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Multiple Endocrine Neoplasia Type 1: Evolving Diagnostic Strategies and Therapeutic Approaches in the Era of Precision Medicine

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Abstract

Multiple endocrine neoplasia type 1 (MEN1) is a rare, autosomal dominant disorder characterized by tumors in the parathyroid glands, gastroenteropancreatic system, and pituitary. This review synthesizes current knowledge on MEN1, from its molecular pathogenesis involving loss-of-function MEN1 gene mutations to its diverse clinical manifestations. We discuss the high penetrance of primary hyperparathyroidism and the significant morbidity associated with neuroendocrine tumors, including gastrinomas and nonfunctional pancreatic lesions. The review outlines a comprehensive diagnostic approach that integrates genetic testing for early identification of at-risk individuals, advanced imaging techniques like ^{68}Ga-DOTATATE PET/CT for tumor localization, and emerging liquid biopsy biomarkers for enhanced detection and monitoring. We also detail contemporary management strategies, emphasizing the need for a multidisciplinary team to navigate complex surgical and medical therapies. The article concludes by highlighting future directions, including the potential for CRISPR gene editing, artificial intelligence in diagnostics, and next-generation therapeutics to improve personalized care and long-term outcomes for MEN1 patients.

Keywords: Multiple Endocrine Neoplasia Type 1; MEN1; Neuroendocrine Tumors

Abbreviations: MEN1: Multiple Endocrine Neoplasia Type 1; DM: Dermatomyositis; IVIG: Intravenous Immunoglobulin; GINA: Genetic Information Nondiscrimination Act; PHPT: Primary Hyperparathyroidism; PTH: Parathyroid Hormone; 4D-CT: Four-Dimensional Computed Tomography; MRI: Magnetic Resonance Imaging; GEP-NETs: Gastroenteropancreatic Neuroendocrine Tumors; VI Pomas: Vasoactive Intestinal Peptide-secreting Tumors; EUS: Endoscopic Ultrasound; WHO: World Health Organization; PitNET: Pituitary Neuroendocrine Tumors; GH: Growth Hormone; AI: Artificial Intelligence; CT: Computed Tomography; PET/CT: Positron Emission Tomography/Computed Tomography; FDG: Fluorodeoxyglucose; ctDNA: Circulating Tumor DNA; miRNAs: microRNAs; PNETs: Pancreatic Neuroendocrine Tumors; SPTX: Subtotal Parathyroidectomy; TPTX: Total Parathyroidectomy; NENs: Neuroendocrine Neoplasms; PRRT: Peptide Receptor Radionuclide Therapy; dpNETs: Duodenopancreatic Neuroendocrine Tumors

Introduction

Multiple endocrine neoplasia type 1 (MEN1), also known as Wermer Syndrome, is a rare, autosomal dominant hereditary disorder that predisposes individuals to develop a range of endocrine tumors [1]. The syndrome is primarily characterized by neoplasms in the parathyroid glands, gastroenteropancreatic system, and anterior pituitary gland, which are the most frequently affected organs [2]. However, the clinical manifestations of MEN1 are highly variable and depend on the type, size, and hormonal activity of the associated tumors. A comprehensive and updated understanding of this complex disorder is crucial for the early detection, accurate risk stratification, and effective long-term management of affected individuals [1,3,4]. The pathogenesis of MEN1 is rooted in germline mutations of the MEN1 gene, which encodes the menin tumor suppressor protein [1]. This protein plays a critical role in transcriptional regulation and maintaining genome stability. The loss of its function leads to the development of tumors following the classic "two-hit hypothesis" of tumorigenesis [5-7]. The high penetrance of the inherited mutation means most carriers will develop the syndrome by age 50, underscoring the importance of family-based screening [1]. While the exact reasons for the tissue-specific nature of these tumors remain under investigation, the loss of menin's regulatory role is fundamental to the disease mechanism [1,8,9]. This review aims to provide an up-to-date and integrated synthesis of the current knowledge regarding the clinical spectrum, diagnostic advancements, and therapeutic strategies for MEN1. We will discuss key features of the core tumors, including primary hyperparathyroidism, gastroenteropancreatic neuroendocrine tumors, and pituitary adenomas. We also highlight the importance of genetic testing and imaging, as well as the potential of emerging biomarkers and personalized management approaches to improve patient care and long-term outcomes.

