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MultidisciplinaryPerspectives in Colorectal Polyps and Polyposis Syndromes:Integrating Pharmacotherapy, Laboratory Biomarkers, Diagnostic Imaging, Rehabilitation, and Genetic Profiling

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Abstract

Background: Colorectal polyps are common gastrointestinal lesions with heterogeneous histological, molecular, and malignant potential. Although many polyps are benign, adenomatous and serrated lesions may represent important precursors of colorectal cancer. Hereditary polyposis syndromes further increase cancer risk and require early recognition, genetic assessment, and structured surveillance.

Aim: This review aimed to provide an integrated overview of colorectal polyps, focusing on their classification, etiology, epidemiology, pathophysiology, histopathology, clinical presentation, diagnostic evaluation, differential diagnosis, and contemporary management strategies.

Methods: Relevant clinical and scientific literature addressing colorectal polyps and hereditary polyposis syndromes was reviewed. Evidence concerning genetic mechanisms, environmental risk factors, endoscopic and radiological diagnosis, histopathological classification, colonoscopic polypectomy, advanced endoscopic techniques, surgical interventions, and multidisciplinary management was synthesized.

Results: Colorectal polyps comprise hyperplastic, inflammatory, hamartomatous, adenomatous, and serrated lesions with substantially different biological behaviors. Molecular abnormalities involving *APC*, *KRAS*, *TP53*, mismatch-repair genes, *BRAF*, *STK11*, *SMAD4*, *MUTYH*, and *PTEN* contribute to distinct hereditary and sporadic pathways. Colonoscopy remains central to diagnosis and treatment, allowing simultaneous detection, characterization, biopsy, and removal. Cold and hot snare polypectomy, endoscopic mucosal resection, and endoscopic submucosal dissection provide increasingly tailored approaches for different lesions. Surgical and transanal procedures are reserved for selected advanced, unresectable, malignant, or hereditary disease.

Conclusion: Accurate characterization and complete management of colorectal polyps are essential for colorectal cancer prevention. Integration of endoscopy, pathology, laboratory and molecular testing, radiology, genetics, pharmacy, surgery, and rehabilitation supports individualized treatment and long-term surveillance.

Keywords: Colorectal polyps; colorectal cancer; adenomas; serrated lesions; polyposis syndromes; colonoscopy; polypectomy; histopathology; genetic testing; multidisciplinary management.

Introduction

A colorectal polyp is a localized mass that projects from the mucosal surface into the lumen of the large intestine. Colorectal polyps are common gastrointestinal lesions and may occur as isolated findings or as manifestations of inherited polyposis syndromes. Their clinical importance varies considerably according to size, morphology,

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histological characteristics, number, and molecular features. Based on size, colorectal polyps are generally categorized as diminutive lesions measuring less than 6 mm, small lesions measuring 6–9 mm, and large lesions measuring more than 9 mm. Morphologically, they are classified as either sessile or pedunculated. Sessile polyps have a broad attachment to the mucosal surface and may have a relatively flat configuration, whereas pedunculated polyps are connected to the intestinal wall by a fibrovascular stalk. These morphological characteristics are clinically relevant because they influence endoscopic detection, technical difficulty of removal, and the potential for incomplete resection. Histological classification remains one of the most important determinants of the clinical significance and malignant potential of colorectal polyps. The major histological categories include hyperplastic, inflammatory, and neoplastic polyps.[1] Neoplastic polyps, particularly adenomatous lesions, are of major clinical concern because they represent important precursor lesions in colorectal carcinogenesis and account for a substantial proportion of colorectal cancers (CRCs).[2] Adenomas may develop through progressive accumulation of genetic and molecular abnormalities, resulting in dysplastic transformation and eventual invasive malignancy. Serrated polyps represent another clinically important group and are increasingly recognized as contributors to colorectal carcinogenesis. They are estimated to be associated with approximately 15% to 30% of CRC cases and may progress through molecular pathways that differ from the conventional adenoma–carcinoma sequence.[3] In contrast, hyperplastic and inflammatory polyps generally have limited malignant potential, although their clinical significance depends on their distribution, size, number, and underlying disease context.

Polyposis refers to a condition characterized by the development of multiple polyps throughout the gastrointestinal tract. Although some polyposis conditions are acquired, many clinically important forms are hereditary and are associated with germline genetic abnormalities. Hereditary polyposis syndromes collectively account for approximately 1% to 7% of CRCs and may be accompanied by significant extracolonic manifestations involving multiple organs and tissues. The genetic basis of these syndromes is particularly important because affected individuals and their relatives may have substantially increased lifetime risks of colorectal and other malignancies.[4] The clinical management of colorectal polyps therefore requires an integrated multidisciplinary approach. Endoscopic evaluation provides the principal means of detection and removal, while histopathological assessment establishes the definitive tissue diagnosis. Radiological imaging may contribute to assessment when advanced lesions, complications, or associated malignancy are suspected. Laboratory and molecular investigations can support risk assessment and identify relevant biomarkers or hereditary abnormalities. Genetic evaluation is particularly important in patients with multiple polyps, early-onset disease, a strong family history, or clinical features suggestive of an inherited syndrome. Physiotherapy and rehabilitation may also become relevant in patients undergoing treatment for advanced colorectal disease or major colorectal surgery, particularly when functional impairment, deconditioning, or postoperative complications affect recovery. Early recognition, appropriate surveillance, complete removal of clinically significant lesions, and identification of hereditary risk are therefore essential components of colorectal cancer prevention and long-term patient management [1][2][3][4].

