Sacral Agenesis

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Sacral Agenesis (SA) is a rare congenital anomaly that involves the whole spectrum of aplastic vertebral malformations that are grouped under the entity Caudal Regression Syndrome. Ranging from agenesis of the coccyx to the absence of the sacral, lumbar and even lower thoracic vertebrae. Feller and Sternberg described in 1930 [28] the macro- and microscopic autopsy findings in cases of vertebral abnormalities. 1934 Goldhamer [33] reported a case of SA and reviewed the literature. In 1958 Eckstein described the case history of a female infant where sacrum and coccyx had failed to develop [25]. The term Sacral Agenesis has been used synonymously with caudal agenesis or caudal regression, first described by Duhamel in 1961 [23]. The common features of the caudal regression syndrome include a combination of lumbosacral agenesis, anorectal malformations and urogenital anomalies. Multiple visceral anomalies together with the extensive neurological deficits of SA resulting in stillbirth or neonatal death that the true incidence of caudal agenesis is therefore uncertain.

Etiology

Karyotype screenings on patients with SA have been studied and had found no abnormality [10,69]. Familial occurrences of SA are rare but have been reported [53,57]. Other reported cases of SA are sporadic and strongly associated with maternal diabetes mellitus [3]. The literature shows that 16 % of infants with SA have diabetic mothers [11,59,65], but only 1 % of infants born to diabetic mothers have a SA [2]. In addition, maternal prediabetic and latent diabetic states are also associated with SA [1,2,37,68]. Another explanation is that the maternal diabetic or prediabetic state provides a specific maternal milieu that provokes an abnormal fetal response in the fetal genetic constitution that renders it to the maternal diabetic milieu. Welch and Aterman [70] showed that this susceptibility may be associated with a relatively unusual human leukocyte antigen haplotype.

Not only the maternal diabetes but other extrinsic factors may cause the teratogenic envirements for SA. Because many diabetic mothers of children with SA were insulin users [51,52], insulin itself has been implicated [24,72]. How these noxious agents exert their deleterious effects and are translated into dysmorphogenesis is unknown. A disorder of an axial mesodermal "developmental field" is postulated by Gardner and Nelson [31], responsible for orchestrating migration and determination of prospective caudal eminence cells during gastrulation. Others see the etiology of SA in a defect of genetic material on the sixth chromosome [30].

Classification

In 1924 Foix and Hillemand [29] introduced a simple classification based on the extent of involvement of sacrum and coccyx. A modification by Smith 1963 [62] included cases with a so-called hemisacrum. In 1976 White and Klauber [71] suggested a classification that took into account involvement of the lumbar vertebrae. In a study by Renshaw 1978 [55] four recognizable types were found (Fig. 1):

Type I total or partial unilateral SA; **Type II** partial SA with a partial but bilaterally symmetrical defect and an articulation between the ilia and abnormal or hypoplastic first sacral vertebra (Fig. 2A and B); **Type III** variable lumbar and total SA with the ilia articulating with the sides of the lowest vertebra present; **Type IV** variable lumbar and total SA, the caudal end-plate of the lowest vertebra resting above the fused ilia or an iliac amphiarthrosis.

