A refresher on the primary care and public health management of acute post-streptococcal glomerulonephritis

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Background
Acute post-streptococcal glomerulonephritis (APSGN) is an acute autoimmune kidney condition triggered by skin infection or pharyngitis caused by specific strains of *Streptococcus pyogenes* (Group A streptococcus). In Australia, APSGN is primarily a disease of childhood disadvantage.

Objective
The aim of this review is to draw attention to a preventable childhood condition, detailing the clinical presentation, diagnostic pathway and management.

Discussion
Children typically present with a nephritic clinical picture: oedema, painless haematuria and hypertension. Diagnostic confirmation requires specific laboratory findings or both clinical and laboratory suggestive evidence. 'Probable' cases only require clinical evidence and 'possible' cases only require suggestive laboratory evidence. Treatment is largely supportive, focusing on the management of hypertension and fluid overload. Suspected and confirmed cases must be notified immediately to regional public health authorities. Outbreaks require a broad-based public health response in accordance with state-based guidelines.

IN AUSTRALIA, acute post-streptococcal glomerulonephritis (APSGN) is primarily a disease of childhood disadvantage. It is an acute autoimmune kidney condition that is triggered by skin infection (impetigo/pyoderma) or pharyngitis due to nephritogenic strains of *Streptococcus pyogenes* (Group A streptococcus [Strep A]).[1] The peak age group for APSGN is 5–14 years.

The documented incidence of APSGN is strikingly higher among Aboriginal and Torres Strait Islander people (more than 170 cases per 100,000 population/year compared to the national figure of 11 per 100,000 population/year) than among non-Indigenous Australians.[2–4] Aboriginal and Torres Strait Islander children, especially in regional and remote settings, carry an inequitable burden of Strep A disease compared with non-Indigenous Australians.[5] As such, in high-risk communities, there is usually a background of sporadic disease with intermittent broader outbreaks.[2,6,7]

The diagnosis of APSGN can be elusive; this is a diagnostic hurdle. It is estimated that up to 75% of cases of APSGN are subclinical and go undetected because of few or no symptoms.[8] In the 1993 Far North Queensland impetigo-driven outbreak, only one-third of children with APSGN were symptomatic; the rest were only detected through community screening.[6] Even when there are symptoms, children might not present to the clinic. We already know that in some remote settings, childhood Strep A skin infection is often normalised; it frequently goes unrecognised and untreated.[9]

Aim

The aim of this brief review is to draw attention to an often-missed critical and preventable childhood condition, detailing the clinical presentation, diagnostic pathway and management of APSGN.

Clinical presentation

Children typically present with a nephritic clinical picture: oedema, painless haematuria and hypertension (Table 1).[1] However, it is not always that easy; these features might not manifest together at the same time. In the case of Aboriginal and Torres Strait Islander children, a family member often brings a child into the clinic because of new-onset facial swelling.[7]

Periorbital oedema is also a feature of nephritic syndrome and occurs in approximately two-thirds of symptomatic patients with APSGN.[7,10] Macroscopic haematuria is the other common presentation, and many cases are discovered incidentally from routine urine analysis.

Hypertension (adjusted for age and height) is usually an asymptomatic finding and can

Table 1. Symptoms of and risk factors for acute post-streptococcal glomerulonephritis

Symptoms	Risk factors
Haematuria	Poverty
Hypertension	Household crowding
Facial and/or peripheral oedema	Previous APSGN diagnosis

APSGN, acute post-streptococcal glomerulonephritis.

persist for several weeks, or even for months. Serial blood pressure readings might also need to be done outside the clinic setting because some children might have 'white coat hypertension'. Clinicians should measure a child's height to determine whether their blood pressure is over the 95th percentile for their sex, age and height (Box 1; Table 2). Additional symptoms can include anorexia, malaise, nausea and even vomiting.[10]

The first challenge for the clinician is to think of APSGN. Of course, APSGN also occurs in non-Aboriginal and Torres Strait Islander people and, here, the diagnosis might be even more difficult because of a low index of suspicion. Thus, the initial community clinical assessment should include close inspection for oedema, careful blood pressure measurement and a urine dipstick/urinalysis test.