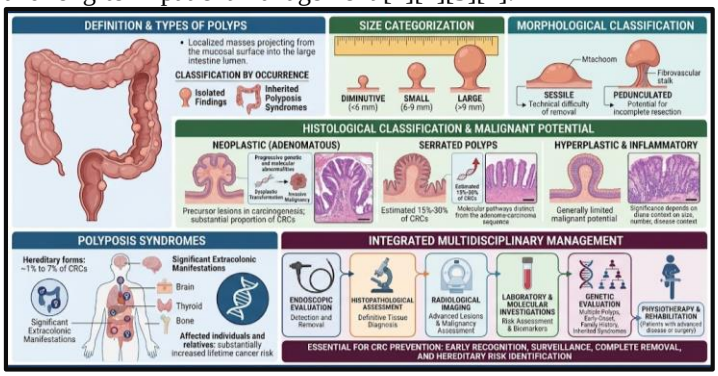

Figure-1: Colorectal Polyps.

Etiology

The development of colorectal polyps is multifactorial and reflects interactions among genetic susceptibility, environmental exposures, lifestyle factors, chronic inflammation, and alterations in the intestinal microenvironment. In many sporadic cases, the precise initiating factor remains uncertain. Neoplastic polyps are particularly associated with the accumulation of genetic and epigenetic abnormalities in colonic epithelial cells, while environmental and behavioral factors may influence the probability of developing these lesions and their subsequent progression. Cigarette smoking is an established risk factor for colorectal polyp formation and may contribute through exposure to carcinogenic compounds, oxidative stress, and cellular DNA damage.[5] Other recognized risk factors include obesity, high consumption of red meat, and inadequate dietary intake of fiber and calcium.[6] These factors may influence intestinal inflammation, metabolic activity, epithelial proliferation, and the composition of the gut microbiota. Conversely, nonsteroidal anti-inflammatory drugs and statins have demonstrated potentially protective effects against colorectal polyp formation, although their routine use specifically for polyp prevention requires consideration of potential adverse effects and individual clinical circumstances.[7] The underlying

etiology also differs according to histological subtype. Serrated adenomas are associated with distinctive molecular abnormalities, including microsatellite instability, hypermethylation of the *MLH1* gene, and mutations involving the *BRAF* gene.[8] Hamartomatous polyps may occur as isolated lesions or as components of inherited polyposis syndromes, including Peutz-Jeghers syndrome (PJS), Cowden syndrome, and juvenile polyposis syndrome (JPS).[9] Inflammatory polyps, commonly referred to as pseudopolyps, are most frequently associated with inflammatory bowel disease (IBD), particularly ulcerative colitis. Similar lesions may develop following infectious or ischemic colitis because of mucosal injury, inflammation, and subsequent regenerative processes.[10] Chronic intestinal inflammation and dysregulation of the gut microbiota may further contribute to epithelial injury and abnormal mucosal proliferation.[11] Several hereditary polyposis syndromes are caused by specific germline mutations. Familial adenomatous polyposis (FAP) is an autosomal dominant disorder associated with mutations in the *APC* gene on chromosome 5q.[12] MUTYH-associated polyposis (MAP) is an autosomal recessive condition caused by biallelic mutations in the *MUTYH* gene, which participates in base-excision DNA repair.[13] PJS is associated with mutations in the *STK11* gene on chromosome 19p,[14] whereas familial juvenile polyposis may result from mutations in the tumor-suppressor gene *SMAD4* on chromosome 10q.[15] PTEN hamartomatous tumor syndromes, including Cowden and Bannayan-Riley-Ruvalcaba syndromes, are associated with abnormalities of the *PTEN* gene on chromosome 10q.[16] Hereditary mixed polyposis syndrome may follow an autosomal dominant pattern involving *SMAD4* and *BMPR1A* abnormalities.[17] In contrast, Cronkhite-Canada syndrome is a rare acquired, nonfamilial disorder characterized by gastrointestinal polyposis of uncertain etiology.[18] Recognition of these diverse causes is essential for appropriate surveillance, genetic counseling, and individualized cancer-risk assessment.

Epidemiology

Colorectal polyps are common lesions, and their epidemiological distribution varies according to age, sex, histological subtype, genetic susceptibility, ethnicity, and exposure to environmental and lifestyle risk factors. Hyperplastic polyps represent the most common histological variant, whereas adenomatous polyps are particularly important because of their established potential to progress toward colorectal cancer. The frequency of colorectal polyps increases substantially with advancing age, reflecting the cumulative effects of somatic genetic alterations, environmental exposures, chronic mucosal injury, and prolonged epithelial turnover. Men generally have a higher prevalence of colorectal adenomas than women, and this sex difference becomes more evident with increasing age. In the United States, adenomatous polyps are detected in approximately 20% to 40% of screening colonoscopies performed in adults older than 50 years. However, colorectal adenomas are not restricted to older populations. Among younger adults, adenomatous polyps are detected in approximately 12% of women and 24% of men. Their occurrence increases progressively with age, reaching approximately 27% in women and 40% in men among adults older than 80 years.[19] This age-related pattern is clinically important because prolonged exposure to carcinogenic and inflammatory processes increases the opportunity for genetic and epigenetic abnormalities to accumulate within colonic epithelial cells. Colorectal polyps are frequently asymptomatic and may therefore remain undetected without screening or diagnostic colonoscopy. In asymptomatic individuals undergoing evaluation, colorectal polyps have been detected in approximately 34.3% of cases.[20,21] A substantial proportion of affected individuals may also have synchronous lesions, with up to 50% presenting with additional polyps. The presence of synchronous lesions emphasizes the importance of complete examination of the colon after identification of an initial polyp because additional lesions may have different histological characteristics and levels of malignant potential. The epidemiology of colorectal polyps differs considerably between adults and children. In pediatric populations, the reported incidence ranges from approximately 4% to 12%, with hamartomatous polyps accounting for most cases.[22] Pediatric colorectal polyps therefore require a different clinical perspective, particularly when multiple lesions, recurrent polyps, or a strong family history is present. Such findings may indicate an underlying hereditary polyposis syndrome and warrant further genetic evaluation. Population differences have also been reported, with colorectal polyps occurring more frequently among non-Caucasian populations.[23] These differences may reflect interactions among genetic background, dietary patterns, lifestyle factors, environmental exposures, healthcare access, and differences in screening practices. Overall, the epidemiology of colorectal polyps demonstrates the importance of age-appropriate screening and surveillance. Early identification and removal of premalignant lesions can reduce the opportunity for progression toward invasive colorectal malignancy, while recognition of early-onset or familial disease can facilitate genetic assessment and targeted surveillance.

