

Introduction: Kennedy's Disease (KD) or [Spinal and Bulbar Muscular Atrophy](#) (SBMA) is a rare, adult-onset, X-linked recessive, lower motor neuron disease caused by trinucleotide CAG repeat expansions in the androgen receptor (AR) gene. In men, SBMA slowly progresses over decades resulting in loss of skeletal and bulbar muscles with weakness, fasciculations, cramps and difficulties in speech and swallowing. Initial symptoms often include fatigue, muscle cramping, fasciculations, tremor, and muscle weakness. However, some men first experience difficulty with swallowing (dysphagia) and speech (dysarthria). As the disease progresses, respiratory function may be impaired by weakening bulbar and respiratory muscles, allowing foreign material to enter and irritate the lungs, reduced cough effectiveness in removing these materials and accumulated mucus, sleep issues, and labored breathing. Left untreated, these issues increase the risk of aspiration pneumonia and respiratory failure, the leading cause of death in SBMA patients (Pradat et al. 2020).

To evaluate respiratory function, the total volume and rate of air flow that can be inhaled and exhaled ([spirometry](#)) was measured in 40 male subjects with SBMA compared to patients with ALS and healthy controls (Yamada et al. 2016). Normalized [peak expiratory flow](#) (%PEF) and [forced vital capacity](#) (%FVC) were decreased with SBMA compared to patients with ALS and healthy controls. In SBMA patients, declines in both PEF and FVC were correlated with declines in trunk muscle strength (Yamada et al. 2016). In 32 SBMA patients that were monitored over time, %PEF declined at 1.3%/year and %FVC declined 0.9%/year after disease onset (Yamada et al. 2016), compared to a ~2%/year decrease in upper and lower extremity muscle strength by quantitative muscle testing (Fernández-Rhodes et al. 2011).

Swallowing Issues: In SBMA, [dysphagia](#) or difficulty in swallowing is associated with weakness of muscles in the mouth, tongue, and throat, which can result in aspiration of solids, liquids or saliva. When foreign material enters the tracheobronchial tree, it can result in inflammation, increased mucus production, recurrent cough, chest congestion and fluid accumulation. Symptoms may develop gradually with increased difficulty breathing when active or lying flat, a feeling of suffocating or drowning, wheezing or gasping for breath, and a productive cough with frothy or foamy sputum.

Swallowing management approaches include: [1] changes in eating habits (posture, location, avoiding distractions); [2] training in safer and more effective swallowing techniques; [3] adjusting food composition (avoid difficult to chew foods), food textures (avoidance of dry crumbly foods), and changing food consistency with thickeners. Nutritional status should be monitored and easy to swallow food supplements should be added to facilitate adequate protein, energy and vitamin intake. For additional information, consult the information sheet "[KD and Swallowing Issues](#)".

Gastroesophageal Reflux Disease ([GERD](#)) can occur when the esophageal sphincter muscles are weakened, allowing stomach content to flow up into the esophagus, causing heartburn, regurgitation, and non-cardiac chest pain. GERD can also result in irritation of the respiratory tract, coughing, wheezing, chest congestion and lung inflammation leading to asthma, bronchitis, or pneumonia (Gaude 2009; Griffiths et al. 2020).

GERD is common in the general population and could be exacerbated by progressive muscle weakness in SBMA. In a study of 49 SBMA patients, [laryngospasm](#) (47%) and heartburn (60%) were common. In patients with both laryngospasm and heartburn, anti-reflux therapy reduced laryngospasm frequency (Sperfeld et al 2005). There are many approaches to treating GERD. These include behavioral changes, dietary changes, medications, and even surgery for particularly refractory cases. Lifestyle modifications for GERD include avoiding eating before lying down, sleeping with the back elevated, and not smoking. Avoiding foods that worsen GERD can help. This includes fatty foods, alcohol, caffeinated beverages, peppermint, and acidic liquids. Medications for GERD range from over-the-counter antacids to H2 receptor blockers and proton pump inhibitors. [Fundoplication](#) is a procedure to tighten the junction between the esophagus and stomach. This has traditionally been done surgically, but there are now endoscopic techniques that are less invasive.

In a case report, a SBMA patient (47 CAG repeats) presented with rapidly worsening bulbar symptoms caused by laryngopharyngeal irritation associated with a viral upper respiratory tract infection, seasonal allergies and laryngopharyngeal reflux, who dramatically improved with multimodality therapy. The patient denied any heartburn or regurgitation. [Videofluoroscopic](#) evaluation of his swallowing revealed mild oropharyngeal dysphagia as well as evidence of esophageal reflux, but no laryngeal penetration or frank tracheal aspiration. Pulmonary function tests (PFT) values were within normal limits. After treatment with prednisone and bronchodilators, dyspnea and wheezing were resolved, but the patient still reported mild residual nasal congestion and frequent throat clearing. He was suspected of having laryngopharyngeal reflux and was treated with esomeprazole, a proton pump inhibitor, along with behavior modification. Ten weeks later, feeling of a lump in the throat (globus pharyngeus) and throat clearing were almost gone, prior baseline chronic dysphagia had resolved, and hoarseness had improved (Diaz-Abad and Porter, 2013).

