

Adolf Kussmaul: Distinguished Clinician and Medical Pioneer

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Increased jugular venous pressure with inspiration is commonly referred to as Kussmaul's sign; and the disappearance of the radial pulse or a drop in systolic blood pressure of 10 mmHg or greater with inspiration is recognized as pulsus paradoxus. Both Kussmaul's sign and pulsus paradoxus are commonly attributed to the discoveries of Dr. Adolf Kussmaul. Together these two clinical signs are important assessors of pericardial or mediastinal disease (table 1).

On February 22, 1822, Adolf Kussmaul (figure 1) was born in the farming community of Graben, Germany.¹ Exposed to medicine at an early age, he accompanied his father, a physician, on house calls and autopsies. At the age of 18, Kussmaul began studying medicine at the University of Heidelberg where he received his doctorate of medicine.² After graduation in 1845, the University of Heidelberg appointed Dr. Kussmaul to Professor of Medicine.³ His intellectual curiosity led him to study and write about many topics including aphasia, ophthalmologic anatomy, gastric lavage, obstetrics, and polyarteritis nodosa.² Among his numerous contributions to the medical field, Kussmaul's sign is considered one of his more significant discoveries and is still used today by astute clinicians, providing important information that frequently helps in directing further investigation.

Kussmaul's Sign

In his 1873 paper entitled "Ueber Schwielige Mediastino-pericarditis und den Paradoxen Puls" ("Concerning Callous Mediastinopericarditis and the Paradoxical Pulse"), Kussmaul described the phenomenon, originally discovered by Greisinger in 1854, in which "the jugular veins became considerably swollen" and "by each inspiration, a slight increase of its contents could be noted."³ Defined by a visualized increase in jugular venous pressure or pulse with inspiration, this occurrence, contrary to the normal physiological event in which jugular venous pressure decreases with inspiration, can be validated with intravascular hemodynamic monitoring and quantitative measurements of pressures in the jugular venous system.

Clinicians use one of two options to determine the appearance of Kussmaul's sign. The more invasive method measures central venous pressure. Central venous pressure monitoring approximates right arterial pressure, which rises during inspiration reflecting impaired venous return to the right heart. The more commonly preferred, non-invasive method to assess right ventricular filling pressure evaluates the jugular venous pressure with a simple flashlight and ruler. First, the clinician positions the patient at a 45-degree angle. Then shines light on the internal jugular vein at an oblique angle and then extends the flashlight

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Figure 1. Adolf Kussmaul (1822-1902). Photo courtesy of the US National Library of Medicine.

horizontally from the highest point of jugular venous pressure pulsations. The increased jugular venous pressure compared to pre-inspiration is consistent with the presence of Kussmaul's sign.

Physiologically, in healthy individuals, pleural pressure approximates pericardial and mediastinal pressure. Inspiration creates negative intrapleural (intrathoracic) pressure, and enhances the pressure gradient and translocation of blood volume between the positive abdominal pressure and negative intrathoracic pressure within the thorax and superior vena cavae, increasing right ventricular pressure and volume, and decreasing right atrial pressure. Furthermore, the increase in negative intrathoracic pressure causes decreased left-atrial and left ventricular filling from the pulmonary venous system due to increased pulmonary pooling of blood volume which in turn causes a slight drop in systolic blood pressure.

The pathophysiological mechanisms responsible for Kussmaul's sign can be explained by conditions which cause right ventricular dysfunction, impair right ventricular filling, and raise atrial pressure (figure 2). The inability for cardiac

chambers to expand due to (1) hypoelasticity or inelasticity of the myocardium caused by conditions such as infection and fibrosis (restrictive cardiomyopathy) (2) mechanical compartmentalization by constrictive pericardial diseases (constrictive pericarditis), or (3) impaired right ventricular function resulting from right-sided myocardial infarction, impede effective right ventricular filling and cause a paradoxical increase in jugular venous pressure during inspiration.⁴ Thus, Kussmaul's sign is seen in conditions that restrict right ventricular filling such as constrictive pericarditis, right-sided heart failure, right-sided heart infarction, tricuspid stenosis and massive pulmonary embolism. Therefore, conditions that raise right atrial and venous pressure are a prerequisite to cause Kussmaul's sign.