Pathophysiology

The pathophysiology of colorectal polyp formation involves a multistep process characterized by progressive genetic, epigenetic, and cellular alterations within the colonic epithelium. The conventional adenoma–carcinoma sequence provides an important model for understanding how normal colonic epithelial cells can undergo transformation

into adenomatous polyps and subsequently develop invasive carcinoma. Somatic mutations involving the *APC* gene are considered an important early event in conventional adenoma formation. These mutations may occur spontaneously within colonic epithelial cells and have been identified in aberrant crypts, supporting their involvement during the initial stages of neoplastic transformation. Loss of normal APC-mediated regulation disrupts cellular growth and differentiation, allowing abnormal epithelial cells to proliferate and form an early adenomatous lesion. Early adenomas may remain benign for many years. However, continued accumulation of molecular abnormalities can promote progression from an early lesion to an intermediate and subsequently advanced adenoma. Alterations involving the *DCC* (deleted in colon cancer) gene have been implicated in the transition from intermediate to late adenoma. The DCC protein functions as a neural cell adhesion molecule receptor and contributes to cellular adhesion, apoptosis, and tumor-suppressive mechanisms. Loss or dysfunction of this pathway may therefore promote abnormal cell survival and progression. Additional alterations involving the *TP53* tumor-suppressor gene are associated with later stages of colorectal tumorigenesis. TP53 plays a central role in DNA damage responses, cell-cycle control, apoptosis, and maintenance of genomic stability. Its dysfunction facilitates survival and expansion of cells carrying potentially oncogenic genetic abnormalities. Activation of oncogenic pathways also contributes to adenoma progression. Mutations involving the *KRAS* oncogene promote uncontrolled colonocyte proliferation and survival, supporting exophytic adenoma growth and progression toward malignancy. *KRAS* alterations are found in a substantial proportion of colorectal cancers and represent an important molecular event within the adenoma–carcinoma sequence.[24] These alterations occur within a broader network of molecular changes rather than acting as an isolated mechanism.

DNA mismatch repair abnormalities represent another major pathway involved in colorectal carcinogenesis. The mismatch repair genes *MLH1*, *MSH2*, and *MSH6* are responsible for recognizing and correcting DNA replication errors. Dysfunction of these genes increases genomic instability and can produce microsatellite instability, thereby facilitating the accumulation of mutations in genes regulating cellular proliferation and apoptosis.[25] This pathway is particularly relevant to hereditary colorectal cancer syndromes and to a subset of sporadic colorectal cancers. Serrated adenomas follow a molecular pathway that differs from the conventional adenoma–carcinoma sequence. Hypermethylation of the *MLH1* gene can impair mismatch repair and contribute to microsatellite instability. Traditional serrated adenomas frequently demonstrate *BRAF* mutations and widespread hypermethylation involving multiple genes, a pattern referred to as the CpG island methylator phenotype (CIMP).[26] In hereditary colorectal cancer syndromes, germline genetic abnormalities create an inherited predisposition to tumor development. Subsequent loss of the remaining functional allele or acquisition of additional somatic abnormalities can accelerate malignant transformation and contribute to the development of invasive cancer at a younger age.[27] Understanding these molecular mechanisms is important for laboratory diagnosis, genetic testing, risk stratification, surveillance, and development of individualized approaches to colorectal cancer prevention and management.

Histopathology

Histopathological examination is central to the diagnosis and risk stratification of colorectal polyps because morphological characteristics provide essential information about their biological behavior and malignant potential. Histological classification broadly separates colorectal polyps into neoplastic, serrated, hyperplastic, inflammatory, and hamartomatous lesions. Neoplastic polyps, particularly adenomas, have the greatest potential for malignant transformation and include tubular, tubulovillous, and villous adenomas. Serrated lesions, particularly sessile serrated lesions and traditional serrated adenomas (TSAs), also have clinically important malignant potential. In contrast, hyperplastic, inflammatory, and most hamartomatous polyps generally demonstrate lower malignant potential, although specific hereditary syndromes may substantially increase the overall cancer risk. Adenomatous polyps characteristically demonstrate increased glandular complexity, crowded and irregular glands, cribriform architectural patterns, and, in more advanced lesions, intraluminal necrotic material. Cytological abnormalities may include loss of normal cellular polarity, nuclear enlargement, prominent nucleoli, altered chromatin distribution, and atypical mitotic activity.[28] Tubular adenomas are the most frequently encountered histological subtype of neoplastic colorectal polyps and account for approximately 65% to 80% of cases. They are commonly pedunculated and are characterized by predominantly tubular and branching glands lined by dysplastic epithelial cells. The degree of cellular atypia may vary, but many tubular adenomas demonstrate relatively limited dysplasia compared with villous lesions. Villous adenomas account for approximately 5% to 10% of neoplastic polyps and are frequently sessile. Histologically, they contain elongated, finger-like villous projections and are more commonly associated with advanced dysplasia and malignant transformation. Tubulovillous adenomas demonstrate a combination of tubular and villous architectural components and account for approximately 10% to 25% of colorectal adenomas.

