| Gene | When to Start Screening | Clinical Screening | Biochemical and Laboratory Screening | Imaging Screening |
|---|---|---|---|---|
| **Cluster 1A** | | | | |
| *SDHA, SDHC, SDHD-pi* | 10-15y | Annual: symptom questionnaire and blood pressure measurement. | Every 2 years: Plasma free or urinary | Every 2-3 years: MRI-HN and MRI-TAP. |
| | Adulthood | Continue as above. | Annual: plasma free metanephrines. | MRI as above. Once: PET/CT ($^{68}$Ga-DOTA-SSA preferred). |
| *SDHB* | 6-10y | Annual: symptom questionnaire and blood pressure measurement. | Every 2 years: Plasma free or urinary | Every 2-3 years: MRI-HN and MRI-TAP. |
| | Adulthood | Continue as above. | Annual: plasma free metanephrines. | MRI as above. Once: PET/CT ($^{68}$Ga-DOTA-SSA preferred). |
| *FH* | 8y | Annual: dermatology evaluation (8y). | | Baseline: MRI Abdomen (8y). Every 6 months: US Abdomen (12y). |
| | Adulthood | Continue as above. Annual: gynecologic evaluation (21y). | | Annual: CT or MRI Abdomen (start at 18y). Annual: US Pelvis (start at 21y). |
| | Diagnosis | | Annual: plasma free (or urinary) metanephrines. | |
| **Cluster 1B** | | | | |
| *VHL* | Before 1y | Every 6-12 months: dilated eye exam. | | |
| | 1y | Continue as above. Annual: history and physical examination. | | |
| | 2y | Continue as above, include BP and pulse on exam. | | |
| | 5y | Continue as above. | Annual: plasma free metanephrines. | |
| | 11y | Continue as above. Every 2 years: audiogram. | Continue as above. | Every 2 years: MRI Brain and Spine w/wo contrast. |
| | 15y | Continue as above. | Continue as above. | Continue as above. Every 2 years: MRI Abdomen w/wo contrast. Once: MRI Internal Auditory Canal. |
| | 30y | Annual: history and physical examination, vital signs (BP and pulse), and dilated eye exam. Every 2 years: audiogram. | Continue as above. | Every 2 years: MRI Brain and Spine w/wo contrast and MRI Abdomen w/wo contrast. |
| | 65y | Annual: history and physical examination, vital signs (BP and pulse), and dilated eye exam. | | |
| | Pregnancy | Preconception: history and physical examination and vital signs (BP and pulse). Preconception and every 6-12 months: dilated eye exam. | Preconception: plasma free metanephrines. | Preconception: MRI Brain and Spine w/wo contrast and MRI Abdomen w/wo contrast. |
| *EPAS1/HIF2A* | 8y | Annual: history and physical examination and vital signs (blood pressure and pulse) measurements. Ophthalmology evaluation at diagnosis. | Annual: plasma free or urinary metanephrines. Monitor hemoglobin and hematocrit (unspecified interval). | Every 1-2 years: MRI-HN and MRI-TAP (at minimum, MRI abdomen). Echocardiogram at diagnosis. |
| | 20y | Continue as above. Assess for symptoms of somatostatinoma and other neuroendocrine tumors (e.g., gastrinoma). | Continue as above. Somatostatin level (unspecified interval). | Continue as above. Negative enteric contrast CT or endoscopy for somatostatinoma (unspecified interval). |
| **Cluster 2** | | | | |
| *RET (MEN2A)* | 3-5y (ATA-MOD) | Every 6-12 months: physical examination. Timing of prophylactic thyroidectomy based on screening data and shared decision-making for ATA-MOD but refer by 5y for ATA-H. | Every 6-12 months: serum calcitonin (those without thyroidectomy). | Every 6-12 months: US Neck (those without thyroidectomy). |
| | 11y (ATA-H) or 16y (ATA-MOD) | Continue as above. | Annual: plasma free metanephrines or 24-hour urinary fractionated metanephrines, ionized (or albumin-corrected) calcium level ± serum intact PTH, and serum calcitonin. | Continue as above. If metanephrine screening positive: MRI or CT Adrenals. |