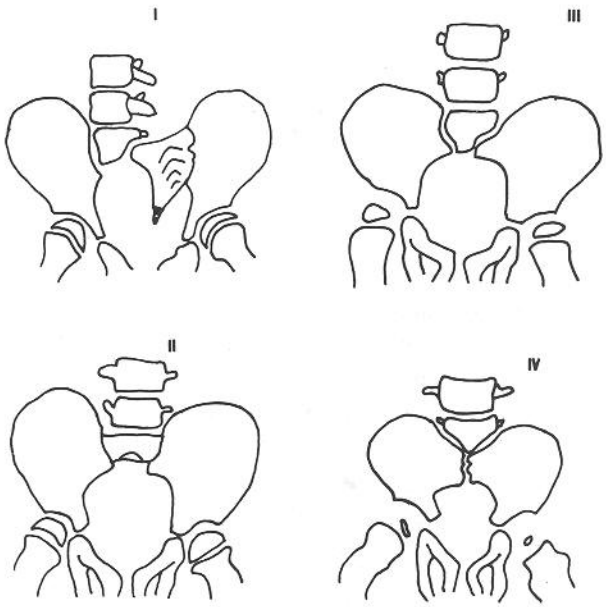


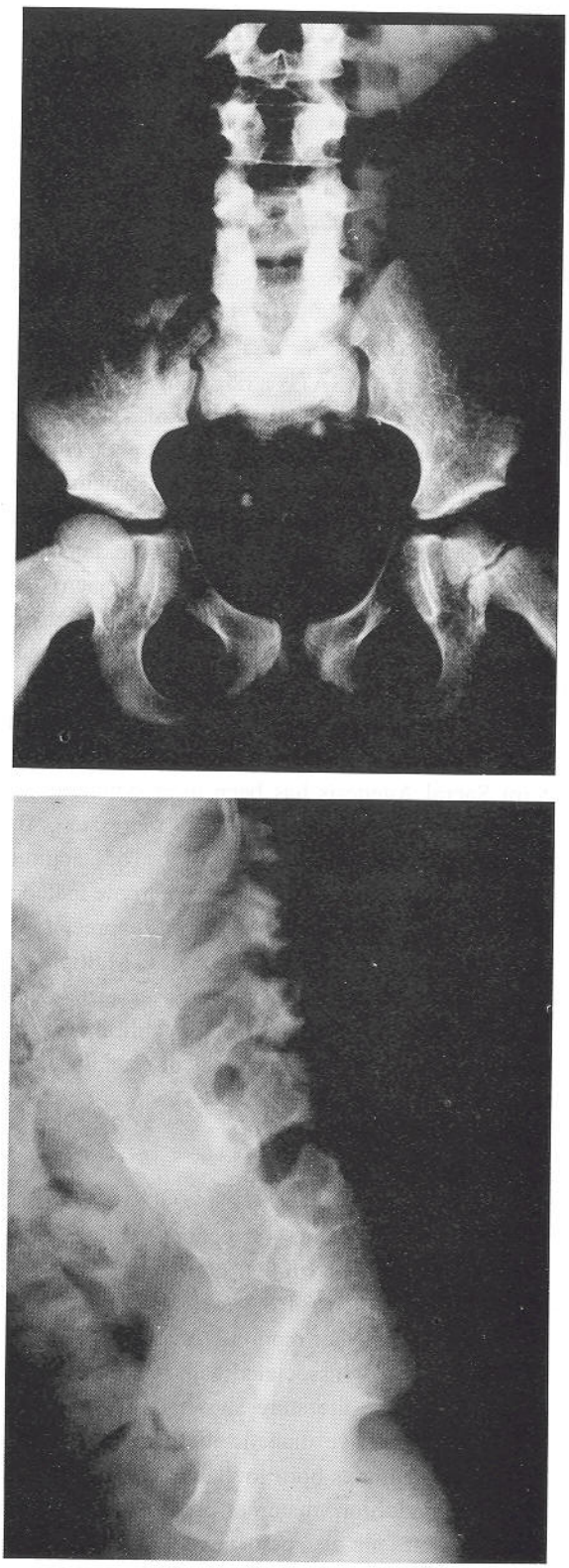
Figure 1. Classification of sacral agenesis by Renshaw [55].

Urologic evaluation and management

One of the most common significant congenital disabilities in consequence of myelodysplasia is a neuropathic bladder dysfunction. Virtually all children with congenital neuropathic bladder dysfunction have a normal excretory urogram at birth [45], and it is only with the course of time that hydronephrosis, vesico-ureteral reflux, renal damage and bladder diverticula develop [15,19,43] as a consequence of functional neurologic obstruction of the bladder outlet [8,66]. The necessity of urologic evaluation is to identify neuropathic voiding dysfunction to institute appropriate therapy. The main elements in such an evaluation are the neuro-urologic history, physical examination, radiographic investigations and specific urodynamic or video urodynamic studies to assess both vesical and urethral sphincter function (Table 1).

Neuro-urologic history should include a careful evaluation of bladder function, inclusive frequency of micturition, caliber and force of the urinary stream. Is the child able to initiate and interrupt a urinary stream? Does the child strain to void? Is there a history of urinary tract infections? What are the characteristics of the urinary incontinence? (When it occurs, frequency, dry interval etc.).

