NTPN Guideline for Investigations in CYP with Neurodevelopement concerns

May 2022

North Thames Paediatric Network

Developmental delay investigation guideline drivers

1. ~20% referrals to tertiary neurology
2. TAT for investigations (Micro array)
3. Access to MRI GA
4. Special Challenges
   - Regression
   - Severe behavioural issues
   - Epilepsy

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Contributions

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Stakeholders

Parent and Patient –Via the YPF @ GOSH

Clinical Nurse Specialist

Advanced Nurse Practitioners

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Pathway for assessment of children presenting with developmental concerns - definitions

ICD-11 (2021) - Disorders of Intellectual Development (6A00)

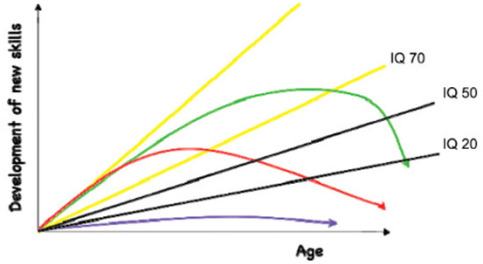
Disorders of intellectual development are a group of etiologically diverse conditions originating during the developmental period characterised by significantly below average intellectual functioning and adaptive behaviour that are approximately two or more standard deviations below the mean (approximately less than the 2.3rd percentile), based on appropriately normed, individually administered standardized tests. Where appropriately normed and standardized tests are not available, diagnosis of disorders of intellectual development requires greater reliance on clinical judgment based on appropriate assessment of comparable behavioural indicators.

In children under 5 years old and unable to engage with standardised tests, **Early developmental impairment (EDI)** may be an appropriate synonymous diagnosis and is coded the same in ICD-11

Commonly used synonyms
Mental retardation
Intellectual developmental disorder
Intellectual disability
intellectual disabilities
developmental delay
Global developmental delay

There are historical pifalls with these synonyms. Definitions of these terms vary with time and some have proven potentially stigmatising or misleading. Terms such as "delay" can give some families false hope about the overall developmental prognosis and do not capture the range of phenotypes each with varying trajectories of development.

Various phenotypes of developmental trajectory. From Horridge, 2011, Assessment and investigation of the child with disordered development. *ADCE&P*;**96:**9-20.



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Pathway for assessment of children presenting with developmental concerns – initial assessment

History	Examination	Growth chart	Review past investigations
Antenatal / perinatal / neonatal	Neurology	Height	Newborn hearing screen (AOAE/AABR)
Medical history	Gait	Weight	Newborn blood spot test (NBBST) – currently 9 conditions: N. Thames Regional Newborn Screening
Developmental history	Gower's test	Head circumference	TORCH screen
Plateauing or regression	Dysmorphism	BMI	Prenatal genetic testing (including NIPT, or invasive CMA & qfPCR)
Diurnal variation in symptoms	Inspection of skin (with Wood's lamp if available)		Previous imaging
Family – 3 generation pedigree, enquire on consanguinity	Organomegaly		Tests taken at other centres, e.g. inpatient ward, or neonatal unit
History of foetal deaths	Hearing & vision		
Vision & hearing	Developmental status		
Functional "collateral" history from educators or other caregivers if available	Consider blood pressure if neurocutaneous stigmata		

