Review Article

Primer on Adhesive Arachnoiditis

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ABSTRACT

This article explores the resurgence of adhesive arachnoiditis (AA), a previously rare disorder, in the 21st century. Historically linked to tuberculosis and other infections, AA's re-emergence is attributed to advancements in MRI technology, aiding in improved diagnosis and an increase in spinal procedures, possibly leading to iatrogenic cases. Complications of AA include chronic pain and motor dysfunction, significantly impacting quality of life. Treatment involves a multidisciplinary approach, including pharmacological and osteopathic treatments, possible surgical interventions, and psychological support. The article provides an in-depth look at AA's epidemiology, clinical profile, causes, diagnosis, and treatment strategies, highlighting its complex nature and the necessity for heightened awareness among medical practitioners.

INTRODUCTION

In 1872, Arachnoiditis (ARC) was defined as inflammation of the arachnoid membrane.[1] The arachnoid is the middle layer of the meninges, the protective covering enveloping and encasing the brain and spinal cord. The outer layer of the spinal canal covering is the dura, and the innermost layer is the arachnoid membrane.

Spinal fluid flows between the arachnoid membrane and the pia mater, the meninges' innermost layer.[2,3] ARC was often called a "Devil's Disease" in the 1800s because it was associated with severe pain, emaciation, suffering, and early death. The usual causes were tuberculosis or syphilis.[4,5]

In 1855, Dr. Thomas Addison published his famous monograph on adrenal insufficiency.[6] About one-third of his eleven cases had postmortem spinal cord pathology compatible with a diagnosis of ARC. There was no treatment in the last two centuries, and even until now, persons with AA may be told it is a hopeless disease and that nothing can be done.

In the early 1900s, Horsley and Harvey, two well-known British physicians who described blood circulation and anatomists, studied postmortem cases. They found adhesions that adhered or glued cauda equina nerve roots to the arachnoid membrane of the lumbar-sacral spinal canal cover.[7,8] Since this discovery, adhesive arachnoiditis (AA) has been used to define the clinical condition whereby some cauda equina nerve roots are adhered by adhesions to the arachnoid membrane. (Figure 1)

Although inflammation of the arachnoid membrane can occur in the brain or upper levels of the spinal cord, lumbar-sacral AA is now diagnosed more frequently in clinical practice. Reported here are the results of our preliminary efforts to study and develop some diagnostic and clinical measures for lumbar-sacral AA and our early clinical experiences.

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EPIDEMIOLOGY

The epidemiology of AA remains challenging to quantify due to its varied clinical presentations and historical underdiagnosis. While exact prevalence and incidence rates need to be well-established, advances in diagnostic imaging and heightened clinical awareness have increased identified cases.[9] Historically linked to complications from specific medical procedures and infections, the condition's re-emergence has paralleled advances in medical technology and increased spinal interventions.[9] Data suggests that while AA is not as standard as widespread conditions like hypertension or diabetes, its impact on affected individuals is significant and merits attention from the medical community.[9] Further epidemiological research is needed to determine the actual burden of AA.

METHODS

Due to the severe nature of AA and the lack of epidemiologic and clinical information, the Tennant Foundation has established an Adhesive Arachnoiditis Study and Education Project. The project aims to collect preliminary demographic and clinical data to help develop diagnostic and therapeutic measures for clinical management. The primary method to collect clinical data is to review AA cases documented by MRI and clinical information. An Institutional Review Committee of the Tennant Foundation has reviewed and approved the project. Cases are voluntarily submitted to us by patients, families, and physicians. To obtain MRI images and case review materials, the project published its desire through AA social media groups recently developed by the re-emergence of AA.

Cases have come to us for review from 50 countries suggesting that increased AA diagnosis is a global development. All cases have signed a release to use their personal information without identification for educational purposes. There has been no financial charge or remuneration for persons with AA who have submitted their MRIs and clinical data to us for review and study. No medications were prescribed, and laboratory tests were performed on cases who participated in the study. Table 1 shows basic information on eighty consecutive cases submitted to and reviewed by the project.