The degree of epithelial dysplasia is an important determinant of malignant potential. Increasing dysplasia is associated with greater architectural complexity and cytological atypia and indicates a higher risk of progression toward invasive carcinoma.[29] For malignant pedunculated polyps, the Haggitt classification provides a standardized assessment of the depth of submucosal invasion and contributes to prognostic evaluation and treatment planning.[30] Haggitt level 0 indicates disease confined to the mucosa. Level 1 represents invasion into the submucosa limited to the head of the polyp. Level 2 indicates invasion into the neck, whereas level 3 represents invasion extending into the stalk. Level 4 describes invasion into the submucosa below the stalk but remaining above the muscularis propria. This classification is particularly useful when determining whether endoscopic excision is adequate or whether additional surgical management should be considered. Serrated lesions are characterized microscopically by prominent epithelial serration accompanied by characteristic architectural abnormalities. These may include asymmetrical proliferation, dilatation of the crypt bases, and serration extending toward the base of the crypts. Approximately 2% to 5% of sessile serrated lesions develop dysplasia. When dysplasia occurs, it may show an abrupt transition between morphologically normal and dysplastic epithelium. Additional architectural abnormalities include villous growth, crypt elongation, glandular crowding, complex branching, cribriform architecture, and either excessive or diminished luminal serration.[31] Traditional serrated adenomas demonstrate a distinctive protruding or villiform architecture, pseudostratified columnar epithelium, ectopic crypt formation, and prominent goblet cells.[32] Hyperplastic polyps are classified within the broader group of serrated polyps but generally have substantially lower malignant potential than sessile serrated lesions and traditional serrated adenomas. They are characterized predominantly by epithelial hyperplasia without significant cytological dysplasia. Hamartomatous and juvenile polyps have a different histological organization and contain variable amounts of connective tissue, including smooth muscle, expanded lamina propria, and inflammatory infiltrates, covered by hypertrophic or regenerative epithelium. Grossly, these lesions may resemble adenomas and are often pedunculated with a characteristic reddish or cherry-red appearance. Inflammatory polyps, commonly termed pseudopolyps, are not true neoplastic polyps. Instead, they represent areas of inflammatory and regenerative tissue associated with mucosal injury, particularly in inflammatory bowel disease. Histologically, pseudopolyps contain islands or projections of relatively preserved and regenerating mucosa surrounded by areas of ulceration, tissue loss, inflammatory infiltration, and architectural distortion. Accurate histopathological differentiation among these entities is essential because morphology directly influences assessment of malignant potential, surveillance requirements, genetic evaluation, and subsequent clinical management.

History and Physical

Most colorectal polyps remain clinically silent and are frequently identified incidentally during screening colonoscopy or evaluation for unrelated gastrointestinal complaints. A focused history should nevertheless assess subtle or intermittent symptoms that may indicate the presence of colorectal lesions. Relevant symptoms include abdominal discomfort, intermittent rectal bleeding, passage of mucus with stool, constipation, diarrhea, altered bowel habits, and a sensation of incomplete evacuation.[33] The nature, duration, frequency, and progression of these symptoms should be documented because they may help distinguish uncomplicated polyps from advanced lesions or other colorectal disorders. Larger polyps may occasionally produce mechanical obstruction, particularly when located in anatomically narrow segments of the colon. Patients may develop progressive abdominal pain, distention, constipation, obstipation, nausea, and feculent vomiting. Chronic occult bleeding from a colorectal polyp may result in iron-deficiency anemia, fatigue, weakness, and pallor. Severe continuous bleeding is uncommon but may occasionally cause substantial blood loss and, rarely, hemorrhagic shock. A detailed personal and family history is particularly important when colorectal polyposis is suspected. Because many colorectal cancers develop through precursor polyps, a history of colorectal cancer, multiple polyps, or early-onset colorectal neoplasia among first-degree relatives should raise suspicion for an inherited cancer syndrome. Familial adenomatous polyposis (FAP) may be associated with extracolonic manifestations, including desmoid tumors, mandibular or other skeletal osteomas, congenital retinal pigment abnormalities, thyroid nodules, and epidermoid cysts involving the face or scalp. Lynch syndrome is associated with increased risks of colorectal cancer and several extracolonic malignancies, including cancers of the endometrium, ovary, stomach, small intestine, urinary tract, biliary tract, brain, skin, pancreas, and prostate.[34] Clinical manifestations of hereditary hamartomatous polyposis syndromes may provide important diagnostic clues. Peutz-Jeghers syndrome may present with characteristic mucocutaneous hyperpigmentation, whereas juvenile polyposis may manifest with rectal bleeding, anemia, or rectal prolapse. Hamartomatous polyps associated with these syndromes may act as lead points for intestinal intussusception, potentially producing acute abdominal pain, obstruction, vomiting, and other features of an acute abdomen.[35] Patients with hypersecretory rectal polyps may develop McKittrick-Wheelock syndrome, characterized by

severe secretory diarrhea, dehydration, oliguria, and, in advanced cases, renal failure. Laboratory abnormalities may include hypokalemia, hyponatremia, and biochemical evidence of uremia.[36] Physical examination should be comprehensive, particularly when a hereditary polyposis syndrome is suspected. Clinicians should assess for cutaneous lesions, mucosal hyperpigmentation, abnormal or supernumerary teeth, mandibular swellings, abdominal wall desmoid tumors, and skeletal abnormalities. Findings suggestive of advanced colorectal malignancy, including cachexia, pallor, left supraclavicular lymphadenopathy, and migratory thrombophlebitis, should also be evaluated.[37] Abdominal examination is particularly important in symptomatic patients and those with suspected obstruction. Digital rectal examination may identify anorectal polyps, palpable masses, tenderness, or evidence of hematochezia.

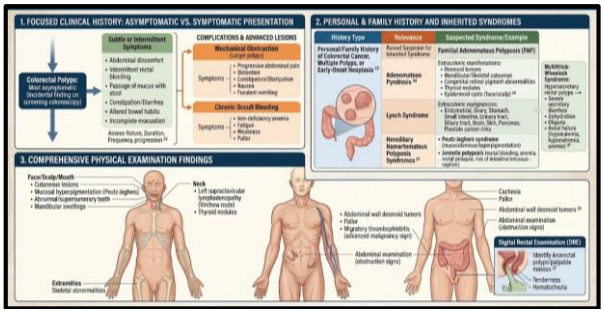

Figure-2: Diagnosis of Colorectal Polyps.