The background history is critical. APSGN usually occurs approximately four weeks after the onset of impetigo and two weeks after Strep A pharyngitis.[10] However, some patients might also have active impetigo when APSGN develops. When patients develop APSGN without clear preceding impetigo or symptomatic pharyngitis, it can be diagnostically challenging.[11]

A household history is also essential. How many people live in the house? Have there been episodes of skin sores or periods of sore throat recently? Is there a household history of APSGN? High community and household burdens of Strep A infection tend to occur in the setting of poverty, household crowding, scabies infections and poor health literacy.[1] In the 2005 Far North Queensland APSGN outbreak, almost half the otherwise healthy 87 children (aged 2–12 years) screened in the community had infected skin sores, and all had scabies.[7] APSGN tends to run in households and families, but this is almost certainly environmental rather than due to genetic susceptibility.

Investigations

When a general practitioner suspects APSGN, the diagnosis must be confirmed. This requires several key investigations (Box 2). Patients with a positive urine dipstick/urinalysis with 2+ or more red blood cells (RBC) in the urine should have samples sent away for microscopy, culture and sensitivity (MCS). Occasional false-positive urine dipstick results necessitate laboratory confirmation with haematuria of >10 RBC/μL.

Clinicians are advised to check serum urea, electrolytes and creatinine. Urea and creatinine might be elevated during the acute phase of the inflammatory process. If raised, clinicians are advised to monitor closely and seek specialist advice.[8] In most children, they resolve after several weeks.

Evidence of a recent Strep A infection can be determined by an elevated or rising anti-streptolysin titre (ASOT), an elevated anti-DNase B titre, recovery of Strep A from the throat or skin sore or a positive Strep A antigen test.[8,12,13] Across rural and remote Australia, these tests might take a week or more to return to the clinic.

Diagnosis

The diagnosis of APSGN can be complicated. Cases of ASPGN can be categorised as 'confirmed', 'probable' and 'possible' on the basis of both available clinical and laboratory evidence (Box 3). 'Confirmed' cases require either definitive laboratory evidence or both suggestive clinical and laboratory evidence. 'Probable' cases only require clinical evidence and 'possible' cases only require suggestive laboratory evidence. These criteria differ somewhat between states and territories in Australia, so if in doubt it is best to check your local guidelines.[8,12,13] All cases, regardless of categorisation, require prompt treatment. We should not wait for all the laboratory results to return.

Management

Approximately two-thirds of children with APSGN can be managed in the community, but approximately one-third will require hospitalisation. Adults with new-onset APSGN tend to have much more severe and prolonged disease and should be referred to the emergency department for further work-up and management. Patients who are managed in remote settings require careful follow-up and distant advice from experienced paediatricians or physicians experienced in APSGN management. Hospitalisation is indicated when hypertension and/or fluid overload cannot be controlled in the community.[14]

In all cases of suspected APSGN, patients should be given intramuscular benzathine

Box 1. Best practice principles of hypertension diagnosis

- Three different blood pressure measures averaged
- The use of appropriately sized cuffs
- Correct patient positioning
- The use of auscultation for at least one measure
- Determined against tables based on age and height to be above the 95th percentile[20]

Box 2. Investigations required to diagnose acute post-streptococcal glomerulonephritis[8]

- Urine microscopy, culture and sensitivity
- Urea, electrolytes and creatine
- C3 and C4 complement
- Anti-streptolysin O titre
- Anti-DNase B
- Throat and/or skin swab microscopy, culture and sensitivity

Table 2. Systolic blood pressure values (95th percentile) for children according to their sex, age and height as per the American Academy of Pediatrics[20]