Radiographic investigations, such as so-



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b

Figure 2A. Anteroposterior x-ray showing a type II sacral agenesis with stable articulation between the ilia and a hypoplastic first sacral vertebra. B). Lateral x-ray showing type II sacral agenesis.

Table 1. Evaluation of children with neurogenic bladder dysfunction

HISTORY
• Bowel and bladder habits
• Pattern of incontinence
• Information regarding birth and development
PHYSICAL EXAMINATION
• Spine
• Lower extremities
1. Reflexes
2. Muscle mass
3. Gait
4. Perineal sensation/tone/reflexes
LABORATORY
• Urine analysis/culture
• Serum creatinine
RADIOLOGIC INVESTIGATIONS
• Sonography
• Excretory urogram
• Voiding cystourethrogram
• Renal scintigram
• Spine
URODYNAMICS
• Flow rate
• Residual urine
• Cystometrogram
• Static and voiding urethral pressure profile

nography of the upper and lower urinary tract together with an excretory urogram or a voiding cystourethrogram, may first suggest the presence of occult spinal dysraphism. A thick walled bladder with severe trabeculation or diverticula in the absence of any anatomical urethral obstruction also suggest the presence of neuropathy (Fig. 3). Renal scintigram should be performed to determine the status of function and drainage of the upper urinary tract.

Urodynamic studies under different techniques are described [6,12]. A very small dose of Meperidine (1 mg/kg of body weight) is administered to children over the age of 1 year to reduce both the discomfort and the axiety while maintaining cooperativeness and responsiveness [27]. Older children are instructed not to empty their bladder for 2 to 3 hours prior to the scheduled appointment. This allows observation for the presence of stress incontinence and the pattern of voiding. A balloon catheter is inserted into the rectum to monitor intraabdominal pressure. Artifacts of movements or straining, which may be confused with contractions of the bladder when one monitors only intravesical pressure, can be eliminated [4,5]. The child is catheterized with either a triple lumen urodynamic catheter or in newborns a

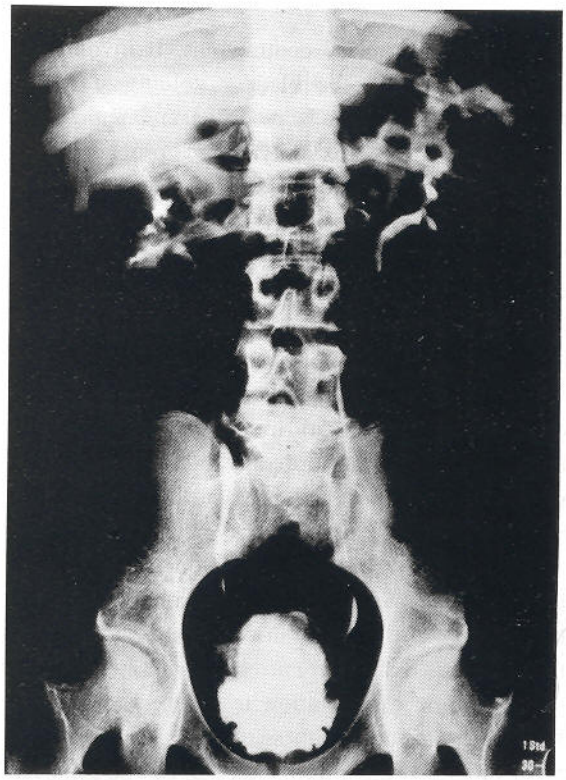

Figure 3. Excretory urogram of a 15-year-old girl managed with intermittent catheterization. Neuropathic bladder with diverticulum-like alterations between the trabeculation.

No.5 feeding tube, because of size restriction of urethra. A hypotonic bladder may not empty completely, even after catheterization.

Urethral pressure profilometry measures the passive resistance of a particular point within the urethra to stretch [32]. Bladder pressure is monitored continuously via the second channel during the urethral pressure study to look for uninhibited contractions. A comparison is made between the pressures within the bladder and the urethra during voiding to determine whether outlet obstruction is present. Saline warmed to body tempature is infused. Filling is performed with the child supine and again when the child is upright. The child is asked to inhibit voiding as long as possible. While voiding, the child is asked to stop urinating so that the physician can determine how strongly the child can block the micturition reflex.

