Ask Mayo Expert: Anemia Workup in 1919

To the Editor: In 1919, death from pernicious anemia was common, with 0.5% to 1% of deaths attributable to the disease.[1] Establishing this diagnosis without modern laboratory testing was challenging. Disseminating Mayo Clinic's knowledge relied on textbooks and could not easily keep pace with rapidly evolving medical knowledge.

In that year, the leading Mayo Clinic expert in the diagnostic workup of anemia was Dr Arthur Hawley Sanford (Figure), who became the director of the clinical laboratories in 1911.[2] In a concise review presented to the Medical Society of the State of New York in 1919, and published via textbook, he outlined Mayo Clinic's state-of-the-art anemia workup.[3]

Dr Sanford began his workup noninvasively. A funduscopic examination of the "eye grounds" was performed. Blood was drawn for a series of tests including a manual blood count, observation of the sedimentation rate, and measurement of the average red blood cell volume. The Wassermann reaction, in which cardiolipin is mixed with blood, was performed to test for syphilis. Stool samples were examined for ova and parasites. The patient's pharynx was examined to determine if a source of chronic sepsis was present. The osmotic fragility test was performed, which is identical to today's test.

FIGURE. Dr Arthur Hawley Sanford.

More invasive testing followed. The Mayo Clinic Ewald test meal of arrowroot biscuits and water was served to perform analysis of gastric secretion.[3] A nasogastric tube was placed for analysis of aspirated gastric contents. A radiograph was performed to detect perforation. Interpreting the testing was difficult, but the amount of hydrochloric acid present and its neutralization following this standardized meal was theorized to show the patient's susceptibility to ulcers.

Following the Ewald test, the nasogastric tube would be advanced to evaluate the duodenal contents. A new method, referred to as Schneider's method, used spectroscopic analysis of urobilin and urobilinogen content to determine if the duodenal secretion contained urobilinogen. In chronic anemia, the patient would have a normal value of urobilinogen, but in a patient with an elevated urobilinogen, it would be indicative of pernicious anemia.[4]

Contrast Dr Sanford's state-of-the-art workup in 1919 to the similar patient with pernicious anemia presenting in 2019. When physicians have clinical questions they could have AskMayoExpert, developed by a team of Mayo Clinic hematologists and internists accessed in a click and be advised to perform the following workup.[5] A complete blood count would be obtained through an automatic Coulter Counter. The anemia would then be classified as macrocytic based on an elevated mean corpuscular volume (MCV). After classifying the anemia based on MCV, a serum homocysteine, folate, reticulocyte count, and a pernicious anemia cascade would be ordered. The pernicious anemia cascade reflexively checks methylmalonic acid (MMA), gastrin, and intrinsic factor antibodies if the B12 level is low or borderline. The labs would likely result in an elevated MMA and positive anti-intrinsic factor antibodies.

A century separates these diagnostic workups. Whether by 20th-century textbook or by 21st-century Internet, the dissemination of knowledge by Mayo Clinic is key to its mission.

William J. Archibald, MD
Internal Medicine
Mayo Clinic
Rochester, MN

Renee E. Ziemer, BA
Mayo Clinic Historical Unit
Mayo Clinic
Rochester, MN

James S. Newman, MD, MHA
Mayo Clinic College of Medicine
Hospital Internal Medicine
Mayo Clinic
Rochester, MN

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Embolized Spinal Dural AV Fistula Repairs Syringomyelia and Polyradiculopathy

To The Editor: A 68-year-old man presented with 3 years of progressive painful lower extremity weakness. He had urinary retention.