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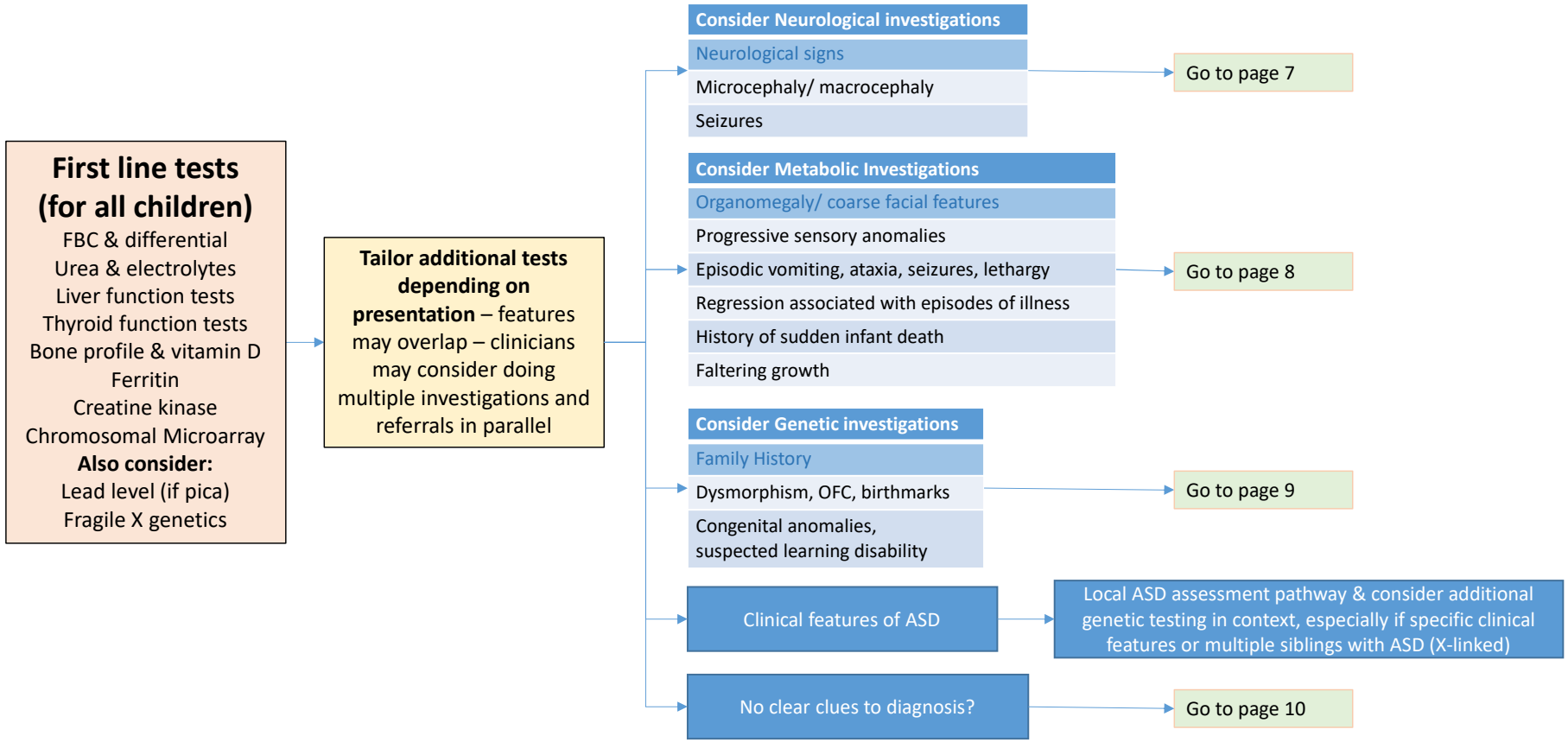
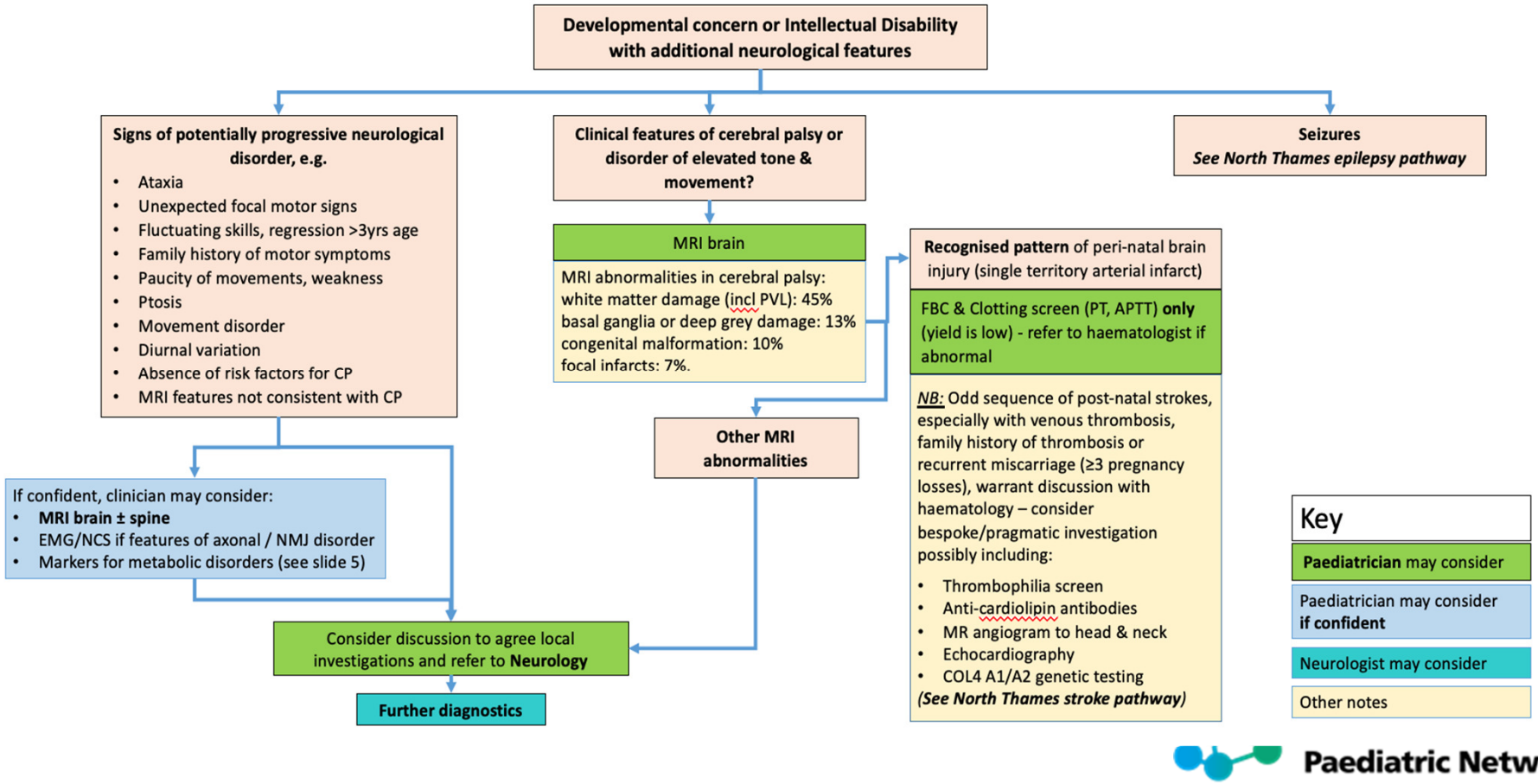
Pathway for Assessment of children presenting with Developmental Concerns – Initial Investigations and what next?