Genetic and Molecular Basis

The MEN1 gene encodes menin, a nuclear tumor suppressor protein involved in transcriptional regulation, genome stability, and cell proliferation [10-13]. Acting as a scaffold, menin interacts with transcription factors and chromatin-modifying complexes like the MLL histone methyltransferase complex, promoting or repressing gene expression depending on context [10,11,14]. Loss-of-function mutations in MEN1 lead to disrupted cell cycle regulation and tumor development, particularly in endocrine tissues, as seen in MEN1 syndrome. These mutations are distributed throughout the gene and typically produce truncated, nonfunctional proteins, though no clear genotype-phenotype correlation has been established [11-13]. The precise reason for tissue-specific tumorigenesis remains unclear, but loss of menin's regulatory role is key to the disease mechanism [10,15,16].

Germline mutations in MEN1 follow an autosomal dominant inheritance pattern, meaning a single pathogenic variant confers a high risk of developing the syndrome, with a 50% chance of transmission to offspring regardless of sex [17-20]. While about 90% of affected individuals inherit the mutation from a parent, ~10% are due to de novo mutations [17-20]. Despite this inheritance pattern, tumor development follows Knudson's two-hit hypothesis, requiring a second somatic mutation for tumorigenesis. Penetrance is high, with most carriers showing symptoms by age 50 [12,20]. There is no clear genotype-phenotype correlation, and clinical variability can exist even within families [12,22]. Genetic counseling is essential for patients and at-risk relatives. Once a familial mutation is identified, predictive testing and reproductive options like prenatal and preimplantation diagnosis are available [17].

In multiple endocrine neoplasia type 1 (MEN1), there are no clear genotype-phenotype correlations associated with MEN1 gene mutations. Most mutations are truncating and dispersed throughout the gene, but their type or location does not reliably predict tumor type, severity, or age of onset [20,23]. Some studies suggest possible associations—for example, mutations in the CHES1-interacting domain (codons 428–610) may correlate with aggressive pancreatic tumors, and large rearrangements with earlier onset [25,26]. Rare variants, like the Burin variant (c.1378C>T), have shown specific tumor patterns within certain families [20]. However, these findings lack consistency and are not robust enough for individualized clinical decision-making. Given the clinical variability, even among family members with the same mutation, other genetic, epigenetic, or environmental factors likely influence disease expression [12,17,20,23,27]. As a result, current clinical management is guided by the clinical diagnosis of MEN1, not specific genotypes.

Emerging molecular biomarkers for MEN1 include circulating microRNAs (miRNAs) and blood-based proteomic signatures. Notably, miR-24-3p (upregulated) and miR-1301-3p (downregulated) have shown strong diagnostic potential, distinguishing MEN1 patients from healthy controls regardless of phenotype or mutation status. miR-24-3p may also play a role in menin silencing and tumorigenesis, suggesting therapeutic relevance [28-30]. Proteomic profiling in MEN1 patients with duodenopancreatic neuroendocrine tumors (dpNETs) has identified circulating proteins linked to oncogenic pathways (e.g., MYCN, YAP1, SMAD targets), which may help predict progression or metastasis [31]. Additionally, epigenetic alterations, including DNA methylation and histone modifications, are under investigation as biomarkers and therapeutic targets, especially in pancreatic neuroendocrine tumors [32]. In summary, miR-24-3p, miR-1301-3p, and circulating proteomic signatures are among the most promising emerging biomarkers for MEN1, with potential for diagnostic, prognostic, and therapeutic use [28-32].

Clinical Spectrum of MEN1-Associated Tumors

Multiple Endocrine Neoplasia Type 1 (MEN1), or Wermer Syndrome, is an autosomal dominant hereditary disorder char-

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acterized by a predisposition to develop neoplasms in multiple endocrine organs. The clinical manifestations of MEN1 vary depending on the type, size, and hormonal activity of the associated tumors. Among these, the most frequently involved organs are the parathyroid glands and the gastroenteropancreatic system. A comprehensive understanding of the clinical spectrum, diagnostic approaches, and pathological features of these tumors is critical for early detection, risk stratification, and management of affected individuals [33].