Ineffective Cough: Coughing can help clear the breathing passages of foreign materials, fluids, irritants, and microbes. However, an effective cough has three phases: [1] deep inhalation; [2] forced exhalation against a closed glottis (opening in the vocal folds); and [3] a violent release of air when the glottis is forced open. The rapid release of air during an effective cough can expel particles and move secretions upward. Coughing also assists in clearing secretions from the lower airway, preventing the pooling of secretions in the air sacs (alveoli) which may reduce oxygen (O₂) and carbon dioxide (CO₂) exchange. However, muscle weakness from SBMA can make it difficult to inhale a large breath, to tightly close the vocal folds preventing air leakage, and then to forcefully exhale. A weak cough due to SBMA can make it more difficult to expel foreign materials leading to inflammation, increased mucus production and infections. In some cases, a weakened cough can lead to formation of mucus plugs that reduce airflow in larger airways and collapsed air sacs (alveoli) in smaller airways. If enough alveoli are blocked, a person's oxygen levels will be negatively impacted over time.

A mechanical insufflator-exsufflator (MI-E) device (Philips Cough Assist™ or [Baxter Synclara](#)) can assist coughing by delivering a brief positive inspiratory pressure to the airway through a facemask or mouthpiece followed by a rapid switch to negative pressure. This simulates a natural cough, increasing inspiratory and expiratory volumes and moving secretions up towards the mouth. Some devices vibrate or oscillate the respiratory system to loosen secretions. MI-E has

been shown to increase Peak Cough Flow (CPF) in patients with neuromuscular disorders (NMD) (Chatwin et al. 2003, Chatwin and Wakeman, 2023). Several men with KD have reported these devices to be very helpful and describe them as a “vacuum cleaner for your lungs” and “pulls the mucus up to your throat where you can spit it out”.

Sleep disorders are common in patients with neuromuscular diseases including SBMA. Pharyngeal and respiratory muscle weakness and hypotonia predispose to airway collapse and obstructive sleep respiratory events especially during REM sleep, when most muscles, other than the respiratory muscles, lose complete muscle tone (atonia). In 9 SBMA patients, the [apnea–hypopnea index \(AHI\)](#) was significantly higher in SBMA than controls with obstructive sleep apnea (OSA) evident in 6/9 patients. REM sleep without atonia was evident in three patients also affected by OSA, indicating that their bodies had adapted to avoid losing muscle tone during REM. SBMA patients showed periodic limb movements in sleep. Sleep quality was poorer in SBMA than in controls (Romigi et al 2014). In a larger study with 23 non-ventilated patients with SBMA, OSA (AHI > 5/h) was more frequent (61%) than in control subjects (26%) and median AHI was significantly higher in patients (9.0/h vs. 3.4/h, $p < 0.01$). Inadequate ventilation (alveolar [hypoventilation](#)) as reflected by increased CO₂ in the blood ([hypercapnia](#)) was found in 3/16 patients. Rapid eye movement (REM) sleep without atonia was present in 44% of SBMA patients but only in 4% of controls ($p < 0.01$). During REM and non-REM sleep, no behavioral abnormalities were observed in either group. Periodic limb movements in sleep (index > 15/h) were frequent in SBMA patients but rarely disrupted sleep (Langenbruch et al. 2021). Sleep apnea can lead to daytime somnolence, hypoventilation, hypertension, and other cardiovascular complications. If sleep apnea is suspected, one should have a sleep evaluation. Sleep apnea can be effectively treated, with CPAP being the most common intervention.

Shortness of breath or [dyspnea](#) is not common in SBMA and non-invasive mechanical ventilation is seldom required (Pradat et al. 2020), though it may be needed if respiratory muscle weakness becomes severe. However, for patients with advanced disease, breathing issues and dyspnea are more common. For some, a [tracheostomy](#) and [mechanical ventilation](#) may eventually be required (Kennedy’s Disease Association, 2022). This becomes necessary if one’s swallowing and coughing impairment becomes so severe that they continually choke on saliva and cannot clear mucus from their lungs. Aspiration pneumonia and respiratory failure is the most common cause of death in SBMA.

References:

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This information sheet is one of a series of documents being developed by the Kennedy's Disease Association to provide information on disease manifestations and management.

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