The presence of Kussmaul's sign in patients with constrictive pericarditis and/or restrictive cardiomyopathy and not cardiac tamponade can be accounted for by the physiological differences in filling patterns and thus provides a physician with useful bedside information for diagnostic decision making. Kussmaul's sign is not seen in patients with cardiac tamponade because even though the increase in pericardial pressure exerts an inward force compressing the entire heart during inspiration, the increase in negative intrathoracic pressure is still able to be transmitted to the right side of the heart and subsequent increase in blood flow to the right atrium ensues.⁵ Conversely, the restriction to diastolic filling of the right ventricle in constrictive pericarditis and restrictive cardiomyopathy by the fixed, less compliant constricting pericardium or myocardium respectively at higher chamber volumes, results in the paradoxical increase in jugular venous pressure referred to as Kussmaul's sign.⁶

Effusive-constrictive pericarditis, a rare condition in which features of constriction by the visceral pericardium occurs concomitantly with pericardial effusion. Signs of constrictive pericarditis become unmasked after pericardiocentesis is performed to drain the exudative effusion. Another distinguishing feature of effusive-constrictive pericarditis is the presence of high right atrial pressure which persists after pericardiocentesis.⁷

Kussmaul Respiration and Coma

In 1874, Dr. Kussmaul detailed physical examination findings he had observed in comatose diabetic patients:

A peculiar type of dyspnea...there is not the least suggestion...that the passage of air to or from the lung has to combat obstruction...everything is

Table 1. Signs commonly associated with Kussmaul.

	Constrictive pericarditis	Restrictive cardiomyopathy	Pericardial tamponade
Kussmaul's sign	Yes	Yes	No
Pulsus paradoxus	Yes	Yes	Yes

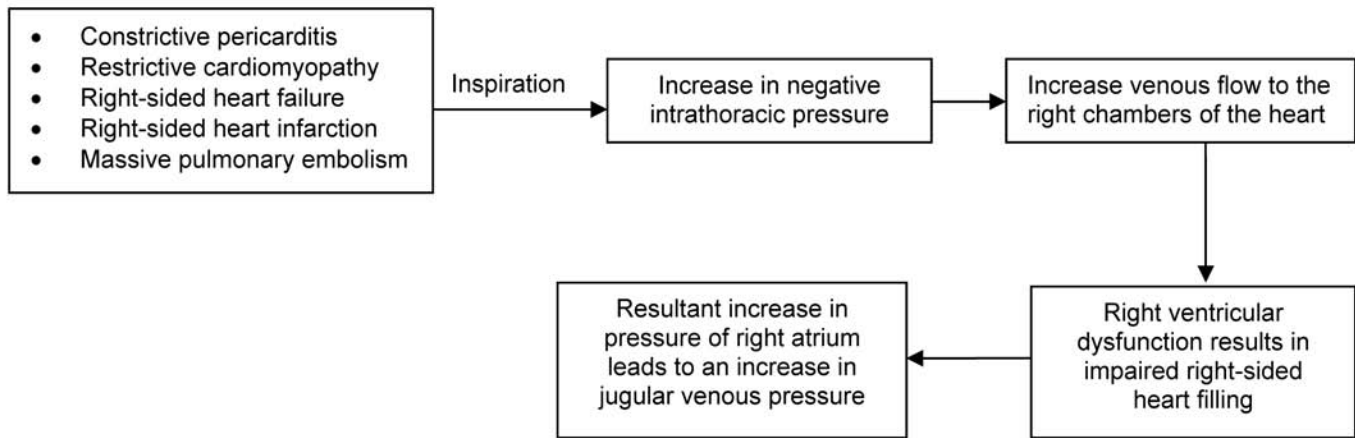


Figure 2. Pathophysiology of Kussmaul's Sign.

indicative of air hunger...even when the patients lies unconscious in deep coma (as translated in reference 2, pg 113 and 114).

The coma that may develop due to diabetic ketoacidosis is sometimes referred to as Kussmaul's coma, and the abnormal respiratory pattern described is called Kussmaul breathing. The definition of Kussmaul breathing varies dependent on the source. Murray and Nadel⁸ define Kussmaul breathing as "a pattern of hyperventilation with deep sighing breaths." Kussmaul breathing may be present in any form of metabolic acidosis. However, in less severe cases of metabolic acidosis, this pattern of breathing may not be detectable. The "air hunger"² described by Kussmaul represents a compensatory increase in minute ventilation to expel carbon dioxide and increase the pH. This compensation occurs rapidly after the decrease in pH with the maximal response expected within 12 to 24 hours post-metabolic acidosis. On an interesting note, there is evidence that this respiratory compensation is not beneficial in chronic metabolic acidosis, as the change in pH towards normal results in less renal excretion of acid over time.⁹

