Bilateral parotid disease has a wide differential diagnosis with an expanding number of available tests. An algorithm, based solely on data obtained from the history and physical in the first encounter, may reduce the differential and aid the clinician in deciding on further workup and treatment. A PubMed search for “bilateral and parotid” revealed 793 results. Eighty-six relevant papers were reviewed to compile a list of disease processes that can cause bilateral parotid masses. A total of 24 disease entities were reviewed. The disease processes were initially subgrouped into 5 categories based on etiology: infection, neoplasm, autoimmune, sialadenosis, iatrogenic, and miscellaneous. For each lesion, the incidence, history and physical examination were compiled in a matrix. Based on these findings, an algorithm was constructed to resourcefully reduce the differential diagnosis of bilateral parotid disease. The proposed algorithm is a retrospective model, which requires further randomized testing in clinical practice to validate.

**RESULTS**

A matrix was built based on the most important factors including disease incidence, bilaterality, timing of onset, nodularity, pain, and presenting skin changes [Table 1]. It appears that the most efficient way to approach bilateral parotid enlargement is to narrow the differential diagnosis first by timing of disease onset, followed by pain, and lastly by nodularity of the lesions [Figure 1]. The approximate percentage of bilateral involvement in parotid enlargement is demonstrated in Figure 2.

**DISCUSSION**

During the review, studies have surfaced that questioned the way we view certain disease entities. Most notably, new studies of diabetes mellitus, cirrhosis, HIV, and viral mumps are summarized as follows.

**Sialadenosis**

Sialadenosis (swelling) is associated with nutritional and hormonal disturbances, particularly chronic malnutrition, obesity, diabetes mellitus, alcoholism, liver disease, and eating disorders. Many drugs have been implicated in sialadenosis, most prominently antirheumatics. Some cases of sialadenosis have no known underlying systemic disease.

With the rising incidence of metabolic syndromes, diabetes mellitus is an increasingly important cause of sialadenosis. Scully et al. reported 45% of sialadenitis patients were diabetic, although diabetes and liver disease often coexist in patients. One study showed 24% of 200 diabetic patients had asymptomatic bilateral parotid enlargement. While still controversial, abundant research has focused on the specific changes in secretory protein expression and salivary flow in glandular diabetic patients, which may contribute to the clinical complications of diabetes. In some cases, parotid enlargement preceded the diagnosis of diabetes. Some authors have proposed that asymptomatic parotid gland enlargement warrants a search for diabetes, and that salivary composition and function have potential to contribute to the clinical diagnosis and staging of diabetes.

Sialadenosis is also frequently found in patients with alcoholism and alcoholic cirrhosis, with an estimated incidence of 30-80%. Whether alcoholism without cirrhosis and other causes of cirrhosis can result in sialadenosis has been debated. A recent study found sialadenosis in 26 of 300 liver transplant candidates (9.3%). Among these 28 patients with sialadenosis, 30.3% had alcoholic cirrhosis, and 60.7% had non-alcohol-related liver diseases. The study suggested that cirrhosis, irrespective of its etiology, may lead to the development of sialadenosis.

**Mumps**

Recently, large viral mumps outbreaks have been reported in developed countries. The resurgence of this disease comes with new challenges as its epidemiology has changed. Adolescents and young adults were affected in these outbreaks, and parotid symptoms may be absent in 10-20% of symptomatic cases. The fact that some of the mumps patients had received vaccination brings to light the moderate efficacy of the mumps vaccine. New research is focused on improving the mumps vaccine and studying the immunological markers of mumps immunity.

**HIV**

Since the introduction of HAART in the mid-1990s, there has been a decline of the prevalence of oral manifestations of HIV infection. However, the incidence of HIV-associated salivary gland diseases, mostly involving parotid glands, have remained the same in developing countries, and even increased in developed countries. For example, nodal enlargement reports in lymphoid proliferations have increased in approximately 1% to 10% of HIV-infected patients. Differential diagnosis of parotid enlargement specific to HIV-seropositive patients includes hyperplastic lymphadenopathy, benign lymphoid lesions (BLLS), and diffuse infiltrative lymphocytic syndrome (DILS).

BILDE occurs in 2% to 6% of HIV-positive adults, and in 1% to 10% of HIV-positive children. BILDE presents early in the course of HIV infection with slowly progressive, but asymptomatic parotid gland enlargement. In the era before the widespread use of HAART, the prevalence of DILS was at 3-4% of HIV-positive patients. Buse et al. reported a diminishing frequency of DILS in the HAART treated patients, suggesting the success of antiretroviral therapy in treating extraglandular involvement. Despite the success of HAART, Cabral-Saldivia et al. reported increased incidence of parotid gland enlargement in HIV-positive patients by 4.8% on HAART. A lessen adverse effect of protease inhibitors is fat accumulation in various areas of the body such as the back of the neck (buffalo hump) and intra-abdominal region. Protease inhibitors have been suggested to cause fatity infiltration of the parotid gland or parotid sialadenosis resulting in glandular swelling.

**CONCLUSIONS**

History and physical exam findings such as disease onset, pain, and nodularity are key elements in the algorithm to quickly narrow the differential diagnosis of bilateral parotid enlargement. New research and case reports will allow continued update and improvement of the diagnostic algorithm.

**REFERENCES**