95th SBP percentile for males (left) and females (right) by age and height															
Age (years)	BP percentile	SBP (mmHg) Measured height							SBP (mmHg) Measured height						
1	Height (cm)	77.2	78.3	80.2	82.4	84.6	86.7	87.9	75.4	76.6	78.6	80.8	83	84.9	86.1
	95th	102	102	103	103	104	105	105	101	102	102	103	104	105	105
2	Height (cm)	86.1	87.4	89.6	92.1	94.7	97.1	98.5	84.9	86.3	88.6	91.1	93.7	96	97.4
	95th	104	105	105	106	107	107	108	104	105	106	106	107	108	109
3	Height (cm)	92.5	93.9	96.3	99	101.8	104.3	105.8	91	92.4	94.9	97.6	100.5	103.1	104.6
	95th	106	106	107	107	108	109	109	106	106	107	108	109	110	110
4	Height (cm)	98.5	100.2	102.9	105.9	108.9	111.5	113.2	97.2	98.8	101.4	104.5	107.6	110.5	112.2
	95th	107	107	108	108	109	110	110	107	108	109	109	110	111	112
5	Height (cm)	104.4	106.2	109.1	112.4	115.7	118.6	120.3	103.6	105.3	108.2	111.5	114.9	118.1	120
	95th	107	108	109	109	110	111	112	108	109	109	110	111	112	113
6	Height (cm)	110.3	112.2	115.3	118.9	122.4	125.6	127.5	110	111.8	114.9	118.4	122.1	125.6	127.7
	95th	108	109	110	111	112	113	114	109	109	110	111	112	113	114
7	Height (cm)	116.1	118	121.4	125.1	128.9	132.4	134.5	115.9	117.8	121.1	124.9	128.8	132.5	134.7
	95th	110	110	111	112	114	115	116	109	110	111	112	113	114	115
8	Height (cm)	121.4	123.5	127	131	135.1	138.8	141	121	123	126.5	130.6	134.7	138.5	140.9
	95th	111	112	112	114	115	116	117	110	111	112	113	115	116	117
9	Height (cm)	126	128.3	132.1	136.3	140.7	144.7	147.1	125.3	127.6	131.3	135.6	140.1	144.1	146.6
	95th	112	112	113	115	116	118	119	112	112	113	114	116	117	118
10	Height (cm)	130.2	132.7	136.7	141.3	145.9	150.1	152.7	129.7	132.2	136.3	141	145.8	150.2	152.8
	95th	112	113	114	116	118	120	121	113	114	114	116	117	119	120
11	Height (cm)	134.7	137.3	141.5	146.4	151.3	155.8	158.6	135.6	138.3	142.8	147.8	152.8	157.3	160
	95th	114	114	116	118	120	123	124	115	116	117	118	120	123	124
12	Height (cm)	140.3	143	147.5	152.7	157.9	162.6	165.5	142.8	145.5	149.9	154.8	159.6	163.8	166.4
	95th	116	117	118	121	124	126	128	118	119	120	122	124	125	126
13	Height (cm)	147	150	154.9	160.3	165.7	170.5	173.4	148.1	150.6	154.7	159.2	163.7	167.8	170.2
	95th	119	120	122	125	128	130	131	121	122	123	124	126	126	127
14	Height (cm)	153.8	156.9	162	167.5	172.7	177.4	180.1	150.6	153	156.9	161.3	165.7	169.7	172.1
	95th	123	125	127	130	132	133	134	123	123	124	125	126	127	127
15	Height (cm)	159	162	166.9	172.2	177.2	181.6	184.2	151.7	154	157.9	162.3	166.7	170.6	173
	95th	127	129	131	132	134	135	135	124	124	125	126	127	127	128
16	Height (cm)	162.1	165	169.6	174.6	179.5	183.8	186.4	152.1	154.5	158.4	162.8	167.1	171.1	173.4
	95th	130	131	133	134	135	136	137	124	125	125	127	127	128	128
17	Height (cm)	163.8	166.5	170.9	175.8	180.7	184.9	187.5	152.4	154.7	158.7	163.0	167.4	171.3	173.7
	95th	132	133	134	135	137	138	138	125	125	126	127	128	128	128

BP, blood pressure; SBP, systolic blood pressure.

