PART 1

Dr. Jeremy Aldritch examined the four-month-old infant that had been admitted to Legacy Emanuel Hospital earlier in the day. The baby's parents, Jayne and Michael Banks, had brought young Alvin to the emergency room because he had been suffering from a chronic cough and diarrhea for almost a week. In addition, they said that Alvin sometimes would "wheeze" a lot more than they thought was normal for a child with a cold. Their pediatrician had told them that Alvin had a cold and would be better in a few days.

Upon arriving at the emergency room, the attending pediatrician detected a possible ear infection and noted that salt crystals were present on Alvin's skin. Chest auscultation revealed the presence of rhonchi in the right upper lobe (RUL) of the lung. The attending pediatrician had Alvin admitted immediately and called Dr. Aldritch, a pediatric pulmonologist. After Dr. Aldritch completed his examination, he asked Alvin's parents to sit with him in his office to discuss Alvin's situation.

What are possible diagnoses for Alvin at this point? What is the evidence for or against each possible diagnosis?

What diagnostic tests or other assessments would you recommend? Why?
PART 2

Dr. Aldritch asks Alvin’s parents about family history of cystic fibrosis. Jayne explains that Alvin cannot possibly have cystic fibrosis. Dr. Aldritch then asks for more details. Jayne has two sisters, neither have CF. Her older sister has one daughter, who is healthy. Neither of Jayne’s parents have CF, but one of Jayne’s cousins on her mother’s side has a son who was diagnosed with CF. Neither Michael’s sister nor brother have CF, nor do his mother or father. However, his paternal uncle died of CF before Michael was born.

Draw the pedigree of these families. Is it possible that Jayne and Michael could both be carriers of the mutated CF allele?
Dr. Aldrich examines the pedigrees and explains to Jayne and Michael that they must both be carriers of the mutated CF allele and therefore each passed this allele on to Alvin. Jayne again assures Dr. Aldrich that Alvin cannot have CF. She explains that, since both she and Michael have a family history of CF, they both underwent genetic testing to find out if they were carriers of the mutated allele. The genetic test was negative for both Jayne and Michael.

Jayne and Michael Banks are of Asian Indian descent. Neither of them carries the most common mutated CF allele, ΔF508. Nor do either of them carry any of the other 22 most common mutated CF alleles. Complete sequencing of their CFTR genes, along with complete sequencing of Alvin’s CFTR gene shows that they all possess a rare variant of the CFTR gene (T6), which has not been found in Caucasian populations, but has been reported in Asians.

Jayne and Michael are very upset with this news. Assume that you are the one on the team whose job is to describe these results.

How will you respond in order to address what is going on with Alvin?
PART 4

Your laboratory results are below.

Complete Blood Count with differential (not necessary to make the diagnosis)

Complete Metabolic Panel (not necessary to make the diagnosis but helpful in the management and monitoring of cystic fibrosis)

OTHER:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase (units/L)</td>
<td>5</td>
<td>0-60</td>
</tr>
<tr>
<td>Lipase (units/L)</td>
<td>15</td>
<td>20-140</td>
</tr>
<tr>
<td>Sweat Chloride (mmol/L)*</td>
<td>56</td>
<td>≤29</td>
</tr>
<tr>
<td>Trypsin/Chymotrypsin</td>
<td>Positive (normal)</td>
<td></td>
</tr>
<tr>
<td>Nasal potential difference</td>
<td>Patient too young for this test</td>
<td></td>
</tr>
<tr>
<td>CFTR multimutation panel†</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>CFTR mutation expanded panel</td>
<td>CFTR gene (T6)</td>
<td></td>
</tr>
</tbody>
</table>

*For infants younger than six months of age, a wide intermediate range is used because sweat chloride concentrations in healthy newborns gradually decrease during the first weeks of life. Sweat chloride results for this age group are interpreted as follows (from UpToDate):
- ≤29 mmol/L: Normal (CF very unlikely)
- 30 to 59 mmol/L: Intermediate (Possible CF)
- ≥60 mmol/L: Abnormal (Diagnosis of CF)

†only identifies common CFTR mutations (23 in number).

Are these results adequate to support the diagnosis of cystic fibrosis?

List some common impairments (or functional limitations resulting from these impairments) of various body systems associated with cystic fibrosis.
PART 5

What impact on family routines and activities can be expected related to Alvin’s CF and what can you and your teammates do to help them prepare to adapt to those challenges and manage as normal a family life as possible?

Assume that you are working with the family and Alvin is now 6 years old, how would your team address the following complications/situations?

-Due to many processes in the lungs and other areas of the body, people with CF are predisposed to infections. How would you manage this risk?

-People with CF also have malnutrition because of the insufficiency of pancreatic enzymes. Because of this failure, these individuals have decreased bone mineral content which increases their risk for fractures. Furthermore, sweating abnormalities make them prone to heat stroke. What would you advise regarding school activities, such as PE and sports participation?

-Currently, the median age of survival for a person with cystic fibrosis is 37 years. Is there a way or a time to discuss this mortality issue with the family? How? When?
Jayne and Michael are appalled that they were not offered a genetic test for one of the possible CFTR alleles. If they had known they were both carriers, their decision to have children could have been completely different.

One of Michael’s work colleagues suggests that he and Jayne should sue their genetic counselor for “wrongful birth.” Michael consults an attorney and finds that courts have allowed parents to recover damages for the cost of caring for a child born with a disability if it can be shown that medical personnel were negligent.

There are over 1000 different mutations of the CFTR gene that can result in cystic fibrosis. Most of them are exceedingly rare. Indeed, some have been identified in only a single family. As stated above, individuals are generally tested for the 23 alleles that account for over 99% of all cystic fibrosis-causing mutations. Michael and Jayne each possess mutated alleles that are not among the 23 alleles commonly tested. Was it negligent for the genetic counselor not to offer additional tests to Jayne and Michael? They were both told that they had tested “negative” for the CF-causing allele. How could this counseling session have been handled to avoid litigation?

What are some of the risks and benefits of genetic testing as it relates to legal (not medical) issues?

Do you think an unintended consequence of genetic testing could be that people would be less liable to seek medical care out of fear that they could later be denied life or health insurance? What laws should be used to govern the use of genetic data of this type?