ONGOING ROLE OF PRIMARY CARE CLINICIAN

Coordinating Care:

1. Genetic Counselling / Medical Genetics
2. Paediatrics (for ages 0–17)
3. Dermatology/Plastic Surgery
4. Ophthalmology
5. Neurology / Neurosurgery
6. Orthopaedics
7. Endocrinology
8. Oncology
9. Psychology / Mental Health
10. High-Risk Breast Screening Clinic (for NF1 women)

LONG-TERM MONITORING AND SURVEILLANCE CHECK LIST

- ✔Annual BP (children: every 6 months)
- ✔Growth, development, head circumference
- ✔Motor coordination; PT/OT needs
- ✔School performance & learning concerns
- ✔Pain, functional changes, or change in size/texture of masses. Pain that seems disproportionate or deeply located may suggest plexiform neurofibroma.
- ✔Vitamin D status & bone health monitoring
- ✔Hearing & balance (NF2-related schwannomatosis)
- ✔Vision screening annually in children
- ✔Mental health screening
- ✔Breast cancer risk discussion (start annual MRI screening at age 30 in NF1 patients – mammography if MRI access is limited)
- ✔MRI Imaging based on symptoms
  - Plexiform neurofibromas: every 6–12 months if growing;
  - Plexiform neurofibromas every 1–3 years if stable
  - Known Optic Pathway Glioma: every 3 months → every 6 months → yearly (if stable)
  - Whole-Body MRI: every 2–3 years in selected patients
  - Suspected Malignant Peripheral Nerve Sheath Tumour: urgent MRI + diffusion

RED FLAGS FOR MALIGNANT PERIPHERAL NERVE SHEATH TUMOURS (MPNST)FINDINGS

- New persistent deep pain
- Night pain
- Firmness or change in texture of a known plexiform
- Neurologic deficit near lesion
- Rapid growth

Non-contrast MRI first; gadolinium when clinical benefit outweighs theoretical risk

MRI INDICATIONS:

- Progressive neurologic symptoms
- New vision changes
- New or enlarging mass
- Persistent deep or night pain
- Change in tumour texture
- Suspected spinal cord compression
- Rapid scoliosis progression
- Suspicion for Optic Pathway Glioma

MRI NOT ROUTINELY INDICATED FOR:

- Stable cutaneous neurofibromas
- Asymptomatic individuals without concerning features
- Learning disability alone
- Stable mild headaches

NEUROFIBROMATOSIS SOCIETY OF ONTARIO

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Disclaimer: This brochure is for general guidance only. It does not replace clinical judgment. Surveillance and imaging should be determined according to each patient's individual needs.

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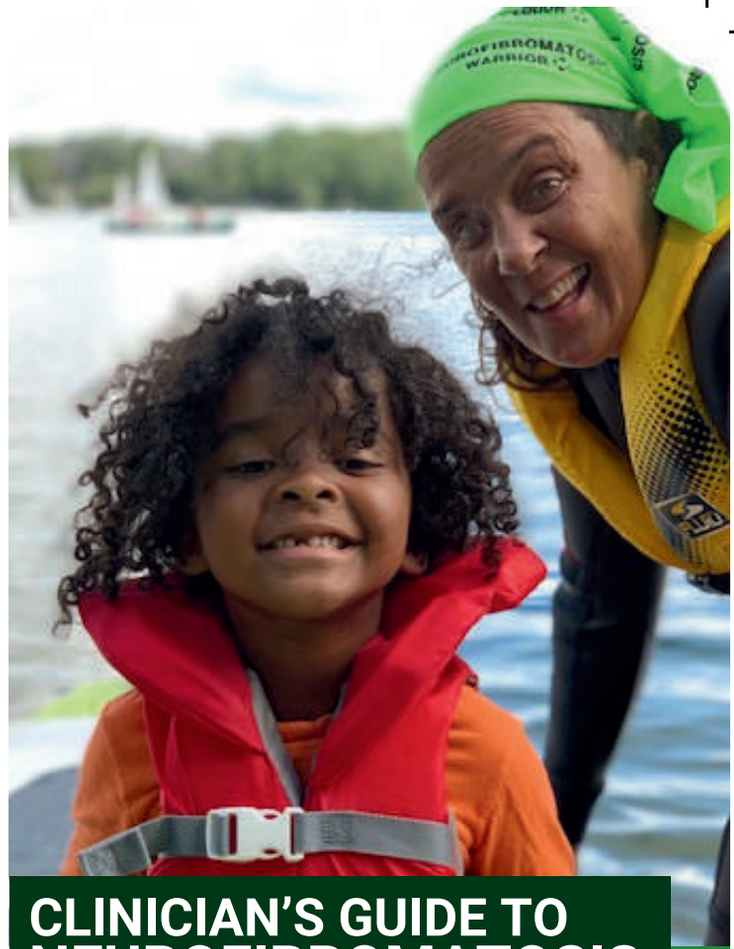