Diagnostic and treatment measures reported here come primarily from a review of published literature and clinical and anecdotal observations from twenty-five MRI-documented cases of AA treated in Dr. (redacted for peer review) clinical practice.[10,11,12-16]

CLINICAL CAUSES

Several epidemiologic studies and reports show that back pain has increased this century.[13-24] The reasons for this increase appear to be multifactorial and include a sedentary lifestyle, obesity, bucket seats, diet, and poor posture.[18-24] Although the precise reasons for the increased diagnosis of AA in this century are somewhat unclear, it has paralleled the rise in the incidence of back pain.[25-27]

The increase in AA diagnoses could be attributed to advancements in MRI technology. These newer techniques enhance the contrast and clarity between spinal fluid and solid tissues, thereby improving the ability to identify AA accurately.[25-27, 28-30] This technological progress in medical imaging may be a critical factor in heightened detection and diagnosis of the condition. People identified with AA today have multiple possible causes and risk factors. Herniated discs are probably the most common precursor of AA.[25,26]

Risk factors that may predispose a person to AA include genetic connective tissue diseases such as Ehlers-Danlos Syndrome, autoimmune disorders such as systemic lupus erythematosus and rheumatoid spondylitis, trauma, and anatomic spine defects such as scoliosis and spondylolisthesis. Medical procedures, especially epidural injections and surgery, are highly associated with AA. Still, these procedures treat AA's precursors and risk factors, so they are not the singular cause of the disease.[27,28] In summary, cases of AA observed in this century have multiple precursors and risk factors that precede its development.

RE-EMERGENCE

After treatment for tuberculosis and syphilis were developed in the first half of the last century, AA essentially disappeared.[4,5] AA re-emerged in the mid-1900s when some toxic dyes (i.e., Pantopaque™) were injected into the spinal canal to perform myelograms.[10,31] Unfortunately, a small percentage of people who received the dyes developed AA.[10,12,31] Toxic myelogram dyes continued until Magnetic Resonance Imaging (MRI) was developed in the late 1980s. At that time, AA again disappeared to a point where it was classified as a rare disease. During this century, AA is being increasingly identified and treated.[32] It is currently unknown whether it is becoming more common or whether there is a growing awareness and better diagnosis of the condition. However, it is not as common as such prevalent diseases as hypertension, diabetes, and asthma.[28,33-35] Just as in past times, persons with AA in this century suffer greatly from intractable pain, multiple neurologic complications, and stifling immobility.[13-16]

CLINICAL PROFILE

AA usually presents to the clinical setting as back pain that hasn't responded to standard therapies. Table 1 shows the clinical profile of eighty consecutive cases of MRI-documented AA that we reviewed in our study project in 2022. The predominant group with AA in this review was a middle-aged female who had an anatomic abnormality of the spine and had undergone multiple epidural injections and spine surgery. Major symptoms were constant pain relieved by standing and worsened by lying flat or raising one's leg. Urination difficulties and blurred vision were common. An interesting symptom is that patients had sensations of insects crawling or water running down their legs.

PHYSICAL EXAMINATION

There are no physical signs that specifically identify AA. Some abnormal physical symptoms, however, are almost always present. There may be lower extremity weakness and a diminution of reflexes. Pain is usually elucidated on straight leg raising. Contractions and indentation of muscles and soft tissues are commonly observed on examination of the back. These anatomic distortions occur due to splinting caused by pain and spinal fluid leakage into the soft tissues of the back. Spinal fluid is a toxic irritant to the muscles and soft tissues between the spinal column and skin surface.

LABORATORY TESTING

AA is an inflammatory disease.[1,8,36] It will usually produce hematologic evidence of excess inflammation.[32] White blood cell count, erythrocyte sedimentation rate, C-reactive protein, and several cytokines may elevate. The latter may also elevate since degenerated intervertebral D discs elevate cytokine levels, typical in patients with AA.[25,37,38] (Table 1). An MRI is required to validate the presence of AA, but abnormal laboratory tests may indicate a need for MRI confirmation.

STAGING AND CLASSIFICATION

AA can be staged or classified as mild, moderate, severe, or catastrophic.[39] (Table 3) Unfortunately, AA may progress through the stages from mild to fatal. The mechanism of progression is a spread of inflammation inside the spinal canal with subsequent scarring and even calcification of nerve roots.[15] In the late stages (Table 3), a person may become seriously debilitated, immobile, and bed-bound.[39] The bowl and bladder routinely become dysfunctional, and immune deficiency may subject the patient to serious systemic infections. Persons with AA in the catastrophic stage require palliative pain care.