Polyarteritis Nodosa

Working alongside pathologist Rodolf Maier in 1866, Kussmaul's description of what he termed "periarteritis [polyarteritis] nodosa" carried a greater significance than either of them could have envisioned.¹ The lasting impact of this event on medicine is a result of a methodology employed by Kussmaul that was light-years ahead of its time, and would become a model for future physicians and researchers. Understanding and defining disease through laboratory testing coupled with complete clinical evaluation, including patient history and physical, became the standard for future clinicians.¹⁰ With the use of the microscope, Maier and Kussmaul were the first to analyze the histological characteristics of a disease and combine them with the clinical description to arrive at an appropriate diagnosis.¹⁰ While Viennese pathologist Carl von Rokitansky (1804-1878) published the first case of polyarteritis nodosa, his narrow focus on the histopathology

prevented him from fully understanding the true nature of the disease.¹⁰

Pulsus Paradoxus

In the same 1873 manuscript in which he describes Kussmaul's sign, Kussmaul writes of another phenomenon seen in patients with constrictive pericarditis (table 2):

...this affliction results in the symptoms associated with chronic infection of the pericardium, as well as...a pronounced arterial pulse phenomenon...the pulsations of all arteries become smaller or disappear completely...and return with expiration...I propose to call this pulse action paradoxical (as translated in an editorial in reference 1).

Table 2. Causes of pulsus paradoxus.

Cardiac causes

- Cardiac tamponade
- Pericardial effusion
- Constrictive pericarditis
- Pulmonary embolism
- Cardiogenic shock
- Restrictive cardiomyopathy
- Acute myocardial infarction

Extracardiac pulmonary causes

- Bronchial asthma
- Tension pneumothorax

Extracardiac non-pulmonary causes

- Extreme obesity
- Superior vena caval obstruction
- Volvolus of stomach
- Diaphragmatic hernia
- Anaphylactic shock

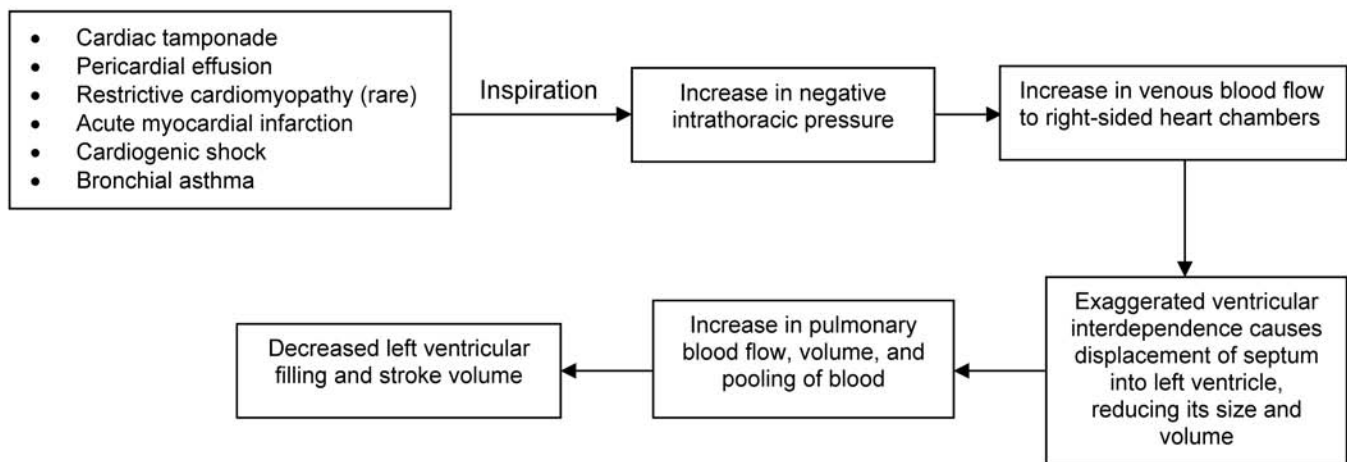


Figure 3. Pathophysiology of Pulsus Paradoxus.

Thus, the paradox Kussmaul describes is that the peripheral pulse disappears while the central heartbeat is still present. Formally defined as a decrease in systolic blood pressure of more than 10 mmHg during inspiration, pulsus paradoxus is an exaggeration of the cardiovascular physiological response to arterial pressure with normal inspiration. The paradox Kussmaul refers to is twofold: (1) a strongly beating heart with weak or absent peripheral pulses, and (2) pulses that seem irregular but actually follow a pattern.