During emptying, pressures are recorded continuously in the bladder and urethra to determine whether there is increased resistance to flow. The cystometrogram is a clinical test of bladder function designed to measure the post-voiding residual, the effective bladder storage capacity, the presence or

absence of involuntary contractions. If involuntary contractions occur, the bladder volume at which they become manifest is recorded and anticholinergic medications (oxybutynin or propantheline) may be administered to asses their efficacy in abolishing these contractions [6]. The failure of the urethral sphincter mechanism to relax during micturition is responsible for the development of increased intravesical pressures and incomplete bladder emptying, which in turn results in the development of vesicoureteral reflux, hydronephrosis, renal damage and urinary tract infections [46]. Similary, severe sphincteric denervation as manifested by electromyogaphic activity typically results in a continual dribbling incontinence [47].

The primary treatment in children with neuropathic urethrovesical dysfunction aims to preserve the integrity of the upper urinary tract, prevent urinary infection and control urinary incontinence.

Endoscopic examination is a necessary part of the work-up in some of these children, depending on the disorder and the information that can be achieved with less invasive means. Radiographic examinations have replaced cystoscopy as routine examinations in many centers, but it may be necessary to examine the urethra, bladder neck area and bladder under direct vision in certain instances.

Management of vesicoureteral reflux

a) Intermittent catheterization

Renal damage in children with neurologic urethrovesical dysfunction is the direct result of urinary infection and obstruction combined with vesicoureteral reflux [42]. Clean intermittent catheterization permits the effective control of urinary obstruction by completely emptying the bladder at regular intervals before there is an unphysiologic increase in the intravesical pressure. To facilitate control of this process, anticholinergic medications are required to decrease the frequency of the involuntary, high pressure contractions, thus increasing the effective low-pressure urinary storage capacity of the bladder.

This abnormal bladder function is successfully managed by intermittent catheterization, that spontaneous resolution of the reflux can be expected in up to 50 % of children with moderate degrees of reflux [36]. Non operative management consisting of clean intermittent catheterization, appropriate pharmacologic agents, prophylactic antimicrobials and periodic urine cultures to exclude the possibility of occult infections. Table 2 lists the patients with SA treated at the Department Pediatric Surgery in Graz. This protocol is continued unless there is evidence of breakthrough infections or progressive renal damage. Children with higher grades of reflux as grade 4 and 5 [36] usually require surgical correction of the reflux. Antireflux operations employing standard techniques can be highly successfull in children with neurovesical dysfunction provided an effective program of bladder management is instituted [41].

b) Cutaneous vesicostomy

Cutaneous vesicostomy is a safe and effective method of providing low pressure bladder drainage [9]. The indications overlap with those for clean intermittent catheterization (ineffective bladder emptying, hydronephrosis, and vesicoureteral reflux). The age of the child, severity of the reflux, renal function and psychosocial circumstances are factors for consideration in deciding between those two management alternatives. In a young child vesicostomy is preferred, particularly when renal function is compromised. Intermittent catheterization is the better alternative in the older cooperative child. Closure of the vesicostomy should be undertaken only if intermittent catheterization as an adequate program is possible. If vesicoureteral reflux has not decreased or resolved by that time antireflux procedure should be performed.

Management of urinary incontinence

Incontinence is the result of a failure to store urine effectively as a consequence of involuntary detrusor contractions, inadequate urethral resistance, or, more commonly both [21]. Catheterization is usually started, when the child is mature enough to accept responsibility and expresses a genuine interest usually between 4 and 8 years of age. Anticholinergic medications will effectively control the involuntary detrusor contractions and increase the effective low pressure reservoir capacity of the bladder [56]. When urethral resistance is low, alpha-adrenergic medication is administered to stimulate alpha-receptors in the bladder neck and urethra, increase the in-

Table 2. Patients with SA: etiology, classificaton, urological anomalies.