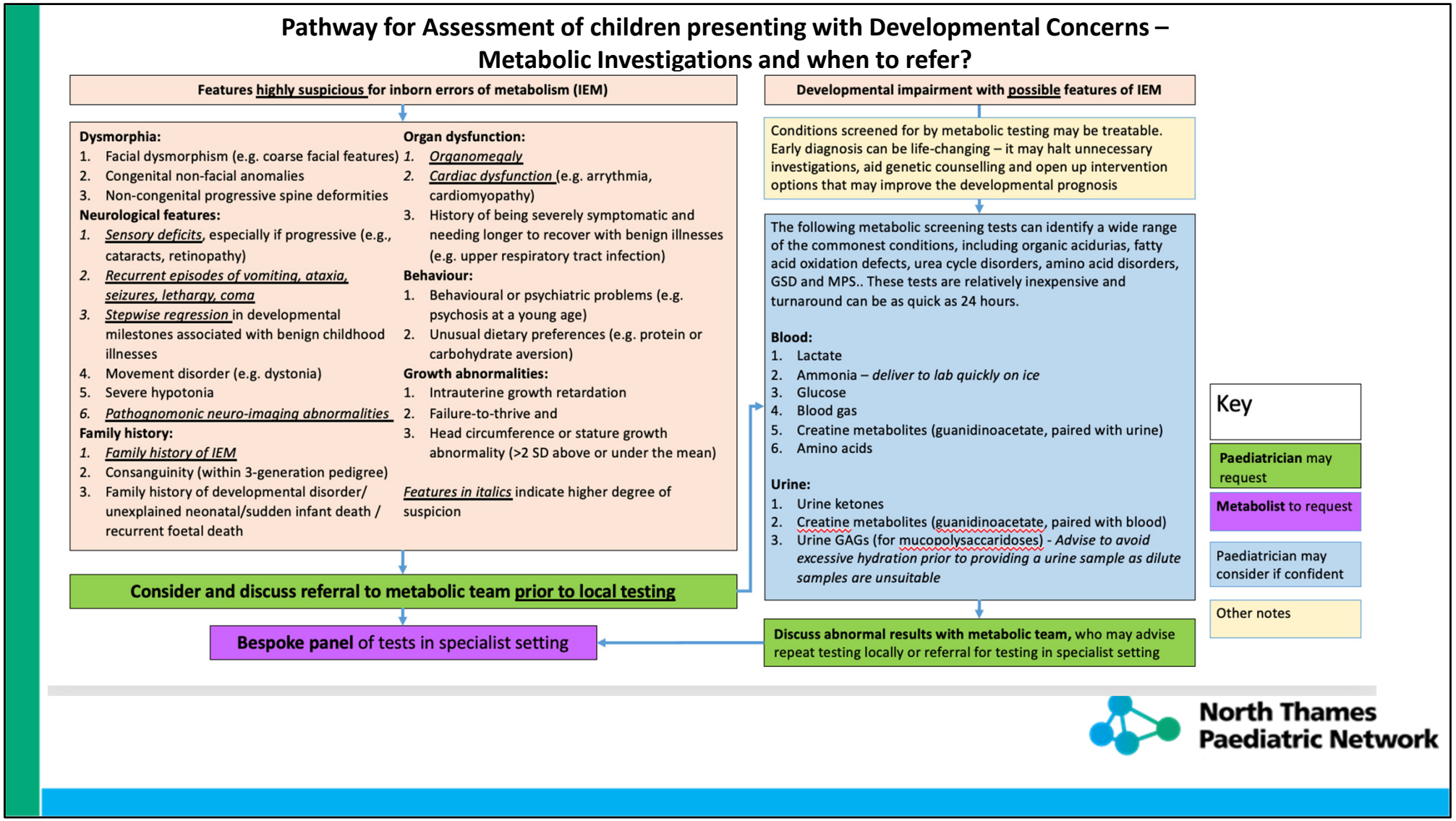


Pathway for Assessment of children presenting with Developmental Concerns – Neurological Investigations and when to refer?