This sign can be tested by placing a sphygmomanometer over the arm and deflating the cuff slowly. The systolic pressure at which the first Korotkoff sounds can be heard during expiration should be recorded. The cuff is then deflated (1 mm per heartbeat) while listening for uniformly loud Korotkoff sounds in both expiration and inspiration. The systolic blood pressure at which Korotkoff sounds can be heard during both phases of respiration should be recorded. The second recorded systolic pressure should be subtracted from the first, and if this value is >10 mmHg, pulsus paradoxus is considered to be present. Palpation of peripheral pulses, especially radial pulses, for decreased force during inspiration, as Kussmaul initially did, is a less formal evaluation for pulsus paradoxus.¹¹ If a patient has an arterial catheter in place, pulsus paradoxus can be detected on the arterial waveform, and this method is the most sensitive for detecting pulsus paradoxus.¹¹ Studying pulse-oximetry waveforms for a reduced plethysmographic peak with inspiration is another noninvasive method for evaluating for the presence of pulsus paradoxus.^{12,13}

Alteration in the normal physiologic mechanisms that govern ventricular filling provides an explanation of the pathophysiology of pulsus paradoxus. During inspiration there is a decrease in intrathoracic pressure accompanied by an increase in the venous flow to the right ventricle. The increased right ventricular volume and pressure from increased venous return causes the interventricular septum to be displaced into the left ventricle reducing its size and volume thereby compromising ventricular filling and compliance.¹⁴ This phenomenon is referred to as ventricular interdependence.

Additionally, the increased negative intrathoracic pressure (1) enhances the pressure gradient (afterload) between the heart and the systemic arterial and venous system and (2) increases pulmonary blood flow, volume, and pooling of blood resulting in decreased left ventricular filling and stroke volume. The final consequence is a decrease in arterial pressure and pulse during inspiration.^{15,16}

Pulsus paradoxus thus occurs as a result of conditions that exaggerate the basic physiological mechanism that occurs during inspiration (figure 3). The following pathologic events operate either alone or concurrently to cause pulsus paradoxus: (1) larger increases in venous blood flow to the right ventricle, (2) greater than normal pooling of blood in the pulmonary venous circulation, (3) decreased pressure gradient between the pulmonary veins and left atrium, and (4) wide deviations in the intrathoracic pressure during inspiration.^{6,14} Apart from being an indicator of pericardial tamponade, increasing pulsus paradoxus magnitude has also been shown to correlate with decreased stroke volume and cardiac output. Therefore, pulsus paradoxus may be used clinically to follow the status of patients with pericardial tamponade.¹⁷

Sensitivity and Specificity of Pulsus Paradoxus

Pulsus paradoxus is often seen in patients with pericardial tamponade because ventricular interdependence is often exaggerated in such cases. Additionally, since there is no impedance towards venous flow to the right ventricle upon inspiration, adequate flow exists in order for the interventricular septum to be displaced.⁵ Pulsus paradoxus shows a sensitivity of 79% for predicting pericardial tamponade, but its specificity is quite low.¹⁷ However, in another study, 98% of patients with pericardial tamponade had pulsus paradoxus.¹⁸ This discrepancy may be explained by the fact that pulsus paradoxus is less likely to be seen in cardiac tamponade when certain comorbidities are present (eg, ventricular hypertrophy, heart failure, severe aortic regurgitation, large atrial septal defect, cardiac adhesions, severe hypotension, and acute left ventricular myocardial infarction).¹¹ These certain conditions mask the presence of pulsus paradoxus because they counteract

the mechanisms responsible for pulsus paradoxus by either decreasing right-sided filling of the heart, increasing filling of the left atrium during diastole, or causing a more subtle shift of the interventricular septum.¹⁴ Echocardiography showing evidence of right ventricular collapse has been more sensitive (93%) and much more specific (100%) than pulsus paradoxus for diagnosing tamponade.¹⁷

