inability to regulate blood glucose, typically due to insulin resistance. There is still much about the on-set and progression of TIIDM that the medical profession does not yet understand. What has been well demonstrated, though, is that TIIDM can lead to several, sometimes serious, health complications including problems with the skin, eyes, nervous system, kidneys, stomach, and feet. TIIDM can also increase the risk for stroke. These complications are more likely to arise when TIIDM is not well managed, or is uncontrolled, meaning blood glucose levels are consistently too high and not maintained within healthy ranges. One of the most common complications among diabetics is disruption of the nervous system; roughly 50% of diabetic patients experience some form of nerve damage.”

Jorge understood what she was saying, but replied, “I’ve been trying to manage my condition, but life is so stressful with my job and kids and everything else going on. I’ve been exercising once a week, but I know I need to do more. I’ve been cooking healthy meals to take for lunch, but that doesn’t seem to be helping.” He paused for a moment, and then with a look of embarrassment, confessed, “I’ve also been smoking again. I quit for a while, but life has been very stressful and smoking helps. It also reduces my cravings for sweets and gives me a reason to take a break from my desk at work. But I don’t drink alcohol.”

Dr. Gupta continued, “You were doing a great job previously and we had your TIIDM in a manageable, controlled state. But sometimes things change. Based on your results and new symptoms, I’m worried about changes in your blood glucose and secondary complications to other physiological systems, especially your nervous system. Consistently high blood glucose over an extended period of time can damage the blood vessels throughout the body, which can result in damaged nerve cells (neurons), and the nerves themselves, leaving them unable to function properly. It doesn’t seem like our plan of diet and exercise is working anymore. We’ll want to continue with this behavioral intervention, but I will likely add medication to your treatment plan. I also want to find a way to help you manage stress and stop smoking. Why don’t we schedule a follow-up appointment to run some additional tests. In the meantime, I’d like you to read through some pamphlets about the nervous system and TIIDM.”

Questions

7. The nervous system is generally split into two branches: the central nervous system (CNS) and the peripheral nervous system (PNS). These two systems are always in communication with one another. Additionally, information is always being processed; signals sensed by the PNS are sent to the CNS and the CNS integrates that information and initiates a response, if necessary. On the following page there is a flow chart and a word bank (Word Bank 1). Place the words into the flow chart so that they accurately describe the CNS and PNS. All words should be used and some may be used more than once.

8. Now use the words in Word Bank 2 to complete the two tables on the next page to describe the sensory system in more detail. All words will be used and some may be used more than once. The first column of “Special Senses” is filled in as an example.

9. Neurons are the basic functional units of the nervous systems. Multiple neurons, combined with astrocytes, glial cells, and other components, comprise a nerve. The stereotypical neuron displayed in textbooks is typically a multipolar motor neuron. Draw a basic motor neuron below. Label the nucleus, cell body, dendrites, axon, axon terminal, myelin sheath, and nodes of Ranvier.
### Word Bank 1
- Brain
- Sympathetic
- Spinal Cord
- Enteric
- "Rest and Digest"
- Sensory
- Autonomic
- Acetylcholine
- Afferent
- Parasympathetic
- Somatic Motor
- Norepinephrine
- Efferent
- Central Nervous System
- Peripheral Nervous System
- Neuromuscular Junction
- "Fight or Flight"

### Periphereral Nervous System

#### Special Senses

<table>
<thead>
<tr>
<th>Sense</th>
<th>Vision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptor Type</td>
<td>Photoreceptors</td>
</tr>
<tr>
<td>Sends Signal to CNS</td>
<td>Optic nerve</td>
</tr>
</tbody>
</table>

#### Somatic Senses

<table>
<thead>
<tr>
<th>Sense</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptor Type</td>
<td></td>
</tr>
<tr>
<td>Sends Signal to CNS</td>
<td></td>
</tr>
</tbody>
</table>

#### Word Bank 2

- Vision
- Itch
- Touch
- Vestibular nerve
- A-beta
- Hearing
- Optic nerve
- Temperature
- Cochlear nerve
- C fibers
- Taste
- Photoreceptors
- Proprioception
- A-beta
- Receptor axons
- Smell
- Chemoreceptors
- Nociceptors
- Olfactory bulb/nerve
- Pain
- Equilibrium
- Mechatoreceptors
- Proprioceptors
- Thermoreceptors
- Cranial nerves VII, IX, X

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"No Longer Living the Sweet Life" by Farih, Lund, Morgan, Turner, & Harris
10. Draw a simple (typical of somatic senses) and a complex (typical of special senses) sensory neuron (receptor). Where applicable, label the cell body, the axon, the nerve endings, myelin, and the axon terminal.