Parathyroid Tumors

Primary hyperparathyroidism (PHPT) is the most prevalent and often the earliest clinical manifestation of MEN1, occurring in more than 90% of mutation carriers, frequently by the third decade of life [33]. The condition arises from hyperplasia or multiple adenomas of the parathyroid glands, in contrast to sporadic PHPT, which typically involves a solitary adenoma. Patients often remain asymptomatic in the early stages; however, over time, the hypersecretion of parathyroid hormone (PTH) leads to hypercalcemia, which manifests clinically as fatigue, polyuria, nephrolithiasis, constipation, neuropsychiatric symptoms, and in severe cases, bone demineralization and fractures [34]. The complications associated with MEN1-related PHPT can be significant. Chronic hypercalcemia may contribute to nephrocalcinosis and renal impairment, and reduced bone mineral density is common due to the prolonged duration of disease before diagnosis. Unlike sporadic forms, the onset of hyperparathyroidism in MEN1 tends to occur at a younger age and follows a more indolent course, often escaping early detection [35].

Biochemical diagnosis of MEN1-associated PHPT is established through elevated serum calcium levels in the presence of an inappropriately high or normal PTH level. Other laboratory findings may include hypophosphatemia and elevated urinary calcium excretion. Imaging plays a secondary role in diagnosis but is crucial in preoperative planning. Neck ultrasound and technetium-99m sestamibi scintigraphy are commonly used to localize abnormal parathyroid glands, although their sensitivity is lower in MEN1 due to multiglandular involvement [36]. Four-dimensional computed tomography (4D-CT) and magnetic resonance imaging (MRI) may be considered in complex or recurrent cases, particularly when planning reoperative surgery [37].

Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)

GEP-NETs represent the second most common manifestation of MEN1, affecting approximately 30–70% of patients, with tumors originating primarily in the duodenum and pancreas [38]. These tumors may be functional—secreting bioactive hormones—or nonfunctional, with the latter often discovered incidentally or through surveillance imaging. Functional GEP-NETs in MEN1 include insulinomas, gastrinomas, and, less commonly, glucagonomas and vasoactive intestinal peptide-secreting tumors (VIPomas). Insulinomas are typically benign and manifest with symptoms of fasting hypoglycemia such as confusion, diaphoresis, and seizures. Biochemically, they are characterized by elevated insulin, C-peptide, and proinsulin levels during episodes of hypoglycemia, often confirmed by a supervised 72-hour fast [39]. In contrast, gastrinomas—frequently located in the duodenum—are the most common functional GEP-NET in MEN1. These tumors result in Zollinger–Ellison syndrome, characterized by severe peptic ulcer disease, gastroesophageal reflux, and chronic diarrhea due to hypergastrinemia and gastric acid hypersecretion [40]. Gastrin levels are typically elevated more than tenfold in the fasting state, especially in the absence of proton pump inhibitors, and are often associated with basal acid hypersecretion.

Nonfunctional pancreatic NETs are increasingly recognized in MEN1 due to regular surveillance imaging. Although clinically silent, they pose a substantial risk due to their potential for malignancy and metastatic spread. Studies indicate that tumor size and growth rate are key predictors of malignant transformation, with tumors greater than 2 cm associated with higher rates of metastasis [41]. Hence, size-based criteria are often used to guide the timing of surgical intervention. The diagnostic workup of GEP-NETs relies on a combination of biochemical assays and imaging. Chromogranin A and pancreatic polypeptide are non-specific markers often elevated in functional and nonfunctional NETs. Localization of GEP-NETs may involve contrast-enhanced MRI, CT, or endoscopic ultrasound (EUS), which is particularly effective for small pancreatic lesions. Functional imaging, such as somatostatin receptor scintigraphy (Octreoscan) or Ga-68 DOTATATE PET/CT, provides high sensitivity for detecting both primary and metastatic lesions and is instrumental in staging and management planning [42]. Histopathologically, MEN1-associated NETs exhibit well-differentiated neuroendocrine morphology, with positive immunohistochemical staining for neuroendocrine markers such as synaptophysin, chromogranin A, and hormone-specific peptides (e.g., insulin, gastrin). Ki-67 index and mitotic rate are essential for tumor grading according to the World Health Organization (WHO) classification, guiding prognostication and therapeutic decision-making [43].