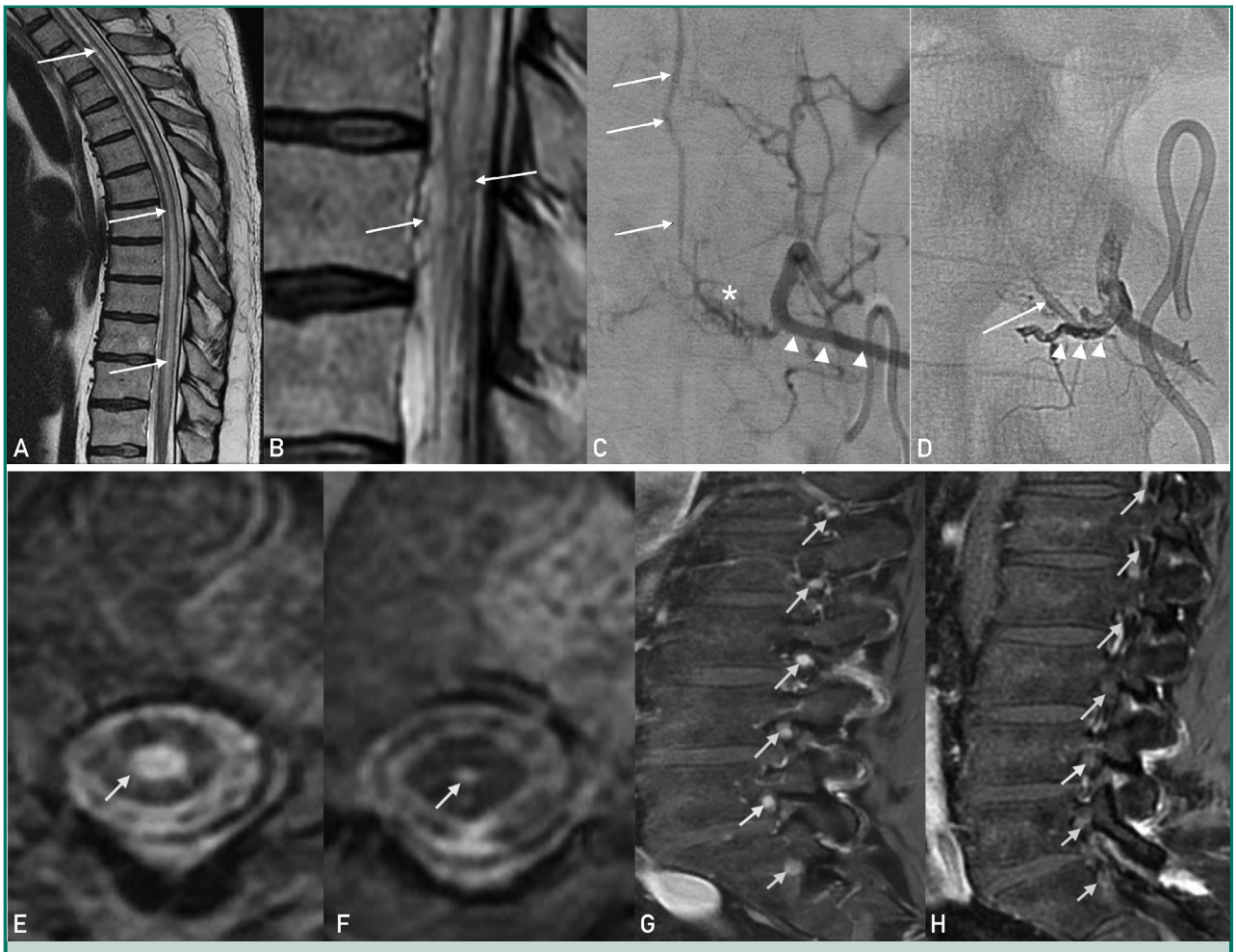

FIGURE. (A), Sagittal T2-weighted magnetic resonance imaging (MRI) scan shows the longitudinally expansive spinal syringomyelia in the described patient (**white arrows**). **(B),** Sagittal T2- weighted MRI revealing subtle intrathecal flow voids within the thoracolumbar spinal canal (**white arrows**). **(C),** Spinal angiogram radiograph demonstrates an abnormal draining vein (**white arrows),** a spinal dural AV fistula (**asterisk**) arising from the left L1 lumbar artery (**white arrow heads**). **(D),** Postembolization shows resolution of the fistula by embolization material (**white arrow**), with persistence of the lumbar artery (**arrow heads**). **(E and G),** Pre-embolization. **(E),** Axial T2-weighted MRI shows the syrinx (**white arrow**) at the C7 level; **(G)** postcontrast sagittal T1-weighted MRI shows enlargement and enhancement of the lumbosacral spinal roots (**white arrows**), also seen at thoracic and cervical levels (not shown). **(F and H),** Three months postembolization; **(F)** axial T2- weighted MRI demonstrates a decrease of the syrinx (**white arrow**) maximal diameter from 6 mm to 2 mm at C7 level; **(H)** postcontrast sagittal T1-weighted MRI shows resolution of the lumbosacral root enlargements and enhancement.