CLINICIAN'S GUIDE TO NEUROFIBROMATOSIS

RECOGNITION
SURVEILLANCE
REFERRAL PATHWAY
PRIMARY CARE MANAGEMENT

NFON
Neurofibromatosis Society of Ontario

Neurofibromatosis is a **complex, multi-system progressive** disorder. Clinical features vary widely, with individuals experiencing symptoms that range from very mild to severe.

This guide helps clinicians identify and manage features of Neurofibromatosis including Neurofibromatosis Type 1, Neurofibromatosis Type 2-related schwannomatosis, and schwannomatosis. Referral to a NF-specialty clinic is recommended whenever available. Where no NF clinic exists, these recommendations support primary care monitoring and referral.

RECOGNIZING NEUROFIBROMATOSIS IN PRIMARY CARE

No single individual exhibits the full range of Neurofibromatosis features; presentation varies widely

SKIN & PIGMENTARY FINDINGS

- ≥6 café-au-lait macules (most common) (5mm prepubertal, 15 mm postpubertal) in the absence of another diagnosis
- Axillary or inguinal freckling (most common)
- ≥ 2 Cutaneous (soft, skin-coloured papules or nodules arising from small peripheral nerves in the dermis) or subcutaneous neurofibromas (firmer, deeper nodules located beneath the skin and may be tender to palpation) OR
- One Plexiform neurofibroma (complex nerve-sheath tumour-Soft, spreading masses that feel like a cluster of twisted cords on examination)

OPHTHALMOLOGIC FEATURES

- Reduced vision, proptosis, strabismus
- Visual field changes
- 2 or more Lisch nodules (Rare <5 years) or 2 or more choroidal abnormalities
- Optic pathway glioma (OPG) (NF1)
- Cataracts in childhood (NF2 feature)

NEUROLOGIC FEATURES

- Persistent or progressive headaches
- Seizures
- Focal deficits
- Ataxia or gait changes
- Neuropathic pain or weakness near a lesion

DEVELOPMENTAL FEATURES

- Speech Delay, verbal apraxia, articulation difficulties
- Learning disabilities
- ADHD features
- Autism spectrum traits
- Large head circumference
- Short stature
- Fine and gross-motor coordination difficulties

HEARING

- Progressive hearing loss, tinnitus, balance issues (consider NF2-related schwannomatosis)

SKELETAL FINDINGS

- Early-onset or atypical scoliosis
- Long-bone bowing / tibial dysplasia / suspected tibial pseudoarthrosis
- Craniofacial asymmetry
- Sphenoid wing dysplasia

FAMILY HISTORY

- First-degree relative with Neurofibromatosis or similar manifestations
- Approximately 50% of individuals diagnosed with Neurofibromatosis develop the condition due to a spontaneous (de novo) mutation with no prior family history

INITIAL WORK-UP IN PRIMARY CARE

PHYSICAL EXAM

- Full skin examination (café-au-lait, presence of neurofibroma, plexiform neurofibroma)
- Vision concerns or ocular asymmetry
- Neurologic exam
- Spine alignment
- Long-bone alignment
- Growth parameters (height, weight, head circumference)
- Blood pressure (pheochromocytoma risk increases with age)

BASELINE INVESTIGATIONS (SUGGESTED PANEL)

- CBC
- CMP / electrolytes/Renal function, LFTs
- Glucose
- Protein
- TSH
- Vitamin D (25-OH) – deficiency is common
- Calcium & phosphate
- ESR/CRP if pain or inflammation reported
- 24-hour urine metanephrines (to rule out pheochromocytoma when indicated: hypertension, tachycardia, sweating, episodic headaches)

IMAGING

MRI is preferred for evaluation of brain, spine, and plexiform tumours. MRI provides superior visualization of nerve-sheath tumours and the optic pathway without radiation exposure.