| *RET (MEN2B)* | Before 1y (ATA-HST) | Routine physical examinations. Refer for prophylactic thyroidectomy. | Every 6-12 months: serum calcitonin (those without thyroidectomy, start at 6mo). | Every 6-12 months: US Neck (those without thyroidectomy). |
| | 11y (ATA-HST) | Routine physical examinations. | Annual: plasma free metanephrines or 24-hour urinary fractionated metanephrines. | If metanephrine screening positive: MRI or CT Adrenals. |
| *NF1* | 1-12 months | At diagnosis: physical examination (especially cardiac, neurologic, dermatologic, and skeletal). Annual: ophthalmologic examination. Pediatric standards (timing varies): growth curves and developmental evaluation. | | As needed based on physical examination findings. |
| | 1-5y | Annual: measure HC and BP, physical examination (especially neurologic, dermatologic, and skeletal), ophthalmologic examination, assess for precocious puberty. Pediatric standards (timing varies): growth curves and developmental evaluation. | | As needed based on physical examination findings. |
| | 5y-Puberty | Annual: monitor growth, measure HC and BP, physical examination (especially neurologic, dermatologic, and skeletal), ophthalmologic examination, assess for precocious puberty. At least once: developmental evaluation and discuss reproductive planning. | | As needed based on physical examination findings. |
| | Adolescence | Annual: blood pressure measurement, physical examination (especially neurologic, dermatologic, and skeletal). At least once: developmental evaluation and discuss reproductive planning. As needed: ophthalmologic examination. | Every 3 years: plasma free (or 24-hour urinary fractionated) metanephrines (start at 10-14y). | If metanephrine screening positive: MRA/MRI -AP (add functional imaging [MIBG or F-DOPA PET/CT] if negative). |
| | Adults | Annual: NF1-focused medical history and physical examination, blood pressure measurement. | Continue metanephrine screening as above (also check if symptomatic and hypertensive). Monitor and supplement to maintain 25-hydroxyvitamin D levels in sufficient range. | Consider baseline MRI for plexiform neurofibromas. Hypertensive (if < 30y, pregnant, or abdominal bruits): MRA abdomen. If metanephrine screening positive: MRA/MRI-AP (add functional imaging [MIBG or F-DOPA PET/CT] if negative). Annual (females): mammography (starting at 30y) and consider MRI Breast with contrast (30-50y). |
| *MAX* | Diagnosis | Annual: history and physical examination. | At diagnosis: plasma (or urinary) metanephrines, anterior pituitary endocrine panel, ionized (or albumin-corrected) calcium level, serum intact PTH. | At diagnosis: MRI-HN, MRI-TAP. Consider functional imaging ($^{68}$Ga-DOTATATE or F-DOPA PET/CT). |
| *TMEM127* | 22y | Annual: history and physical examination. | Annual: plasma free (or 24-hour urinary fractionated) metanephrines. | Every 1-3 years: MRI-AP. |
| *MET* | 18y | Annual: history and physical examination. | | Baseline: CT or MRI abdomen, then every 2 years (by 30y or sooner). |
| *H3F3A* | Diagnosis, for p.(G34W) | Annual: history and physical examination. | At diagnosis: plasma (or urinary) metanephrines. | At diagnosis: MRI-AP and skeletal survey. |

Table 2. Recommended screening for PPGL syndromes according to genetic classification. Adapted with permission from Kuo and Pacak 2025 (44). ATA-H, American Thyroid Association (ATA) high risk; ATA-HST, ATA highest risk; ATA-MOD, ATA moderate risk; BP, blood pressure; HC, head circumference; MRI-AP, MRI of abdomen and pelvis; MRI-HN, MRI of head and neck; MRI-TAP, MRI of thorax, abdomen, and pelvis; PTH, parathyroid hormone; SDHD-pi, paternally inherited SDHD pathogenic variant; MEN, multiple neuroendocrine neoplasia; CS, Carney syndrome; CSS, Carney-Stratakis syndrome; 3PA, 3 P association; NF1, neurofibromatosis type 1; TSC, tuberous sclerosis complex.