Evaluation

The evaluation of colorectal polyps requires integration of clinical assessment, laboratory investigations, stool-based testing, endoscopic examination, histopathology, and appropriate imaging. The principal objectives are to identify colorectal lesions, determine their number, size, morphology, and location, establish their histological characteristics, and assess their potential for malignant transformation. Laboratory investigations provide supportive information and may identify complications associated with bleeding or hypersecretory lesions. A complete blood count is useful for detecting anemia related to chronic occult gastrointestinal blood loss. Serum creatinine and electrolyte measurements are particularly important in patients with large or hypersecretory adenomas because substantial fluid and electrolyte losses may occur. Carcinoembryonic antigen may be assessed when invasive malignancy is suspected, although it is not a diagnostic test for colorectal polyps. Stool-based tests can detect occult gastrointestinal bleeding and contribute to colorectal cancer screening. Conventional fecal occult blood testing has limited sensitivity for small polyps because these lesions may not bleed consistently. Larger lesions, particularly those exceeding 2 cm, and polyps undergoing malignant transformation are more likely to produce detectable blood in stool.[38] Fecal immunochemical testing uses antibodies directed against the globin component of human hemoglobin and generally provides greater sensitivity than traditional fecal occult blood testing. However, despite its usefulness for colorectal cancer screening, its ability to identify advanced adenomas remains inferior to direct colonoscopic examination.[39] Colonoscopy remains the principal and most comprehensive diagnostic method for colorectal polyps because it permits direct visualization, characterization, biopsy, and complete endoscopic removal of many lesions. Nevertheless, colonoscopy does not detect every lesion. The overall missed-polyp rate has been reported at approximately 22%, with diminutive lesions being particularly susceptible to non-detection.[40,41] Screening recommendations vary according to age, individual risk, family history, and underlying hereditary conditions. Average-risk individuals generally begin screening during mid-adulthood, whereas patients with hereditary syndromes require substantially earlier and more intensive surveillance.[42] In FAP, surveillance may begin during adolescence, while patients with Lynch syndrome require early and frequent colonoscopic assessment.[43]

The Paris classification provides a standardized framework for describing colorectal polyp morphology and surface characteristics.[44] Protruding lesions include pedunculated (Ip) and sessile (Is) types, whereas nonprotruding lesions include slightly elevated (IIa), completely flat (IIb), and slightly depressed (IIc) forms. Excavated lesions are classified as type III. Accurate morphological classification helps determine the likelihood of advanced pathology and guides endoscopic treatment planning. Image-enhanced colonoscopy provides additional information beyond conventional white-light examination. Techniques such as narrow-band imaging and near-infrared autofluorescence can improve assessment of vascular and mucosal patterns and support prediction of histological characteristics. These technologies have demonstrated improvements in diagnostic sensitivity and specificity, with reported values approaching 80% and 90%, respectively.[45] Endocytoscopy and artificial intelligence-assisted image analysis represent further developments intended to improve detection and real-time characterization of colorectal lesions.[46] Radiological assessment provides important complementary information when conventional colonoscopy is incomplete, contraindicated, or unsuitable. CT colonography, also known as virtual colonoscopy, uses a prepared and distended colon to generate two- and three-dimensional images of the colorectal lumen. It can detect more than 90% of polyps larger than 5 mm when interpreted by experienced radiologists.[47] Its major limitation is that it cannot obtain tissue samples or perform polypectomy, meaning that patients with significant

detected lesions generally require subsequent colonoscopy. CT colonography is also unsuitable in several high-risk situations, including selected patients with FAP or Lynch syndrome, active colitis, intestinal obstruction, and recent polypectomy.[48] MR colonography provides an alternative imaging approach, particularly when CT is unsuitable. Although its diagnostic accuracy is generally lower than that of CT colonography, reported sensitivity exceeds 88% for lesions larger than 10 mm.[49] Capsule endoscopy has a limited role in colorectal polyp assessment because its sensitivity and specificity are considerably lower than those of conventional colonoscopy.[50] Molecular stool testing provides another noninvasive approach by detecting biomarkers such as *KRAS* mutations, methylated *BMP3*, *NDRG4*, and β-actin. Although fecal DNA testing is established for colorectal cancer screening, its sensitivity for advanced adenomas is approximately 57%, while detection of high-grade dysplasia may reach 83%.[51,52] Collectively, these diagnostic modalities provide complementary information and allow colorectal polyp evaluation to integrate endoscopic, histological, radiological, laboratory, and molecular perspectives.

Treatment / Management

Management of colorectal polyps is determined by the lesion's size, morphology, number, anatomical location, histological characteristics, and estimated malignant potential. The principal objective is complete removal of lesions with malignant potential while minimizing procedural complications and preserving colorectal function. Colonoscopic removal is the preferred treatment for most detectable colorectal polyps because it permits simultaneous visualization, resection, and tissue retrieval for histopathological assessment. The choice of endoscopic technique depends on whether the lesion is pedunculated or nonpedunculated, its dimensions, depth of suspected invasion, and the likelihood of complete and safe resection. Patients with multiple polyps or suspected hereditary polyposis syndromes require additional consideration because management extends beyond removal of individual lesions and may involve genetic assessment, intensive surveillance, chemoprevention, or prophylactic surgery.