Box 3. Evidence required to diagnose acute post-streptococcal glomerulonephritis[12]

Laboratory definitive evidence

- Renal biopsy suggestive of acute post-streptococcal glomerulonephritis

Laboratory suggestive evidence (all three criteria must be met)

- Haematuria on microscopy (red blood cells >10/μL)
- Evidence of recent Group A streptococcus infection (elevated anti-streptolysin O titre or anti-DNase B or positive Group A streptococcus on skin/throat culture)
- Reduced C3 level

Clinical evidence (at least two of the three criteria must be met)

- Facial and/or peripheral oedema
- Moderate haematuria
- Hypertension, according to age/sex and height percentiles

benzylpenicillin to eradicate any Strep A. However, this does not alter the autoimmune process (Table 3). Intramuscular benzathine benzylpenicillin is a painful injection that must only be given by someone properly trained and skilled in the procedure.[15] If the patient with suspected APSGN is allergic to penicillin, they should receive oral trimethoprim and sulfamethoxazole as per the Australian Therapeutic Guidelines (eTG).[13,16] The management of any child whose systolic blood pressure is greater than the 95th percentile for sex, age and height should be promptly discussed with a paediatrician. An antihypertensive agent will probably be required and will be selected based on the patient's clinical and fluid status.

The covering paediatrician will help with follow-up. This might include weekly blood pressure and urine dipstick checks for six to eight weeks after presentation. Most children with APSGN tend to clinically recover over about six weeks. Macroscopic haematuria, hypertension and low C3 usually also normalise within 6–8 weeks. However, microscopic haematuria can persist for up to two years.[10] If there is persistent haematuria and/or hypertension and/or proteinuria and/or kidney function impairment, patients should be followed up at least until these manifestations have completely resolved. There is evolving evidence to suggest that it might be best to follow children with APSGN into adulthood. At the present time, it is impossible to assess and monitor any subtle glomerular injuries left behind, but we now know they have an impact later in life.[17] Early intervention is needed to improve the chances of preventing APSGN-related chronic kidney disease.[17]

Table 3. Intramuscular benzathine benzylpenicillin weight-based dosing[21]

Weight	Dose
<10 kg	450,000 IU
10–20 kg	600,000 IU
>20 kg	1,200,000 IU

Public health implications

General practitioners are encouraged to notify their local public health service immediately whenever they encounter a suspected case of APSGN, even before the confirmatory tests results have become available. As of 2024, APSGN is notifiable in the Northern Territory, Western Australia and, more recently, Queensland.[8,12,13]

Confirmed and probable APSGN cases require household contact tracing. All individuals living in the house over the two weeks prior to symptom onset (or positive laboratory tests) need to be assessed for skin sores, sore throats, scabies, hypertension, oedema and haematuria. In addition, the family, household and close contacts of a confirmed APSGN patient who have stayed in the household in the two weeks preceding the onset of APSGN require treatment.[13] Intramuscular LA Bicillin (benzathine benzylpenicillin) must be administered to all contacts aged between one and 17 years and all adults aged 17 years and over who have skin sores.[13]

When a public health unit declares an outbreak, as determined by local guidelines, the primary aim is to reduce Strep A transmission and prevent further cases of APSGN. This involves screening all children aged between one and 17 years, as above, followed by appropriate management. This public health response requires close partnerships with local primary healthcare facilities and community leaders.[18]

When there is an outbreak, Strep A cultured from cases or contacts will be sent to a reference laboratory and genotyped to determine the M protein gene (*emm*) type. The villain or villains might turn out to be well-known nephritogenic strains, such as *emm* type 55, or even newly recognised strains.[19]

Prevention

The prevention of Strep A requires well-resourced health promotion programs and annual health checks in communities at risk. This requires a strengths-based approach, led by Aboriginal and Torres Strait Islander health workers based in the community. Until the primordial causative factors for APSGN (poverty and a lack of housing, employment and health education) are addressed by the wider community, there are no other viable preventative mechanisms.

Key points

- APSGN is largely unrecognised and undetected.
- APSGN is primarily a disease of childhood disadvantage. APSGN in adults is relatively rare, but usually more severe. The diagnosis of APSGN is guided by a clear set of criteria.
- Although there appears to be early clinical recovery (>90%), childhood APSGN is a strong risk factor for chronic kidney disease in later life.
- Treatment is largely supportive, with a focus on hypertension and fluid overload. Prevention of APSGN at the community level requires eternal vigilance.
- Suspected and confirmed cases of APSGN must be notified immediately to regional public health authorities.

- Outbreaks of APSGN require a broad-based public health response in accordance with state-based guidelines.

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