Pituitary Adenomas

Pituitary Neuroendocrine tumors (PitNET) are benign neoplasms originating from the anterior pituitary gland, situated within the Sella turca at the base of the brain [44]. They represent approximately 10% of all intracranial tumors. Studies report an annual incidence ranging from 3.9 to 7.4 cases per 100,000 individuals, with a prevalence estimated between 76 and 116 cases per 100,000 population [45]. These tumors are classified as either functional or non-functional, based on their capacity to secrete biologically active hormones and the specific type of hormone produced [46]. Signs and symptoms of hyperprolactinemia, such

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as hypogonadism, amenorrhea, galactorrhea, hemianopia bitemporal [47]. Non-functional adenomas typically do not exhibit hormonal activity and are more likely to present with symptoms related to mass effect [48]. In MEN1 syndrome, pituitary adenomas most commonly include lactotrophs, followed by silent, somatotroph, and corticotroph subtypes [49]. Genetic plays an important role in the pathogenesis of the disease, the MEN1 gene, located on chromosome 11q13.1, is in charge of encoding a cell cycle regulatory cofactor; somatic MEN1 mutations are observed in sporadic adenomas. Approximately 10% of MEN1-related cases arise from de novo mutations, occasionally presenting as mosaicism [50].

Diagnosis of pituitary tumors is based on a combination of clinical presentation and imaging findings [51]. MRI is the gold standard for anatomical evaluation; the most utilized sequences include non-contrast spin-echo T1-weighted images in sagittal and coronal planes, fast spin-echo T2-weighted coronal images, and gadolinium-enhanced T1-weighted coronal sequences [52]. Management strategies are tailored according to the tumor type and the specific hormone secreted. In the most common subtype, prolactinomas, cabergoline has demonstrated superior efficacy compared to bromocriptine. Both are dopamine agonists, but cabergoline is associated with a more favorable side effect profile. For growth hormone (GH)-secreting adenomas, somatostatin analogs have shown significant therapeutic benefit and remain a cornerstone of medical management. Surgical evaluation is recommended in cases where the tumor is close to the optic chiasm, is associated with anterior hypopituitarism, demonstrates progressive enlargement, or presents with risk factors for apoplexy. Additionally, neuro-ophthalmologic assessment is advised at baseline and 6-month follow-up in cases where there is evidence of tumor impingement on the optic chiasm [53].

Other Less Common Tumors

While pituitary adenomas, parathyroid hyperplasia, and pancreatic neuroendocrine tumors dominate the clinical spectrum of MEN1, several other tumours are less common but warrant clinical attention. For instance, thymic carcinoids, although rare, predominantly affect men and carry significant morbidity due to their aggressive behaviour and higher malignancy potential [54]. Bronchial carcinoids also occur and tend to be less aggressive compared to thymic variants; however, vigilant monitoring is necessary due to their metastatic potential [55]. Moreover, adrenal involvement in MEN1 typically presents as benign adrenal cortical adenomas, hyperplasia, or infrequently, pheochromocytomas [56]. Although these adrenal manifestations are often asymptomatic and detected incidentally during imaging studies, hormonal evaluation is recommended, especially to rule out functional adrenal lesions [56]. In addition, cutaneous manifestations such as skin angiofibromas, collagenomas, and lipomas are frequently overlooked, but are clinically relevant markers of MEN1 [57]. These lesions are benign and commonly appear as small, reddish-brown papules on the nose and cheeks. Their presence may serve as an early clinical indicator of underlying MEN1, especially in otherwise asymptomatic individuals [57]. Even though skin lesions are not pathognomonic, recognizing them plays an important role in the timely identification and management of patients with MEN1 [57].

Advances in Diagnostic Strategies

Genetic Testing and Counseling

The cornerstone of early and accurate diagnosis in Multiple Endocrine Neoplasia Type 1 (MEN1) is genetic testing, particularly targeting the MEN1 gene, which encodes the tumor suppressor protein menin. Genetic testing is indicated in patients with clinical features suggestive of MEN1, such as parathyroid adenomas, pancreatic neuroendocrine tumors, and pituitary adenomas, especially when these occur at a young age or in combination [11]. Individuals diagnosed with a single MEN1-associated tumor before age 30 should be considered for genetic evaluation, as this could indicate a germline mutation [58]. Family screening plays a crucial role, given the autosomal dominant inheritance pattern of MEN1. Once a pathogenic MEN1 mutation is identified in a proband, first-degree relatives should be offered predictive genetic testing. Early identification of asymptomatic mutation carriers allows for proactive surveillance and early intervention, which significantly improves prognosis [59]. However, this strategy necessitates comprehensive genetic counseling to ensure individuals understand the implications of testing, including the psychosocial impact of a positive result and the potential for insurance or employment discrimination, despite protections under laws such as the Genetic Information Nondiscrimination Act (GINA) in the United States [60]. Ethically, genetic testing raises questions about consent, especially in children. Testing minors is generally recommended only if early surveillance or intervention will benefit the child during childhood or adolescence. Therefore, a balance must be struck between respecting future autonomy and preventing morbidity through early diagnosis [61].