Colonoscopic Polypectomy

Colonoscopic polypectomy is the principal definitive treatment for most colorectal polyps and can generally be performed during the same colonoscopic examination in which the lesion is identified. The decision to remove a lesion is influenced by its size, morphology, location, number, and endoscopic appearance. Pedunculated lesions are usually technically accessible and can often be removed using standard snare techniques, whereas sessile and laterally spreading lesions may require advanced resection methods. Complete excision is important because residual adenomatous or serrated tissue can contribute to recurrence and may retain malignant potential. Diminutive polyps measuring less than 6 mm identified by CT colonography may not require immediate excision and can instead be managed according to appropriate imaging-based surveillance strategies. Lesions larger than 6 mm generally warrant removal and histopathological examination to establish their precise diagnosis and determine subsequent surveillance requirements.[53] Several techniques are available for colonoscopic polypectomy. Conventional biopsy forceps are primarily used for very small lesions. Standard forceps can generally be used for polyps smaller than approximately 3 mm, whereas large-cup or jumbo forceps may facilitate removal of lesions up to approximately 6 mm. The forceps grasp the lesion and remove the tissue directly through repeated or single bites, depending on its size and configuration. Although technically straightforward, forceps removal may result in incomplete excision, particularly when the lesion is larger than the capacity of the forceps or has a broad attachment. Therefore, appropriate lesion selection is essential when this technique is used. Cold snare polypectomy is an important method for removing small to intermediate colorectal polyps without applying electrocautery. The snare is positioned around the lesion with an approximately 1- to 2-mm margin of surrounding normal mucosa before mechanical transection. The specimen is subsequently retrieved through the colonoscope for pathological examination. Cold snare techniques are particularly useful for nonpedunculated lesions measuring approximately 6 to 9 mm and 10 to 19 mm, while specific pedunculated lesions may also be managed according to their stalk characteristics.[54] Avoidance of electrocautery reduces thermal injury and may decrease the risk of delayed bleeding and deep tissue damage in appropriately selected lesions.

Hot snare polypectomy uses electrocautery to facilitate tissue transection and hemostasis. It may be used for selected pedunculated lesions and nonpedunculated noninvasive lesions of intermediate size. The snare is positioned around the polyp while maintaining a small margin of normal tissue, followed by gradual closure and application of electrical current. Careful technique is required because excessive thermal penetration may increase the risk of deep mural injury or perforation. For large nonpedunculated lesions, particularly those exceeding 20 mm, endoscopic mucosal resection (EMR) is an established advanced technique. EMR involves injection of fluid into the submucosal layer to elevate the lesion from the muscularis propria, thereby creating a safety plane for subsequent snare resection. Depending on lesion size and morphology, EMR may be performed en bloc or in multiple fragments. Complete documentation of the lesion and careful pathological assessment are particularly important when piecemeal resection is necessary.

Endoscopic submucosal dissection (ESD) is a more technically demanding procedure that permits en bloc removal of selected large or suspicious colorectal lesions. It is particularly useful when superficial submucosal invasion is suspected and precise pathological assessment of the entire lesion is required. The lesion is first marked, generally leaving a several-millimeter margin, followed by submucosal injection. The mucosa surrounding the lesion is then circumferentially incised using an electrosurgical endoscopic knife, after which the lesion is dissected from the underlying submucosal layer. ESD can provide a complete specimen with clearly defined margins, which is valuable for determining the depth and characteristics of invasion and assessing whether endoscopic treatment has been curative.[54] Although colonoscopic polypectomy is generally safe, complications can occur. Bleeding is the most frequent adverse event and is usually limited after removal of diminutive lesions but becomes more clinically relevant with larger lesions and advanced procedures such as EMR and ESD. Perforation represents a more serious complication and may occur because of mechanical injury or excessive thermal penetration. Reported perforation rates may reach approximately 1.5% with EMR and 10% with ESD, although many cases can be managed using endoscopic closure techniques when recognized promptly. Postpolypectomy coagulation syndrome is an uncommon complication resulting from transmural thermal injury without frank perforation. It produces localized peritoneal inflammation and may present with abdominal pain, fever, and systemic inflammatory manifestations. Reported rates range from approximately 1.3% to 3.7%. Colonic stricture is an uncommon late complication, particularly after extensive circumferential or large-area EMR and ESD.[55] Appropriate patient selection, meticulous technique, recognition of high-risk lesions, and postprocedural monitoring are therefore essential for minimizing adverse outcomes.

Surgical Interventions

Surgical treatment is reserved for colorectal polyps that cannot be safely or completely removed endoscopically, lesions with invasive malignancy requiring oncological resection, selected hereditary polyposis syndromes, and symptomatic polyposis conditions. Surgery may be indicated when a sessile lesion is technically irretrievable, when an endoscopic resection is incomplete, or when histopathological examination demonstrates invasive carcinoma extending into a stalk or deeper bowel layers. Prophylactic colorectal surgery is also an important component of management for selected hereditary syndromes, particularly familial adenomatous polyposis (FAP), in which the extensive adenomatous burden and high lifetime risk of colorectal cancer may make repeated endoscopic removal impractical or insufficient.[56] Patients with irretrievable colorectal polyps also require careful surgical consideration because the risk of occult carcinoma in this population may be substantial, with reported cancer incidence reaching 17.7%.[57] When invasive malignancy is identified or strongly suspected, surgical management should follow appropriate oncological principles. Depending on tumor location and disease extent, this may include complete mesocolic excision or total mesorectal excision, central vascular ligation, and regional lymphadenectomy. The objective is not simply removal of the visible polyp but adequate resection of the involved bowel segment and associated lymphovascular structures when malignant invasion is present. Histopathological examination of the surgical specimen remains essential for determining tumor stage, margin status, lymph-node involvement, depth of invasion, lymphovascular invasion, and other pathological characteristics that guide further management. Patients with FAP require individualized surgical planning based on polyp burden, rectal involvement, age, family history, functional considerations, and patient preferences. Surgical options include total colectomy with ileorectal anastomosis and total proctocolectomy with ileal pouch-anal anastomosis. Total colectomy with preservation of the rectum avoids extensive pelvic dissection and is therefore generally associated with lower risks of pelvic sexual and urological dysfunction. However, the remaining rectal mucosa continues to carry a risk of adenoma development and malignant transformation. Lifelong or long-term proctoscopic surveillance is consequently required, and proctectomy may become necessary when rectal disease becomes extensive or clinically concerning. In contrast, total proctocolectomy with ileal pouch-anal anastomosis removes the colon and rectum and provides definitive removal of the principal colorectal mucosal substrate at risk. Nevertheless, this approach involves substantial pelvic surgery and may be associated with complications such as anastomotic leakage, pouch-related fistulas, pouchitis, fecal incontinence, and urinary or sexual dysfunction.