Neurological examination showed spastic paraparesis (Medical Research Council grades 1 to 3, worst at ankles and thighs). Reflexes were diffusely reduced with bilateral Babinski signs. There was symmetric loss of vibration and pain detection extending to the umbilicus and hands. He required 2-person assistance to stand and walk. A large cervicothoracic syrinx was seen on magnetic resonance imaging (MRI) in association with cervical stenosis. Despite cervical decompression fusion at C5-C6, he continued to worsen. Repeated MRI with contrast identified enlargement and enhancement of all roots. Electromyography and nerve conductions identified an axonal predominant chronic-active polyradiculopathy C5-T1 and L2-S1 with fibrillations extending to paraspinal muscles. Cerebrospinal fluid (CSF) protein

was elevated at 102 mg/dL, and an inflammatory myelopolyradiculopathy with syrinx was postulated, with no other explanation found. He did not respond to weekly intravenous immunoglobulin (IVIG) and intravenous (IV) methylprednisolone, which were discontinued after 6 months.

In referral, we noted that the syrinx was associated with thoracolumbar flow voids, raising the possibility of a spinal dural arteriovenous fistula (SDAVF) (Figure). Spinal angiogram confirmed the SDAVF, arising from the left L1 lumbar artery, which was treated by transarterial embolization (Figure). Three months after the procedure, he had normal power and near-normal gait, with resumption of outdoor hiking. Babinski signs and urinary retention persisted, but reflexes returned, and sensation improved. Repeated MRI of the spine showed the cervicothoracic syrinx resolved, and all roots had normalized: no longer enlarged or enhancing (Figure).

Syringomyelia is the result of an expansion of CSF in the spinal cord. It has been most commonly recognized in association with Chiari malformation-type 1 (CM-1), but also in spinal cord tumors, trauma, ischemia, infection, and inflammatory arachnoiditis.[1] In CM-1, CSF blockage at the foramen magnum results in venous congestion and the formation of the syrinx.[2] In our case, once the SDAVF was embolized, the spinal root and central canal congestion resolved, leading to the dramatic clinical and radiographic improvements (Figure). Our patient still has urinary retention, and like CM-1 patients status post-foramen magnum decompression, some extent of myelomalacia is predicted in chronic disease. There are only 2 other cases reported in the literature of SDAVF associated with syrinx, and polyradicular features were not highlighted.[3,4] We believe that our patient, and possibly others with SDAVF and syringomyelia, may have a significant clinical polyradicular component responsive to embolization.

This case highlights that idiopathic syringomyelia should not be diagnosed without serious consideration of SDAVF. Lower-extremity weakness, episodes of acute worsening, sensory level, or sphincter dysfunction should raise the possibility of SDAVF. A decision to move to spinal angiogram can be assisted by observation of venous congestion on routine MRI as witnessed by flow voids on T2 imaging most commonly seen on sagittal images (Figure). Early diagnosis may help prevent permanent myelomalacia, polyradicular injury, and poor prognosis.[5] Neural injury from chronic congestion of spinal roots may be more likely to reverse rapidly compared with the direct congestion within the spinal cord central canal after SDAVF closure.

Marcus V. Pinto, MD
Department of Neurology
Mayo Clinic
Rochester, MN

Harry Cloft, MD, PhD
Department of Radiology
Mayo Clinic
Rochester, MN

Christopher J. Klein, MD
Department of Neurology, and Department of Laboratory Medicine and Pathology
Mayo Clinic
Rochester, MN

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Quality of Life of Patients With Marfan Syndrome After Valve-Sparing or Valve-Replacement Operations

To the Editor: Few studies have evaluated quality of life (QOL) in patients with Marfan syndrome (MFS). Most patients with MFS are dissatisfied with their self-image, report low self-esteem, and express difficulty coping with the ramifications of their condition.[1] A recent surgical-series study, however, showed that patients with MFS who underwent thoracoabdominal aortic repair rated their physical and mental component scores higher than those of the general population.[2] As options for prolonging life expectancy of patients with MFS increase,[3] assessing the impact of these interventions on QOL becomes even more important. Although studies have reported late outcomes of operations for aortic aneurysms in patients with MFS, to our knowledge, no studies have examined the QOL of patients with MFS stratified by type of operation.

This study included patients with MFS and aortic root aneurysms who underwent either aortic valve-sparing (AVS) root repair or aortic valve and root replacement (composite AVR) from February 11, 2005, through September 3, 2010,