TABLE 1.
Clinical Profile of 80 MRI-Documented Cases of Adhesive Arachnoiditis

	No.
1. Females	65 – 81%
2. Males	15 – 19%
3. Age Range in Years	18 – 80
4. Mean Age ± S.D. in Years	48.9 ± 13.7
5. No. with a Predisposing Spinal Condition*	61 – 76.3%
a. Herniated discs	44 – 55%
b. Spondylolisthesis	17 – 21.25%
c. Osteoporosis	6 – 7.5%
d. Spine arthritis	23 – 28.75%
e. Scoliosis	9 – 11.25%
f. Tarlov cysts	9 – 11.25%
6. No. with One or More Spinal Surgeries	43 – 53.8%
7. Total No. of Spine Surgeries in 43 Cases	91
8. Range of Surgeries in 43 Cases	1 to 8
9. No. Who Had Two or More Spine Surgeries	22 – 27.5%
10. No. Who Had One or More Epidural Injections	69 – 86.3%
11. Total No. Epidural Injections in 69 Cases	236
12. Range of Epidural Injections in 69 Cases	1 to 20
13. No. Reported Over 8 Epidural Injections	16 – 20.0%
14. Symptoms and Complications Reported by Over 55% of Cases	
a. Pain Relief on Standing	70 – 87.5%
b. Standing too Long Causes Need to Lie Down	69 – 86.3%
c. Hurts to Lie Flat on Back	67 – 83.8%
d. Pain Always Present	66 – 82.5%
e. Shooting Pains, Tremors, or Jerking in Legs	64 – 78.8%
f. Burning Pains in Feet	63 – 78.8%
g. Cold Hands or Feet	58 – 72.5%
h. Crawling of Insects on Skin	58 – 72.5%
i. Water Dripping/Running Down Legs	52 – 66.3%
j. Difficulties Starting Urination/Defecation	51 – 63.8%
k. Leg Raise Hurts Back	50 – 62.5%
l. Blurred Vision	47 – 58.8%
m. Pain Behind Eyes	45 – 56.3%

COMPLICATIONS

AA may produce several complications and consequences, summarized in Table 2.[33] Pain can become highly debilitating and require the most potent pain relief measures. Nerve roots entrapped in the mass may connect to the bladder, intestine, stomach, sex, organs, and lower extremities.[40] Patients may experience radiating pain in waves that causes lower extremity jerking, spasms, and burning sensations in the buttocks, hips, legs, or feet. Weakness of the legs requiring ambulation assistance with a cane, walker, or wheelchair is common in severe cases. The intraspinal mass of AA may impair spinal fluid flow and produce blurred vision, tinnitus, headaches, and possibly dementia if spinal fluid flow isn't normalized.[31] Anorexia, malnutrition, and a bed-bound state occur in advanced stages.[39] (Table 3) Spinal fluid leakage may occur because the inflammatory mass of AA can erode through the spinal canal covering. Premature deaths likely occur due to sepsis and cardiovascular or adrenal failure.

TREATMENT

In the past, patients were usually told, "Nothing can be done." Today, this is not true. Although no specific pharmacologic agent is labeled for the treatment of AA, treatment measures reported to us in our Study and Education Project by patients and physicians indicate positive outcomes. Treatment efforts reported to us have resulted in pain relief, improved mental and physical function, and apparent cessation of disease progression.

Since there is no single treatment agent, we advocate a three-component medical approach: (1) suppression of neuroinflammation, (2) neuroregeneration, and (3) pain control. Unless the patient is on daily opioid drugs, our first choice for pain relief and suppression of inflammation is low-dose naltrexone. The starting dosage is 7.0 mg, given twice a day and then titrated upward over time, according to patient symptoms. The maximum dosage is 14 mg a day. Our patients have responded well to low doses, intermittent ketorolac, and methylprednisolone or dexamethasone to control neuroinflammation. Side effects and complications of these agents are avoided by use of only one to three times a week. Single ketorolac dosages are usually 10 to 30 mg, methylprednisolone 2 to 4.0 mg, and dexamethasone .5 to .75 mg. Ketorolac can be administered by injection, troche, or oral routes. Some mild to moderate cases of AA have responded to the anti-inflammatories diclofenac, meloxicam, or indomethacin.