Management of selected rectal polyps can involve organ-preserving transanal procedures rather than radical rectal resection. Transanal excision (TAE), transanal minimally invasive surgery (TAMIS), and transanal endoscopic microsurgery (TEM) may be considered for appropriately selected large benign lesions and early malignant polyps with superficial submucosal invasion. Appropriate candidates generally have favorable histological characteristics, including well or moderately differentiated tumors without evidence of lymph-node metastasis.[58] Careful preoperative staging is particularly important when malignancy is suspected. High-resolution pelvic magnetic resonance imaging provides detailed assessment of the rectal wall and surrounding tissues and can identify adverse features

such as lymphadenopathy, tumor deposits, and extramural vascular invasion. Contrast-enhanced computed tomography of the thorax and abdomen is used to evaluate for distant metastatic disease. These investigations allow the multidisciplinary team to determine whether local excision is oncologically appropriate or whether radical resection is required. TAE is generally suitable for selected rectal lesions that are relatively small, accessible through the anal canal, and limited to superficial disease. The technique involves direct exposure of the lesion with anal retractors, placement of traction sutures, and circumferential incision with an appropriate margin. Full-thickness excision is then performed, and the resulting defect may either be closed or allowed to heal secondarily. TAE has the advantage of being relatively simple and avoids abdominal or extensive pelvic surgery, but its applicability is limited by lesion size, location, depth, and the ability to obtain adequate margins. TAMIS provides a minimally invasive platform for transanal removal of rectal lesions and can be used for benign polyps and selected T1 cancers with curative intent. It may also have a palliative role in advanced disease when radical resection is inappropriate or cannot be performed. One of its principal advantages is the ability to access lesions in different quadrants of the rectum. A single-port device is inserted through the anal canal, and continuous carbon dioxide insufflation creates an operative working space. Conventional laparoscopic instruments are then used to dissect the lesion, followed by either closure of the defect or healing without closure when clinically appropriate.

TEM is another specialized local excision technique and is particularly useful for lesions located in the middle and upper rectum and rectosigmoid region. Lesions can be accessed at considerable distance from the anal verge, including those located up to approximately 20 cm away. The procedure uses an operating proctoscope through which specialized instruments are introduced while continuous carbon dioxide insufflation maintains visualization and working space. The lesion is dissected under direct vision and removed through the proctoscope. TEM may be particularly advantageous for appropriately selected lesions located at anatomically difficult positions, including the anterior and posterior aspects of the rectal wall.[59] Transanal procedures generally have lower physiological burden than radical colorectal surgery but are not free from complications. Potential adverse outcomes include urinary retention, urinary tract infection, postoperative bleeding, perianal abscess, and transient fecal incontinence. TAMIS and TAE may additionally be complicated by rectal or bowel perforation, pelvic abscess, rectal stenosis, and rectovaginal or rectovesical fistula formation. Appropriate patient selection, accurate preoperative staging, experienced surgical technique, and postoperative surveillance are therefore essential. Overall, treatment of colorectal polyps should be individualized according to the biological behavior and anatomical characteristics of the lesion rather than based on size alone. Endoscopic removal remains the central therapeutic strategy for most lesions, while EMR and ESD provide advanced options for larger or technically challenging polyps. Surgical resection is reserved for lesions that cannot be adequately treated endoscopically, lesions demonstrating invasive malignancy, and selected hereditary or symptomatic polyposis syndromes. Because treatment decisions may depend on endoscopic morphology, histopathological findings, molecular characteristics, imaging results, and hereditary risk, optimal management requires coordinated input from gastroenterologists, colorectal surgeons, pathologists, radiologists, laboratory specialists, genetic professionals, pharmacists, and rehabilitation teams. This multidisciplinary approach supports complete lesion control, appropriate cancer prevention, preservation of function, and individualized long-term surveillance.

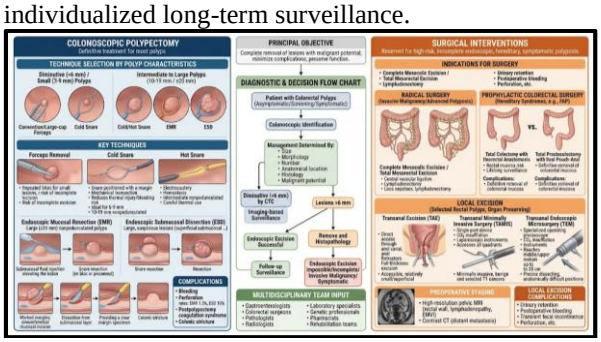

Figure-3: Treatment and management of colorectal polyps.

Differential Diagnosis

The differential diagnosis of colorectal polyps is broad and includes hereditary polyposis syndromes, sporadic epithelial lesions, inflammatory conditions, hamartomatous disorders, mesenchymal lesions, and pseudopolyps that may mimic true mucosal polyps during endoscopic examination. Accurate differentiation is clinically important because apparently similar lesions may have substantially different malignant potential, genetic implications, surveillance requirements, and treatment strategies. Diagnosis should therefore integrate the number and distribution of lesions, age at presentation, endoscopic morphology, histopathological characteristics, extracolonic manifestations, and relevant family history. When the phenotype suggests an inherited syndrome, molecular genetic testing and genetic counseling may be required to establish the underlying diagnosis and facilitate evaluation of at-risk relatives. Hereditary colorectal polyposis syndromes constitute an important component of the differential diagnosis, particularly in patients presenting with numerous adenomas, early-onset colorectal neoplasia, multiple

gastrointestinal polyps, or a strong family history of colorectal or extracolonic malignancy. Familial adenomatous polyposis (FAP) occurs in classical and attenuated forms. Classical FAP is typically characterized by the development of more than 100 colorectal adenomas, often beginning at a relatively young age. The extensive adenomatous burden may involve the entire colon and rectum and may be accompanied by extracolonic manifestations. Attenuated FAP generally produces a lower adenoma burden, commonly ranging from 10 to 100 adenomas, with a tendency toward later clinical presentation. These phenotypes should be distinguished from MUTYH-associated polyposis (MAP), an inherited disorder that may present with more than 20 adenomas and generally becomes clinically apparent later in life, commonly during the fourth to seventh decades. Differentiating FAP from MAP is particularly important because their inheritance patterns and molecular mechanisms differ, with implications for genetic counseling and family screening.