Imaging Techniques

The diagnostic landscape for MEN1 has evolved substantially with advancements in imaging technologies. Conventional imaging modalities such as magnetic resonance imaging (MRI) and computed tomography (CT) remain essential tools, particularly for the evaluation of pituitary adenomas and pancreatic lesions [62]. However, these methods are often limited in sensitivity, especially for detecting small or functionally silent tumors. In contrast, functional imaging techniques have markedly enhanced the detection and characterization of MEN1-associated neuroendocrine tumors (NETs). Among these, 68Ga-DOTATATE PET/CT has emerged as a superior modality for identifying well-differentiated NETs due to its high affinity for somatostatin receptors, offering improved resolution and accuracy compared to traditional somatostatin receptor scintigraphy [63]. PET/CT with 18F-FDG may also be utilized in more aggressive or poorly differentiated cases, aiding in risk stratification [64]. Current surveillance protocols integrate a

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combination of imaging and biochemical markers, tailored to the individual's mutation status, age, and family history. For mutation carriers, imaging usually begins in childhood or adolescence and is repeated at regular intervals to monitor for the development of MEN1-associated tumors. These protocols are essential for early detection and improved clinical outcomes, particularly in asymptomatic individuals identified through family screening [65].

Biomarkers and Liquid Biopsy

In parallel with imaging advancements, interest has grown in biomarkers and liquid biopsy techniques as non-invasive diagnostic tools for MEN1. Traditional biochemical markers such as serum calcium, parathyroid hormone, prolactin, insulin, and gastrin levels remain critical in the initial evaluation and monitoring of MEN1-associated tumors [66]. However, these tests often lack specificity or may become elevated only after significant disease progression. Emerging approaches like circulating tumor DNA (ctDNA), microRNA profiling, and methylation signatures from blood samples represent the frontier of MEN1 diagnostics. These liquid biopsy techniques offer the promise of earlier detection, real-time monitoring of tumor dynamics, and even treatment response assessment without the need for invasive procedures [67]. While still largely investigational in MEN1, initial studies have demonstrated their potential in related neuroendocrine tumor syndromes, paving the way for future integration into routine care [68].

Therapeutic Approaches in the Era of Precision Medicine

Surgical Management

Surgical excision is the only potential cure for non-metastatic PNETs, but it's often challenging in MEN1 patients due to multiple, potentially malignant tumors of varying sizes [69,70]. While most microadenomas are stable, larger tumors (2-3cm and >4cm) have high rates of lymph node and liver metastasis, respectively [71,72]. Because of these challenges, survival is linked to non-metastatic disease, and many patients require additional therapies beyond surgery [73].

Subtotal Parathyroidectomy (SPTX): SPTX involves removing three parathyroid glands and part of the fourth, or preserving a normal fourth gland, to prevent permanent hypoparathyroidism and reduce early postoperative hypocalcemia [71]. This is often the surgical choice when one gland can't be found. However, its effectiveness is debated as it's difficult to determine which gland to preserve, and the maneuver risks damaging blood supply, causing permanent hypoparathyroidism or cell seeding that could lead to recurrence [72].

Total Parathyroidectomy (TPTX): TPTX involves completely removing all parathyroid tissue, including a transcervical thymectomy to address potential occult glands. The goal is to prevent difficult-to-treat cervical recurrences by radically removing all parathyroid tissue, and to reduce the risk of permanent hypoparathyroidism by autotransplanting some tissue, usually to the non-dominant forearm [73].

Pancreatic surgeries for neuroendocrine tumors fall into two main categories: tissue-sparing (enucleation) and tissue-resection (pancreatoduodenectomy, distal pancreatectomy). Enucleation is a preferred method for small tumors away from the pancreatic duct because it reduces the risk of complications like endocrine or exocrine insufficiency, leading to shorter hospital stays and lower costs [69,70].