Case	sex	First seen	diabetic mother	Typ of SA (Renshaw)	urological anomalies and treatment	orthopedic status and treatment	Anorectal status	other Anomalies
E.T.	f	2 yrs.	—	I	NBD → Oxybutynin, IMC, VUR 4°-5° bilat.→ Cohen bilat.	muscular atrophia lower leg → physiotherapy pes pronatus et abductus right → cast pes pronatus et adductus left → achillotomy spondylolisthesis L_5 → OP	continent	anomalous rips
T.S.	f	3 wks.	+	II	NBD → Oxybutynin, IMC UTI → antibiotic Th. VUR 2° bilat. → kons.	—	obstipation	—
D.U.	f	6 wks.	+	IV	NBD → Oxybutynin, IMC VUR 3° bilat. → Cohen bilat.	hip dysplasia → cast hip contracture → Physio-therapy pes supinatus bilat. → med. Release and talus-osteotomy bilat.	AS → dilata-tion continent	aortic stenosis
I.M.	m	2 wks.	—	III	spontaneous miktion NBD?	—	normal	tethered cord
D.A.	f	2 wks.	—	III	NBD → Oxybutynin, IMC VUR 3°-4° left, 1° right → Cohen bilat.	congential scoliosis → kons., Hip dislocation right → open reduction, cast coxa valga left → intertrochan-teric osteotomy club foot bilat → achillotomy, hip and knee flexion contractures → physiotherapy	obstipation (digital removal)	—
G.M.	f	1 yr.	—	II	NBD → Oxybutynin, IMC	—	normal	anomalies of the cervical spine
S.N.	f	1 day	—	II	NBD → IMC	—	IA → Pena continent	coarctation of the aorta
K.B.	f	1 day	—	II	—	—	IA	EA, RA left, SCH, †
P.S.	f	1 day	—	II	NBD → IMC	—	IA - Pena continent	vagina duplex, ectopic, urether right, persistent cloaca

IA: imperforate anus, AS: anal stenosis, RA: renal agenesis, VUR: vesico ureteral reflux, IMC: intermittent catheterization, NBD: neurogenic bladder dysfunction, EA: esophageal atresia, SCH: severe congenital heart defect, IRDS: idiopatic respiratory distress syndrome.

traurethral pressure and reduce urinary incontinence has been possible in up to 90 % of children [40].

If incontinence is a significant problem additional surgical treatment may be considered. If the urethral sphincter mechanism is adequate and incontinence results from a small capacity bladder, augmentation can improve urinary continence [39]. If incontinence is a problem of inadequate sphincter mechanism, two surgical alternatives are available: The first is to create a sphincter mechanism as described by Dees [17], and Leadbetter [44]. The most commonly employed surgical alternative for urinary incontinence is the artificial urinary sphincter described by Scott [60]. The success rate for the artificial sphincter in children with neurogenic incontinence has been reported to be as high as 90 % [16,34].

Anorectal malformations

Anorectal malformations may be associated with bony spinal deformities and with variable degrees of neurologic deficit [38]. Duhamel correctly identified patients with anorectal malformations as having a regional defect, "a syndrome of caudal regression" [23], including the VATER association (Vertebral anomaly, Anal imperforation, Tracheo-esophageal fistula, and Renal/Radial anomalies) thought to represent a defect in mesodermal development at the primitive streak level [23], and the OEIS complex (Omphalocele, Cloacal Exstrophy, Imperforate anus, Spinal deformities) [13]. SA is found in between 13 and 54 % of patients with imperforate anus [18,22,48] and is three times more common in patients with high imperforate anus than those with low lesions [14], according to the classification by Stephens and Smith [64].

The muscles most commonly involved are those supplied by the S2-S5 cord levels, which include muscles of the perineum and pelvic sling. The perineal and pelvic motor paralysis account for the abnormality of the urethral and anal sphincters [49]. So disorders of the anorectal area have dif-

ferent variations, fecal incontinence, anal stenosis and imperforate anus are possible.

Therapy

Children with anal stenosis dilatation is necessary but a following fecal incontinence may be possible [49]. For patients with imperforate anus and sacral anomalies the pull-through procedure described by deVries and Peña [20] is indicated. One group of patients should be carefully assesed before undergoing this procedure: those with neurogenic bladder. This condition is almost always present in patients with an absent sacrum below S1 or S2 [63]. Children with these severe spinal anomalies suggest a deficiency of sacral innervations and have a weakness or absence of external sphincter muscle function in response to electrical stimulation. In such children, the prospects for fecal continence are poor and a pull-through procedure should probably not be attempted. In previous studies neurogenic bladder was found in approximately 7 to 29 % of children with imperforate anus [7,35,57,67]. Boemers et al demonstrated that SA and associated neuropathological correlate is the most common cause of neurogenic bladder sphincter dysfunction in children with the caudal regression syndrome [12]. So the possible complications of posterior sagittal anorectoplasty, namely enuresis or fecal incontinence from trauma to the pelvic nerve plexus and urethral sphincter may be incorrectly attributed to the pull-through procedure [38,50].

