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| **Name:** |
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| Group 4B - 5 |
| **Basic Science Question:** |
| What is Alagille Syndrome? |
| **Report:** |
| Alagille Syndrome (ALGS) is a genetic, multisystemic disorder that affects individual patients in different capacities (Saleh, et al., 2016). It was originally described by Daniel Alagille and his colleagues in 1969, and is considered a rare disease primarily characterized by a decreased number of small hepatic bile ducts (Berniczei-Royko, et al., 2014). In order to be diagnosed with ALGS, a patient must not only present with a reduced number of bile ducts, but also with abnormalities in at least two other organs including the heart, eyes, spine, and facial features (Berniczei-Royko, et al., 2014). Alagille Syndrome is an autosomal dominant condition that results in mutations of the JAG1 and/or NOTCH2 genes (Saleh, et al., 2016). Mutation of the JAG1 gene is far more common than NOTCH2, and it results in disruptions of the signaling pathway during development, leading to developmental errors in the previously listed organs (Berniczei-Royko, et al., 2014). Although ALGS only affects 1 in every 70,000 live births, it can be inherited from only one parent, meaning there is a 50% chance that each child will develop this disorder (Berniczei-Royko, et al., 2014).  Diagnosis of Alagille Syndrome is relatively difficult, but has traditionally included histological evaluation to identify the decreased number of bile ducts in the liver (Saleh, et al., 2016). As of recent, diagnosis has been accomplished based on clinical presentation criteria and genetic testing (Berniczei-Royko, et al., 2014). These criteria are based on the five main systems that are affected by the genetic mutation of the JAG1 gene: the liver, the skeletal system, the heart, the eyes, and facial features (Berniczei-Royko, et al., 2014). In infancy, the liver is affected by a decreased number of small bile ducts which, in severe cases, can potentially lead to liver failure. This is also known as cholestasis, a decreased flow of bile from the liver to the small intestine (Saleh, et al., 2016). The skeletal system is affected in that the thoracic vertebrae primarily present as “‘butterfly’ hemivertebrae” where the anterior vertebral arches fail to fuse resulting in a sagittal cleft (Berniczei-Royko, et al., 2014). This is present in 70% of patients. Heart abnormalities are present in roughly 90% of patients and can include findings ranging from benign heart murmurs to structural defects (Saleh, et al., 2016). The most common ocular manifestation in patients with ALGS is posterior embryotoxon, a defect in the anterior chamber of the eye (Saleh, et al., 2016). It can be diagnosed by slit-lamp examination and is reported in up to 90% of individuals with ALGS (Saleh, et al., 2016). Finally, facial abnormalities are among the most noticeable symptoms in a patient with Alagille Syndrome. These abnormalities include a prominent forehead, deep set eyes, a straight nose with a flattened, bulbous tip, a delicate pointed chin, and large ears (Berniczei-Royko, et al., 2014). These features are not very prominent before one year of age, but later in life typically develop in about 95% of cases, causing the face to appear as an inverted triangle (Berniczei-Royko, et al., 2014).  In terms of dental manifestations, Alagille Syndrome can damage many structures in or around the dentition including the teeth, salivary glands, the periodontium, and mucous membranes (Berniczei-Royko, et al. 2014). Although not primary features the disorder, these manifestations “occur as a complication of the long-lasting cholestasis and are linked to hyperbilirubinemia” (Berniczei-Royko, et al., 2014). During the formation of the dentition, cholestasis causes enamel opacities, hypomineralization, and hypoplasia of tooth enamel (Berniczei-Royko, et al., 2014). Alagille Syndrome, in conjunction with liver disease, can also have significant impacts on oral health due to food deficiency, lack of immunity, and coagulation disorders (Berniczei-Royko, et al., 2014). |
| **References:** |
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