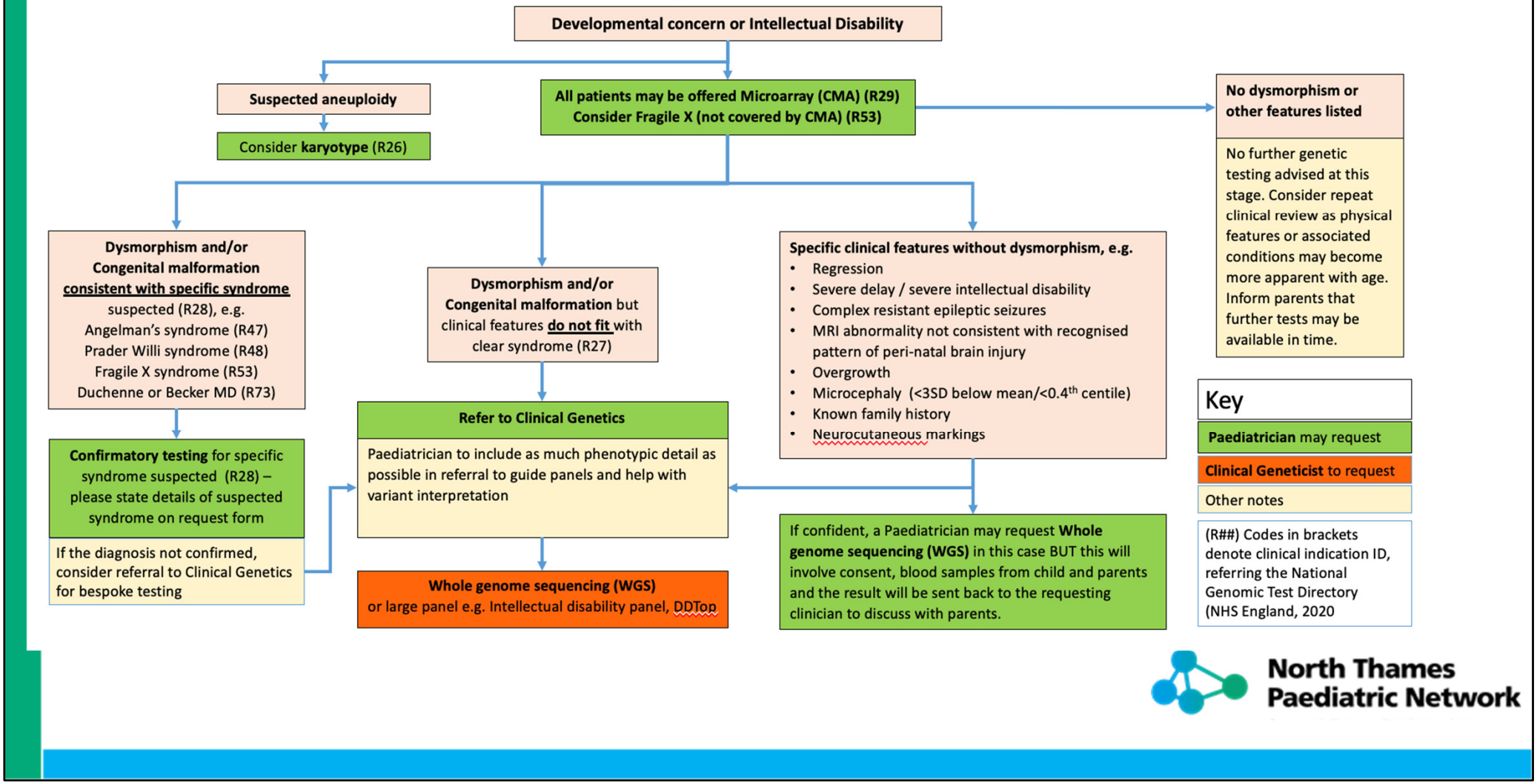
NICE guidelines says MRI scan NOT needed for diagnosis – can be made clinically

Pathway for Assessment of children presenting with Developmental Concerns – Metabolic Investigations and when to refer?