Orthopedic Aspects

External features and neurological deficit

The failure of development of the sacrum ranges from absence of only the lower coccygeal segment which often goes unnoticed, to partial absence of the sacrum or absence of all lumbar and sacral vertebrae according to the classification of Renshaw [55]. In the milder form the spinal defect may only be recognized in the course of clinical and radiologic investigations of patients with deformities in the lower limb or neurological changes, similar as in patients with spina bifida. In patients with complete SA different variations of characteristic pictures are seen. If the entire sacrum was missing and the ilia articulate or fuse with each other below the last vertebra, the transverse pelvic diameter will be greatly reduced and the hip look narrow compared with the thorax, with a mermaid-like appearance. Incomplete absence of the lumbar and sacral vertebrae, the lower limbs are characteristically abduced and flexed at the hips, flexed at the knee and plantar flexed at the ankles, so that the patient sits in the so-called "Buddha" position.

Pang found in his study of 1993 that patients with high motor levels and paralysis of "long muscles" across the ankle had severe deformities, but patients with low motor levels and "intrinsic muscle" paralysis had lesser deformities such as high pedal arches and hammer toes. The motor deficits in SA tend to parallel the extent of the bony deficit. The most commonly involved muscles are those supplied by the S2-S5 cord levels. The second frequently involved muscle groups are those by L5-S1. In contrast with motor function the sensory findings were not predictable from the radiographic appearance of the sacrum. The lowest functional motor level was higher than the last sensory level, sometimes by 4-5 segments [49].

Treatment

Most children born with SA have normal intelligence. Orthopedic management should be directed to correcting lower limb deformities, making the best use of any active lower limb muscle and stabilization of the spine and pelvis [55]. Observations of spontaneous movements in the lower limbs and electrical stimulation of the limb muscles allows a good estimation within the first weeks of life of future potential for walking and orthotic requirements.

Scoliosis is the most common spinal anomaly associated with SA [55]. Scoliosis is mostly associated with congenital hemisacrum and if there is progressive kyphosis surgical stabilisation by spinal osteotomy or fusion of the affected hemivertebrae may be needed.

Hip dislocation is caused by muscle imbalance and not by acetabular malposition alone. If the hips are dislocated, it is usually better to leave them in the dislocated position, where they will form an abnormal but stable false joint. On the other hand many surgical procedures may be necessary to achieve this goal [61].

Complete motor paralysis occurs in complete ab-

sence of the whole lumbar spine and sacrum. Severe flexion contractures of the hip and knees are common and responsible for the functionless condition of the lower extremities. Attempt to correct the deformities by soft tissue release and osteotomy may fail due to circulatory inadequacy and together with a significant sensory loss may make it impossible to fit the limbs with a prosthesis. Elting and Allen advise bilateral subtrochanteric amputation with subsequent prosthesis to be the treatment of choice [26]. Subtrochanteric amputation is preferable to hip disarticulation because it provides an wider sitting base and a better prosthetic accommodation. This operation is done between the age of 4 and 7 years. If it is possible to demonstrate the presence of intact sensory supply or a skin biopsy shows intact sensory endings, then correction of deformity should be attempted [61].

Knee joint contracture is reflected by muscle imbalance together wih capsular contracture and skin webbing, that soft tissue release and sometimes a supracondylar osteotomy are necessary for sufficient correction of the deformity.

Deformity of the foot is the result either from muscle imbalance or from positional contracture. If the sensation of the foot is intact a correction should be done between the age of 6 months to 2 years to allow the child to learn to walk. Several procedures of treatment are used to release the deformity including serial application of casts, tendon transfers, soft tissue release and extra- and intra-atricular arthrodesis. The physiotherapeutic measures required in the rehabilitation of these patients are complex and need not only acknowledgement of neurological problems but the use and management of prostheses, well described by Rosenfelder [58].

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