CT Scans – Use Cautiously

- CT involves ionising radiation.
- With repeated CT exposure, there is an increased long-term risk of Leukemia and brain tumours.
- CT should be used only when MRI is unavailable, contraindicated, or required for acute/emergent care.
- Use lowest radiation dose possible.

Gadolinium Contrast in MRI

- **Evidence of gadolinium accumulation in the brain and other tissues after repeated contrast exposure.**
- **No direct proven clinical harm to date, but long-term effects remain uncertain.**
- **Risk for nephrogenic systemic fibrosis (NSF) in patients with significant renal impairment**

USE GADOLINIUM ONLY WHEN THE DIAGNOSTIC BENEFIT OUTWEIGHS THE THEORETICAL RISK

REFERRAL PATHWAY BY SPECIALTY

1. Medical Genetics / Genetic Counselling

- Confirm diagnosis (Neurofibromatosis Type 1, Neurofibromatosis Type 2-related schwannomatosis, schwannomatosis)
- Genetic Counselling
- Variant interpretation
- Family Planning (when applicable)

Clinical features remain the primary basis for diagnosing Neurofibromatosis. Genetic testing can support diagnosis but may not always fully confirm Neurofibromatosis, particularly in cases involving de-novo mutations or variants that current testing methods may not detect.

A NEGATIVE GENETIC TEST DOES NOT RULE OUT NEUROFIBROMATOSIS IF CLINICAL FEATURES ARE PRESENT

If available, refer to Adult or Paediatric Neurofibromatosis Specialty Clinic for initial evaluation, development, and coordinated surveillance. If no Neurofibromatosis clinic is accessible, refer children to Paediatrics and adults to specialty care if clinically indicated

2. Dermatology/Plastic Surgery

- Symptomatic, painful, or rapidly changing neurofibromas
- Cosmetic concerns
- Identifies benign vs malignant changes of neurofibromas and superficial plexiform

3. Ophthalmology / Neuro-Ophthalmology

- All children with suspected or confirmed NF1 (baseline + early childhood annual exams)
- Assess for Optic Pathway Glioma (NF1)
- Visual decline, strabismus, proptosis
- Orbital tumours
- Sphenoid dysplasia involving the orbit
- Cataracts in Children (NF2- related schwannomatosis)

Optic pathway gliomas may impair hormonal regulation if they extend to or compress the hypothalamus. This can result in endocrine complications, including precocious puberty, growth hormone deficiency, altered appetite, temperature dysregulation, and sleep disturbances. (Refer to endocrinology if indicated)

4. Neurology / Neurosurgery

- Seizures
- Progressive headaches
- Focal neurologic deficits
- Suspected CNS tumours
- Symptomatic plexiform lesions affecting nerves or spine
- Increased Pain

Urgent Evaluation/MRI Required For:

- Rapidly enlarging mass
- New neurologic deficits
- Persistent or rapidly worsening pain
- New asymmetric weakness
- Acute vision change
- New bowel/bladder dysfunction

5. Orthopaedics

- Scoliosis (early or rapidly progressing curves)
- Long-bone bowing / tibial dysplasia
- Suspected pseudoarthrosis
- Craniofacial or sphenoid bone abnormalities (joint care with Ophthalmology/Neurosurgery)
- Recurrent or low-energy fractures → consider endocrine/metabolic bone referral

6. Endocrinology & Metabolic Bone

- Precocious puberty
- Growth abnormalities
- Vitamin D deficiency and low bone mineral density
- Osteopenia / osteoporosis
- Fracture risk
- Hormonal drivers of bone fragility
- Assess for pheochromocytoma when symptomatic: hypertension, sweating, tachycardia, episodic headaches

7. Oncology

- Rapidly enlarging, firm, or newly painful masses
- Concern for MPNST
- Symptomatic Optic Glioma or other CNS tumours
- Suspected Neurofibromatosis-associated malignancies
- Complex nerve-sheath tumours (plexiform neurofibromas)
- Monitoring concerning changes suggesting malignant peripheral nerve sheath tumour (MPNST)- May require Neurosurgery