11. What is myelin? What type of cells makes myelin in the PNS? In the CNS?

12. What is the purpose of myelin?

13. Are all neurons in the human body myelinated?

14. Apply the above information you just reviewed about the nervous system to our patient, Jorge. According to Jorge’s symptoms, which branch of his nervous system is most affected? How can you tell?
Part IV – Nervous System Tests

After handing Jorge the pamphlets about the nervous system and TIIDM to read, Dr. Gupta was ready to share her thoughts. “I think you have a form of peripheral neuropathy. More specifically, I think your sensory neurons are being affected as a result of your TIIDM. But, I’d like to run a few more tests to help us determine which neurons are being affected the most.” Jorge was concerned but also happy that he and Dr. Gupta might be able to pinpoint what was wrong so that they could better manage his condition.

“So what exactly is peripheral neuropathy, and what additional tests do I still need to have?”

“Peripheral neuropathy is a generic term to describe damage or lack of function in the neurons, and thus nerves, of the peripheral nervous system. If you recall, the PNS conveys signals between the CNS and the body. Nerves are collections of neurons and supporting cell types, such as Schwann cells, glial cells, and astrocytes. Damage to the nerves can result in several problems, including a failure to transmit signals, sending signals too quickly or too slowly, or sending signals at the wrong times. This problem can affect the autonomic, sensory, and/or motor divisions of the peripheral nervous system. Additionally, this condition can affect a single nerve (mononeuropathy), more than one nerve in separate areas (multiple mononeuropathy), or can affect multiple diffuse nerves (polyneuropathy). There are over 100 different types of peripheral neuropathy, but you likely have what we call diabetic neuropathy. Diabetic neuropathy is a complication of uncontrolled or unmanaged TIIDM. The continually high blood glucose levels can damage the myelin around the neurons, and also the blood vessels that carry oxygen to the neurons, or can damage the axons themselves. Diabetic neuropathy can have various forms, but the most common generally impacts multiple nerves and is termed distal symmetric polyneuropathy. I want to run some tests to make sure we know exactly which division is being impacted. I also want to have you tested for Charcot’s joint, also called Charcot neuroarthropathy, due to your foot pains.”

“Okay, I’ll do whatever is necessary. But what is Charcot’s joint?”

Dr. Gupta replied, “Charcot’s joint is a rare foot disorder that can cause pain, deformity, and disability. It can also lead to ulceration and infection. This can co-occur with peripheral neuropathy, especially in diabetics. Given your foot pains and sore, and the nerve pain, I’d like to have you evaluated for this as well.”

“Thanks, Dr. Gupta. So what do we do if it turns out that I have diabetic neuropathy? Can it be cured? Is my insurance going to cover all these tests?”

“Unfortunately, there is no cure for diabetic neuropathy, but we can manage the pain with medications. We would likely start you on an NSAID and if that doesn’t work we can go to a steroid. We’ll absolutely want to get your blood glucose under control; if we do that we can help prevent worsening of the condition. You will need to make sure you are eating healthy, continuing to limit alcohol intake, and increasing your exercise is important. I’d also like you to work on cutting out the cigarettes and managing your stress levels. I can get you information on free smoking cessation and stress management classes at the hospital. Unfortunately, I’m not sure what your insurance plan will cover, they all differ, so you will have to call your carrier and discuss it with them. But I do want to run all of these tests to make sure we figure out what is going on with your nerves.”

Dr. Gupta advised Jorge to monitor his blood glucose levels very closely. In addition, he should continue with an exercise and diet plan. They set another appointment for next week to run the neuropathy tests and to discuss various medications to help manage his TIIDM. Before leaving the exam room, Dr. Gupta handed Jorge a sheet describing tests that are used to diagnose different types of neuropathy. She also gave him information about free classes on smoking cessation and stress management.

Questions

15. Fill out Table 3 below about the tests you think Dr. Gupta should order for Jorge. We want to maximize data for diagnosis, but at the same time minimize the number of procedures used (extra tests are costly and time consuming).
Table 3. Jorge Alvarez – Possible Tests

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Would You Recommend for Jorge? (Yes/No)</th>
<th>Why or Why Not?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monofilament Test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quantitative Sensory Test (QST)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nerve Condition Velocity (NCV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electromyography (EMG)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autonomic – QSART</td>
<td></td>
<td></td>
</tr>
<tr>
<td>X-Ray</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT Scan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nerve Biopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin Biopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional Blood Tests</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>