Medical Management

Somatostatin analogs (octreotide, lanreotide) are key medical treatments that bind to somatostatin receptors on NENs to stabilize tumor growth and manage symptoms [3,4]. For insulinomas, they are a second-line therapy for controlling hypoglycemia but can paradoxically worsen it in tumors without somatostatin receptors. Other options include pasireotide, everolimus, and chemotherapy [73]. For metastatic GEP-NETs, treatment options are limited. Somatostatin analogs and targeted drugs like everolimus and sunitinib can stabilize the disease for a limited time. A newer, promising option is Peptide Receptor Radionuclide Therapy (PRRT), which delivers radiation directly to tumor cells via radiolabeled somatostatin analogues, offering a more durable response [69,70].

Multidisciplinary and Surveillance Approaches

MEN1 patients benefit from a coordinated, multidisciplinary approach that brings together endocrinologists, geneticists, oncologists, surgeons, radiologists, and nutritionists. This collaborative model is essential due to the syndrome's propensity for multiple synchronous and metachronous tumors, variable tumor behavior, and the need for nuanced risk stratification and management [74-77]. Genetic counseling is a cornerstone, both for affected individuals and at-risk relatives, facilitating early diagnosis, cascade testing, and informed decision-making regarding surveillance and reproductive planning [75,78,79]. Endocrinologists oversee biochemical and clinical monitoring, while oncologists and surgeons contribute to the management of neuroendocrine tumors and parathyroid disease, tailoring interventions to tumor type, size, and growth kinetics [80,81]. Nutritionists play a key role in preventing and managing complications such as osteoporosis and nephrolithiasis, and in supporting patients undergoing pancreatic surgery [76]. This team-based approach ensures that care is both comprehensive and responsive to the evolving needs of MEN1 patients across the lifespan.

Future Directions

The evolving landscape of MEN1 research promises significant advancements in diagnosis and treatment. A major frontier lies in CRISPR and gene editing, which hold the potential to correct the underlying MEN1 gene mutations [10,12,60]. Although still in

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the experimental phase, these technologies may one day offer a curative approach by restoring menin function at a molecular level, preventing the formation of tumors. In diagnostics, artificial intelligence (AI) is poised to transform how we screen and monitor MEN1 patients. AI algorithms could analyze large datasets from diagnostic imaging, such as MRIs and PET/CT scans [42,52], to identify subtle, early tumor changes that are easily missed by the human eye. This could lead to earlier detection of fast-growing or malignant lesions, improving prognosis and guiding timely intervention. Advancements in genomics and bioinformatics are paving the way for personalized risk stratification tools. By combining an individual's specific MEN1 mutation [31,59] with their clinical history, biomarkers [34,68], and other genetic modifiers, new tools could provide more accurate predictions of which tumors are most likely to develop and become aggressive [33]. This would allow for a highly tailored surveillance schedule, minimizing unnecessary testing for low-risk individuals while focusing intensive monitoring on those at greatest risk. The future of MEN1 management is bright with the development of next-generation therapeutics and a push for more clinical trials. Current treatments primarily manage symptoms or remove tumors, but novel targeted therapies are being explored [35,69]. These new drugs could specifically inhibit the molecular pathways that are dysregulated due to menin deficiency. Expanding the number and scope of clinical trials is crucial to rigorously test these new treatments and refine existing ones, ultimately improving patient outcomes and quality of life.

Conclusion

Multiple endocrine neoplasia type 1 is a complex and highly penetrant hereditary syndrome requiring a comprehensive, multidisciplinary approach. While the clinical manifestations are varied, primary hyperparathyroidism, pancreatic neuroendocrine tumors, and pituitary adenomas remain the cardinal features, each demanding tailored diagnostic and therapeutic strategies. Early diagnosis through genetic testing and a consistent, lifelong surveillance protocol are paramount to improving patient outcomes and reducing malignancy-related mortality. Advances in molecular biology, including the identification of novel biomarkers, alongside sophisticated imaging modalities and a growing understanding of the genetic underpinnings of the disease, are paving the way for more personalized and effective care. As research continues into next-generation therapeutics and the application of technologies like AI and gene editing, the future of MEN1 management promises to move beyond symptom control to offer more curative and patient-centered interventions.

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