TABLE 2.
Complications and Consequences of Adhesive Arachnoiditis[33]

COMPLICATIONS	CONSEQUENCES
SPINAL FLUID FLOW OBSTRUCTION	→ Headache → Blurred vision → Tinnitus (Ringing in ears) → Mental impairments (memory, attention, reading, and mathematical ability)
SPINAL FLUID FLOW LEAKAGE	→ Contraction of paraspinal muscles → Tissue over lumbar spine indents or "caves in" → Arms can't extend
SITTING/STANDING ABILITY IMPAIRED	→ Can't sit or stand in one position very long
INTRACTABLE PAIN SYNDROME	→ Constant ("24/7") pain → Cardiovascular, metabolic, and endocrine dysfunctions
NEUROPATHIC SYMPTOMS	→ Burning feet → Shooting pains into buttocks or legs → Radiating type pain
IMPAIRED IMMUNITY	→ Sepsis (infection) → Premature death
LOSS OF BLADDER, BOWEL, AND SEXUAL FUNCTION	→ Urgency, incontinence, hesitancy, or paralysis → Bloating, abdominal pain, alternating constipation, and diarrhea → Sex organs disabled, loss of libido
LEG AND FOOT PARALYSIS	→ Weakness → Inability to stand or walk → Foot drop
BIZARRE NEUROLOGIC SYMPTOMS	→ Sensation of water or insects on legs → Burning of feet or buttocks → Leg jerking, spasms, "restless legs"
DIETARY DYSFUNCTION	→ Loss of appetite → Excess sugar intake → Malnutrition/weight loss → Anorexia

We advocate neuroregeneration strategies, including polypeptides and administering anabolic hormones such as dehydroepiandrosterone (DHEA), colostrum, or nandrolone. The latter carries a specific label for nutritional deficiency states such as AA. A high-protein diet with collagen or amino acid supplements is routinely recommended. Pain control is symptomatic and standard. A neuropathic agent such as a benzodiazepine or gabapentin is routine. In the advanced stages of AA, opioids may be required.

Low or moderate dosages under 90 mg of daily morphine equivalence will almost always suffice. The combination of inflammation suppression and neuroregeneration measures significantly reduces the requirements for opioids. We have seen a significant drop in opioid use in most patients. Daily physical exercise of the lower extremities is recommended to help prevent paralysis of the legs and feet. Leg exercises include straight leg raising, stretching, foot flexing, and walking. Water soaking and electromedical therapies are suggested as ancillary measures.

TABLE 3.
AA Stages[3]

STAGE ONE – MILD
→ Extremities: full range of motion, strength, extension → No urinary or central symptoms* → Normal ambulation → Low-level pain: non-opioid management is sufficient
STAGE TWO – MODERATE
→ Extremities: full range of motion, strength, extension → Some urinary, gastrointestinal tract, and central symptoms* → Normal ambulation → Constant pain: non-opioid management is sufficient
STAGE THREE – SEVERE
→ Extremities: some deficiency in range of motion, strength, extension → Significant urinary, gastrointestinal tract, and central symptoms* → Ambulates with assistance+ → Severe, constant pain that usually requires daily opioids
STAGE FOUR – CATASTROPHIC
→ Extremities: significant deficiency in range of motion, strength, extension → Significant urinary, gastrointestinal tract, and central symptoms* → Bed bound all or part of each day → Ambulation requires assistance → Severe, intractable pain that requires palliative care
Notes on Interpretation ** Central refers to headaches and eye/ear/nasal symptoms such as blurred vision, tinnitus, vertigo, or nasal dripping* *+Ambulation assistance means cane, walker, wheelchair* ***Note:** Categories can overlap. Mild and moderate categories have the best potential for recovery.*