Constrictive Pericarditis and Restrictive Cardiomyopathy

When it comes to differentiating between constrictive pericarditis and other cardiac restrictive disorders, such as restrictive cardiomyopathy, the challenge lies in the hands of the physician. A lack of available clinical resources or tools at the bedside to aid in making the diagnosis and differentiating between the two is greatly enhanced by diagnostic imaging studies, eg, magnetic resonance imaging (MRI) and computerized tomography (CT), and echocardiograms. A late S₃ and in some cases S₄ during diastole and a mitral or tricuspid regurgitation murmur, are subtle signs which may be present in restrictive cardiomyopathy. A pericardial knock or diastolic sound caused by rapid inflow of blood followed by an abrupt cessation of flow may be heard on auscultation in patients with constrictive pericarditis. Management and outcomes are critically dependent on defining the correct diagnosis, since patients with constrictive pericarditis can be cured by pericardectomy, resulting in significantly better outcomes than those seen in patients with restrictive cardiomyopathy.¹⁹

In one study by Ling et al, only 19% of patients with constrictive pericarditis were found to have pulsus paradoxus.²⁰ However, in an older series of patients with constrictive pericarditis, 44% of patients had pulsus paradoxus by the modern definition.²¹ Patients with severe constrictive pericarditis are more likely to display a decrease in pulses with inspiration and have a positive Kussmaul sign.²² Pulsus paradoxus is more commonly seen in the syndrome of effusive-constrictive pericarditis, in which tamponade and pericardial constriction coexist and in one 66% of such patients displayed pulsus paradoxus.⁷ More importantly, pulsus paradoxus is usually absent in patients with more advanced restrictive cardiomyopathy as a result of a non-compliant septum that compromises ventricular interdependence.²³ However, it may be seen in patients with constrictive pericarditis because of the interventricular septal displacement towards the left ventricle during diastole, thus impeding left ventricular filling.

Gastroenterology, Esophagogastroscope, and the First Ophthalmoscope

In an article published in 1869, Kussmaul described the treatment of gastric outlet obstruction with associated dilation by means of a stomach pump.¹⁰ The successful use and treatment of a patient with gastric ectasia through such methods was described, with the patient's symptoms subsided after only a few days. While the stomach pump was used by others at the time, Kussmaul played a key role in popularizing the device.¹ In another example of Kussmaul's sagacity; he

addressed the possibility of treating more complex cases of gastric outlet obstruction:

...whether perhaps bolder species of a distant future will attempt, in such cases through gastrotomy, creation of a gastric fistula and dilatation of the stricture with a knife or probe, to achieve radical successes...who dares today to decide this question? One must fear being softly or loudly ridiculed for just posing it (as translated in reference 10).

In 1881, Christian Billroth (1829-1894) acted upon this suggestion and attempted what was considered at that time an almost impossible feat; a full gastric resection in order to treat a gastric outlet obstruction.²⁴ Also described within the article are the first references towards performing esophageal and gastric endoscopy using a rigid instrument.¹⁰

In a letter written in 1899 to one of his former assistants, Kussmaul described that he had incorporated the use of an endoscope into his clinical practice, visualizing a proximal esophageal carcinoma.¹⁰ After he introduced the idea and demonstrated the benefits of using a gastroscope, subsequent physicians such as Rudolf Schindler and Basil Hirschowitz expanded on the ideas set forth by Kussmaul and advanced the field of endoscopy to where it is today.¹⁰

Even though Kussmaul was unsuccessful in creating a successful final product, he is credited with being the first person to recognize the need for the ophthalmoscope. Kussmaul began his work on creating a tool that could view the interior of the eye at the age of 23, at which time he was a medical student in Heidelberg, Germany.²⁵ In 1845, he wrote a dissertation entitled "Die Farbenerscheinungen im Grunde des menschlichen Auges" ("An Important Description of Colour Phenomena in the Fundus Oculi"), which contained the blueprint for construction of an ophthalmoscope.²⁵ Despite a problem with the fundamental optics of the device, which would later be corrected by Hermann von Helmholtz, Kussmaul undoubtedly played an integral role in the creation of the ophthalmoscope and provided physicians with a tool that enabled them to better understand and treat diseases associated with the interior of the eye.

In the early morning of May 28, 1902, Dr. Kussmaul succumbed to his bout with coronary sclerosis, leaving behind his many contributions to medical science.² In his 80 years of life, Adolf Kussmaul made discoveries seemingly beyond the capabilities of one man. He wrote prolifically in diverse fields (for example, cardiology, rheumatology, endocrinology, gastroenterology, psychiatry, and neurology). Dr. Kussmaul serves as a model for medical professionals and students exemplifying that there are no limits to exploration. Adolf Kussmaul predicated his achievements on the foundations of science: observation, hypothesis, experimentation and analysis, as will future discoverers in the medical sciences.

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