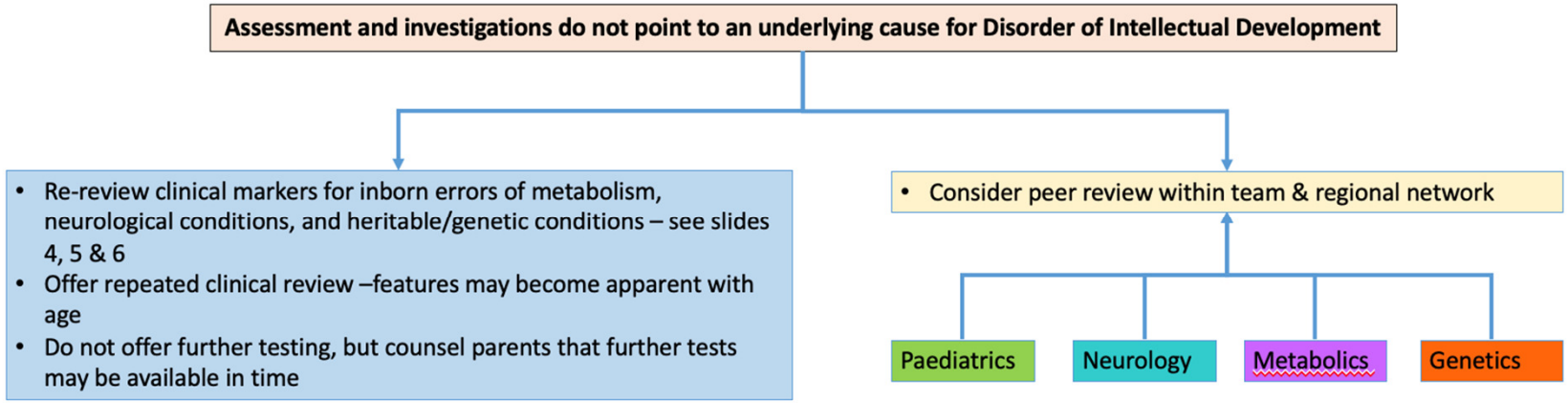
Hypoglycaemia indicates organic aciduria, FAO defects, GSD, or MSUD
Metabolic acidosis (raised anion gap) indicates organic aciduria, FAO defects, or MSUD
Elevated urine ketones indicates MSUD or organic acidurias
Absent urinary ketones indicates FAO defects. Abnormal plasma carnitine in organic acidurias and FAO defects
Elevated ammonia indicates Urea cycle disorder, Organic aciduria or FAO defect
Elevated lactate indicates organic aciduria, FAO defect, or respiratory chain defect
Deranged LFT indicates FAO defects
Plasma Amino acids – high glycine indicates Non-ketotic hyperglycinaemia, or organic aciduria. High BCAAs indicates MSUD. AAs usually abnormal in urea cycle disorders
Abnormal urinary organic acids in MSUD, FAO defects, and organic acidurias
Elevated urine GAGS in MPS

Pathway for Assessment of children presenting with Developmental Concerns – Genetic Investigations and when to refer?



To help simplify the information from the National Genomic Test Directory this flow sheet provides guidance for Paediatricians on Genetic testing for Developmental Delay.
All children with Developmental delay, Intellectual disability and/or autism spectrum disorder should have a microarray. In all cases Fragile X should be considered as this is not covered by the microarray test. If the clinician has suspicion of a particular syndrome this should be specified at the time of the microarray test so that scientists are alerted to apply additional tests should these be required.
If the microarray is normal, further investigation is guided by the patient phenotype. For dysmorphic children or children with congenital malformations a referral should be made to a Clinical geneticist to assess and consider whole genome sequencing. For children who have no dysmorphism or congenital malformations no further genetic testing may be useful as there is very little specificity in the phenotype. Clinicians may wish to review over time as sometimes physical features or medical conditions become more apparent with age. For children with no dysmorphism who have features such as regression, more severe intellectual disability/developmental impairment, abnormal MRI brain or epilepsy, the Paediatrician may order a whole genome sequence (if confident) or refer to a Clinical Geneticist,

Pathway for Assessment of children presenting with Developmental Concerns – No clear clues to diagnosis?



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Future work:

1. Operationalise the guideline – Workshop ie where to send tests
2. Common pitfalls of metabolic tests (Proposal for an audit after implementation)