The underlying cause of carcinoid tumors remains unclear. Some studies have suggested risk factors such as smoking and dietary intake, however, further research is needed to confirm these findings. In the majority of cases tumors are slow-growing and can produce hormonal chemical substances such as serotonin, bradykinins, tachykinins and prostaglandins. If the original carcinoid cells spread (metastasize) to the liver, these substances are no longer broken down to their inactive form and are released into the systemic (main) circulation, causing the signs and symptoms of carcinoid syndrome. When tumors affect organs other than the gastrointestinal tract, such as the ovaries, carcinoid syndrome can occur in the absence of liver metastases. Carcinoid tumors are rare, with only 27 new cases per million diagnosed in the U.S. per year. Of these, only about 10% will develop carcinoid syndrome. The syndrome affects males and females in equal numbers. All races can be affected though there is a slightly increased prevalence in black African males. All ages can be affected but most gastrointestinal cases occur in middle-age. Bronchial (airway) tumors are most often seen in the fifth decade but can affect people at any age. Carcinoid syndrome may be more prevalent than suspected because diagnosis is difficult and sometimes overlooked; some patients may not exhibit all three of the hallmark symptoms of flushing, wheezing, and diarrhea. Diagnosis is best achieved with a multimodality approach including biochemical investigation, radiological and nuclear imaging, and finally histological (tissue biopsy) confirmation where possible. The occurrence of episodic facial flushing and/or chronic diarrhea not diagnosed by standard tests as being a result of more common causes should lead to suspicion of carcinoid syndrome. In the past, measurement of 24-hour urinary excretion of 5-hydroxyendolacetic acid (5-HIAA), a product of the breakdown (metabolism) of serotonin, in a patient on a low serotonin diet was the main lab test used. It is still useful and the level of 5-HIAA will be clearly elevated in 50% of the cases. However, there are also blood tests available, the most useful being chromogranin-A, often in combination with an imaging technique known as octreoscan, that may confirm the diagnosis of carcinoid syndrome even when urinary 5-HIAA is normal. This technique may also be helpful in indicating the presence of carcinoid tumors when the full spectrum of symptoms is not apparent. Other investigations that may be helpful, depending on the location of the primary tumor, include CT scan, ultrasound, MRI and endoscopy. Sometimes the diagnosis is established incidentally at the time of surgery for another suspected condition such as intestinal obstruction or appendicitis.