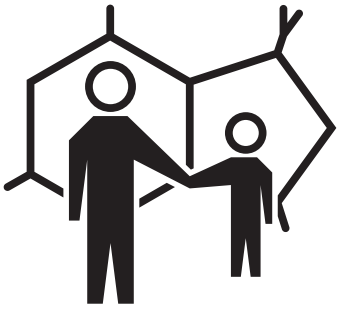
PUMPA

Purine Metabolic Patients' Association

Registered Charity No. 1019792



Information for consultants and general practitioners

This information, compiled with the help of St Thomas' Hospital Purine Research Unit, aims to assist medical professionals by pinpointing significant symptoms.

Purine metabolic disorders are often devastating for the patients involved and their families. Of the twenty-eight known purine metabolic disorders, most have been identified only in the last twenty years and their novelty makes it difficult for clinicians to keep pace. Many existing cases were originally misdiagnosed, or not diagnosed at all until late in life. It is reckoned up to 100 might be born annually in a population of 50 million, on which basis many cases go unrecognised in the UK every year.

Apart from the pain to patients and relatives, the medical cost of misdiagnosis can be immense. Children can be subjected to years of tests and some have progressed to dialysis and transplant.

Symptoms

- Gout in a young man or woman. Gout in people under thirty is always unusual and should be investigated, not just treated with Allopurinol. Too much Allopurinol can cause kidney damage in young patients with genetic gout.
- A history of:
  - infections which do not respond to treatment,
  - 'gravel' on a child's nappy, passage of small stones/loin pain.

If you have patients with these symptoms, please consider referring them to a local specialist.

Incidence of disorders diagnosed

disorder	percentage of total disorders diagnosed
ADA deficiency	20%
LNS	15.65%
XO deficiency	13.04%
HPRT deficiency	13.04%
APRT	8.7%
pyrimidine defects (CDPPT, UMPH, DHPA, DHPD, UMPS)	6.02%
XO/SO deficiency	5.22%
PNP	3.48%
PRPS	3.48%
TPMT	2.61%

Table of abbreviations

ARF	acute renal failure
ADA	adenosine deaminase
APRT	adenine phosphoribosyltransferase
ASA	adenylosuccinase
CDPPT	CDP-choline phosphotransferase
DHPA	dihydropyrimidinase
DHPD	dihydropyrimidine dehydrogenase
FJHN	familial juvenile hyperuricaemic nephropathy
HPRT	hypoxanthine phosphoribosyltransferase
LNS	Lesch Nyhan Disease
MDA	myoadenylate deaminase (muscle)
ODC	orotidine-5'-decarboxylase
OPRT	orotate phosphoribosyltransferase
PNP	purine nucleoside phosphorylase
PRPS	phosphoribosylpyrophosphatesynthetase superactivity
TPMT	thiopurine methyltransferase
UMPH1	uridine monophosphate hydrolase (also known as pyrimidine-5'-nucleotidase)
UMPS	uridine monophosphate synthase (OPRT/ODC)
XDH	xanthine dehydrogenase
XO	xanthine oxidase
XO/SO	combined XO/sulphite oxidase

Abnormalities associated with purine and pyrimidine defects

none – 2; cancers – 2; anaemia – 3; immune – 3; drug metabolism – 5; stones – 5; renal – 7; neuralogical – 9

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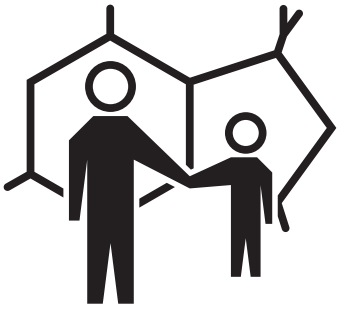

Clinical presentation

disorder	associated symptoms	diagnostic marker	can early diagnosis improve prognosis?
gout and/or renal failure			
unknown	primary gout in middle-aged male	high urate	
LNS	partial HPRT deficiency; adolescent gout, ARF, uric acid lithiasis	high urate	yes (x-linked)
PRPS superactivity	gout, uric acid lithiasis, neurological deficits	high urate	yes (x-linked, females also)
FJHN	adolescent gout/progressive renal disease	raised urate	yes
kidney stones and/or renal failure			
XDH deficiency	xanthine lithiasis, ARF, arthralgia, myopathy	low/absent urate	yes
APRT deficiency	2,8-dihydroxyadenine lithiasis		yes
ARF	*(chemically identical with uric acid stones)*		
neurological deficits			
ASA deficiency	psychomotor retardation with epilepsy		
DHPA deficiency	seizures, developmental retardation, spasticity, microcephaly		yes
DHPD deficiency	microcephaly, retardation, epilepsy		yes
HPRT deficiency	complete HPRT deficiency: LNS, cerebral palsy, self-mutilation, retardation, choreoathetposis, renal complications	high urate	yes
MDA deficiency	muscle cramps, exercise intolerance		
PNP deficiency	developmental delay, spasticity, hypertonia, immunodeficiency	low urate	yes
PRPS superactivity	retarded development, ataxia, inherited deafness, dysmorphic features, renal problems	high urate	yes
XO/SO deficiency	(combined deficiency) neonatal fitting, retardation, ocular lens dislocation		
immunodeficiency			
ADA deficiency	repeated infections, candidiasis, vomiting	severe lymphopenia (no T or B cells)	
PNP deficiency	life-threatening chicken pox, neurological deficits	T cell immunodeficiency, low urate	
UMPS deficiency	cell immunodeficiency, anaemia		
anaemia			
UMPS deficiency	megalobastic anaemia not responsive to treatment, oroticaciduria, neurological deficits	megalobastic anaemia	yes (oroticaciduria)
UMPH1 deficiency	pyrimidine 5'-nucleotidase haemolytic anaemia	T cell immunodeficiency, low urate	
CDPPT	haemolytic anaemia		
other			
ADA deficiency	in pleural/ascites fluid: tuberculosis marker		
TMPT deficiency	sufficiency/superactivity: intolerance or non-responsiveness to azathioprine therapy		