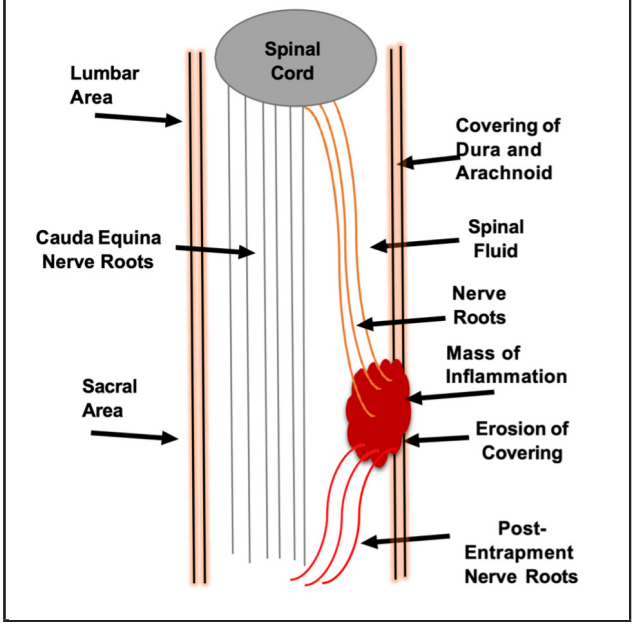
CONCLUSION

The recent resurgence of AA is closely linked to advancements in MRI diagnostics, enhancing its detection. This condition, often associated with chronic back pain unresponsive to standard treatments, manifests through symptoms like urinary dysfunction and neurological discomfort. Its etiology is diverse, encompassing intervertebral disc degeneration, genetic and immunological factors, as well as post-procedural trauma. Despite the absence of controlled pharmaceutical trials, current treatments focusing on inflammation suppression, neuroregeneration, and pain management have shown varying effectiveness. This renewed recognition of AA underscores the imperative for the medical community to adapt and refine their diagnostic and treatment approaches, underlying the necessity for heightened vigilance and proactive management of this complex condition.

AUTHOR DISCLOSURES:

No relevant affiliations or conflicts of interest.

FIGURE 1:
Diagram of Entrapped Nerve Roots in AA[40]



REFERENCES:

1. Thomas J. Arachnitis and Arachnoiditis. In: Comprehensive Medical Dictionary. Philadelphia, PA: J.B. Lippincott & Co; 1873:57.
2. Damkier HH, Brown PD, Praetorius J. Cerebrospinal fluid secretion by the choroid plexus. Physiol Rev. 2013;93(4):1847-1892.
3. Kiiski H, Aanismaa R, Tenhunen J, *et al.* Healthy human CSF promotes glial differentiation of hESC-derived neural cells while retaining spontaneous activity in existing neuronal networks. Biol Open. 2013;2(6):605-612.
4. Aldrete JA. History and evaluation of arachnoiditis: The evidence revealed. Insurgentes Centro 51-A. Col San Rafael, Mexico. 2010:3-14.
5. Aldrete JA. Arachnoiditis: The Silent Epidemic. Mexico: Future Med Publishers; 2003.
6. Addison T. On the Constitutional and Local Effects of Disease of the Supra-Renal Capsules. London, England: Samuel Highley; 1855.
7. Harvey SC. Meningeal adhesions and their significance. Interstate Post Grad Med. 1926;2:27-31.
8. Horsley V. Chronic spinal meningitis: it's differential diagnosis and surgical treatment. Br J Med. 1909;1:513-517.
9. Maillard J, Batista S, Medeiros F, *et al.* Spinal Adhesive Arachnoiditis: A Literature Review. Cureus. 2023;15(1):e33697. Published 2023 Jan 12. doi:10.7759/cureus.33697
10. Quiles M, Marchiselo PJ, Tsairis P. Lumbar adhesive arachnoiditis: Etiologic and pathologic aspects. Spine. 1978;3(1):45-50.
11. Todeschi J, Chibbaro S, Gubian A, Pop R, Proust F, Cebula H. Spinal adhesive arachnoiditis following the rupture of an Adamkiewicz aneurysm: Literature review and a case illustration. Neurochirurgie. 2018 Jun;64(3):177-182.
12. Ross JS, Masaryk TS, Modic MT, *et al.* MRI imaging of lumbar arachnoiditis. AJR Am J Roentgenol. 1987;149(5):1025-1032.
13. Bourne IH. Lumbosacral adhesive arachnoiditis: A review. J R Soc Med. 1990;83(4):262-265.
14. Delamarter RB, Ross JS, Masaryk TS, *et al.* Diagnosis of lumbar arachnoiditis by magnetic resonance imaging. Spine. 1990;15(3):304-310.
15. Shiraishi T, Crook HV, Reynolds A. Spinal arachnoiditis ossificans: Observations on its investigation and treatment. Eur Spine J. 1995;4(1):60-63.
16. Stookey B. Adhesive spinal arachnoiditis simulating spinal cord tumor. Arch Neurol Psychiatry. 1927;17:151-164.
17. Dahlhamer J, Lucas J, Zelaya C, *et al.* Prevalence of chronic and high-impact chronic pain among adults, United States, 2016. MMWR Morb Mortal Wkly Rep. 2018 Sep 14;67(36):1001-1006.
18. Hoy D, March L, Brooks P, *et al.* The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014;73(6):968-974.
19. Smith M, Davis MA, Stano M, *et al.* Aging baby boomers and the rising cost of chronic back pain: secular trend analysis of longitudinal medical expenditures panel survey data from 2000 to 2007. J Manipulative Physiol Ther. 2013;36(1):2-11.
20. Strine TW, Hootman JM. US national prevalence and correlation of low back and neck pain among adults. Arthritis Rheum. 2007;57(3):656-665.
21. Andersson GB. Epidemiological features of chronic low back pain. Lancet. 1999;354(9178):582-585.
22. Deyo RA, Dvorkin SF, Antmann D, *et al.* Report of the NIH Task Force on chronic low back pain research standards. J Pain. 2014;115(2):569-585.
23. Deyo RA, Mirza SK, Martin BI. Back pain prevalence and visit rates: estimates from U.S. national surveys, 2002. Spine. 2006;31(23):2724-2727.
24. Freburger JK, Holmes GM, Agans RP, *et al.* The rising prevalence of chronic low back pain. Arch Intern Med. 2009;169(3):251-258.
25. Jackson A, Isherwood I. Does degenerative disease of the lumbar spine cause arachnoiditis? A magnetic resonance study and review of the literature. Br J Radiol. 1994;67(797):840-847.
26. Jorgenson J, Hansen PH, Steenskoo V, *et al.* A clinical and radiological study of chronic lower spinal arachnoiditis. Neuroradiology. 1975;9(3):139-144.
27. Epstein NE. The risks of epidural and transforaminal steroid injections in the spine: commentary and a comprehensive review of the literature. Surg Neurol Int. 2013;4(Suppl 2):S574-S593.
28. Eisenberg E, Goldman R, Schlag-Eisenberg D, *et al.* Adhesive arachnoiditis following lumbar epidural steroid injections: A report of two cases and literature review. J Pain Res. 2019;12:513-518.
29. Todeschi J, Chibbaro S, Gubian A, Pop R, Proust F, Cebula H. Spinal adhesive arachnoiditis following the rupture of an Adamkiewicz aneurysm: Literature review and a case illustration. Neurochirurgie. 2018 Jun;64(3):177-182.
30. Anderson TL, Morris JM, Wald JT, Kotsenas AL. Imaging Appearance of Advanced Chronic Adhesive Arachnoiditis: A Retrospective Review. AJR Am J Roentgenol. 2017 Sep;209(3):648-655
31. Whedon JM, Glassey D. Cerebrospinal fluid stasis and its clinical significance. Altern Ther Health Med. 2009;15(2):54-60.
32. Tennant F. Adhesive Arachnoiditis: Identification, Treatment, and Management of Inflammatory Pain. Podiatry.com. Accessed January 11, 2024. https://www.podiatry.com/news/459/Adhesive-Arachnoiditis-Identification-Treatment-and-Management-of-Inflammatory-Pain
33. Arachnoiditis Hope website. https://arachnoiditishope.com/diagnosis/. Accessed January 19, 2024.
34. Parenti V, Huda F, Richardson PK, *et al.* Lumbar arachnoiditis: Does imaging associate with clinical features? Clin Neurol Neurosurg. 2020;192:105717.
35. Rodriguez LJG, Sandoval Sanchez V, Benavides Rodriguez D, *et al.* Paraplegia due to adhesive arachnoiditis: a case report. Acta Ortop Mex. 2009;23(4):232-236.
36. Bilello J, Tennant F. Patterns of chronic inflammation in extensively treated patients with arachnoiditis and chronic intractable pain. Postgrad Med. 2016;92(1096):1-5.
37. Zang Y, Chee A, Shi P, *et al.* Intervertebral disc cells produce interleukins found in patients with back pain. Am J Phys Med Rehabil. 2016;95(5):407-415.
38. Burns, L. Effects of Lumbar Lesions. The Educational Department A.T. Still Research Institute; Sunnyslope Laboratories; Academy of Applied Osteopathy.1966:62-63.
39. Arachnoiditis Hope website. https://arachnoiditishope.com/2020-aa-update-report/. Accessed January 19, 2024.
40. Arachnoiditis Hope website. https://arachnoiditishope.com/history/. Accessed January 19, 2024.