Lynch syndrome should also be considered in patients with colorectal neoplasia who do not demonstrate the extensive adenomatous burden characteristic of FAP. Individuals with Lynch syndrome may have relatively few colorectal adenomas, with reported numbers ranging from 0 to approximately 30, but they have an increased lifetime risk of colorectal carcinoma and several extracolonic malignancies. These include cancers of the endometrium, stomach, and urothelial tract, among others.[60] Therefore, the absence of numerous polyps does not exclude a hereditary predisposition. Clinical assessment should consider the patient's age at diagnosis, personal and family history of Lynch-associated cancers, tumor characteristics, and mismatch-repair or microsatellite-instability findings when available. Hamartomatous polyposis syndromes represent another important group of hereditary disorders. Peutz–Jeghers syndrome (PJS) is characterized by gastrointestinal hamartomatous polyps together with characteristic mucocutaneous pigmentation, particularly around the lips and oral cavity. The diagnosis may be supported by the presence of multiple characteristic polyps and a compatible family history or extraintestinal phenotype. Juvenile polyposis syndrome (JPS), in contrast, is characterized by multiple juvenile polyps throughout the gastrointestinal tract or a significant burden of juvenile polyps within the colorectum. Although these lesions are histologically hamartomatous, affected individuals may have an increased risk of gastrointestinal malignancy, making appropriate surveillance essential. Cowden syndrome, also known within the spectrum of PTEN hamartomatous tumor syndromes, should be considered when gastrointestinal polyposis occurs together with mucocutaneous abnormalities or a history suggestive of multiple primary malignancies. Patients may develop polyps involving the stomach, small intestine, and colon, while the broader syndrome is associated with mucocutaneous lesions and increased risks of malignancies involving organs such as the breast, endometrium, and thyroid.[61] The recognition of these extracolonic features can therefore provide an important diagnostic clue when the gastrointestinal phenotype alone is nonspecific.

Sporadic colorectal lesions are substantially more common than hereditary polyposis syndromes and should remain central to the differential diagnosis in patients without strong hereditary features. Inflammatory polyps and pseudopolyps may occur in inflammatory bowel disease, particularly ulcerative colitis, and can also develop in association with infectious or other forms of colitis. These lesions may arise from areas of mucosal regeneration and inflammation rather than representing true neoplastic polyps. Their clinical significance consequently depends not only on their appearance but also on the underlying inflammatory disease and the presence of dysplasia elsewhere in the colon. Hyperplastic polyps constitute another common category of colorectal lesions. In the appropriate clinical and pathological context, multiple proximal hyperplastic lesions may raise consideration of a serrated polyposis phenotype. A pattern involving at least five histologically confirmed lesions proximal to the sigmoid colon, with at least two measuring more than 1 cm, is an important diagnostic criterion in the supplied classification framework.[62] Distinguishing hyperplastic lesions from sessile serrated lesions is particularly important because the latter can participate in serrated colorectal carcinogenesis and therefore carry different implications for surveillance. Hereditary mixed polyposis syndrome should be considered when a patient demonstrates multiple colorectal polyps with differing histological characteristics rather than a uniform population of adenomatous or hamartomatous lesions. The coexistence of different polyp types can complicate endoscopic classification and should prompt consideration of a hereditary disorder when accompanied by an appropriate family history or early-onset disease.[63] Cronkhite–Canada syndrome represents a contrasting acquired condition. It is characterized by extensive hamartomatous-type polyps throughout much of the gastrointestinal tract, with relative sparing of the esophagus. Because this disorder is not a typical inherited polyposis syndrome, its recognition requires consideration of the patient's overall clinical presentation and associated gastrointestinal manifestations.

Other uncommon conditions can mimic conventional colorectal polyposis. Ganglioneuromatous polyposis is characterized by hamartomatous ganglioneuromatous lesions that may

occur synchronously with adenomas and juvenile polyps.[64] Intestinal leiomyomatosis represents another rare differential diagnosis and is associated with proliferation of smooth muscle cells together with hyalinization of vessel walls.[65] These disorders illustrate the importance of histopathological evaluation because endoscopic appearance alone may not reliably distinguish unusual mesenchymal or hamartomatous lesions from more common colorectal polyps. Pneumatosis cystoides intestinalis can also produce a pseudopolypoid appearance. Rather than representing true mucosal neoplasia, this condition is characterized by collections of gas within the intestinal wall, producing submucosal or subserosal lesions that may appear polypoid endoscopically. The terminal ileum is a common location, and characteristic imaging findings may include intramural gas, ascites, and portal venous air.[66] Recognition is important because these findings can otherwise be mistaken for intraluminal polyps or other pathological masses. Finally, nonpolypoid submucosal lesions should be distinguished from mucosal colorectal polyps. Lipomas, gastrointestinal stromal tumors, and neuroendocrine tumors may present as protruding lesions but arise from different tissue layers and possess different biological behaviors and management requirements. Hemorrhoids may also be mistaken for distal rectal or anal polyps, particularly when the examination is limited or the lesion is viewed without adequate anatomical orientation. Endoscopic characterization, targeted biopsy or resection when appropriate, and histopathological assessment are therefore fundamental to establishing the correct diagnosis.

Conclusion:

Colorectal polyps represent a heterogeneous group of lesions ranging from benign, low-risk abnormalities to clinically important precursors of colorectal cancer and manifestations of hereditary cancer syndromes. Their clinical significance depends on histological subtype, size, morphology, distribution, dysplasia, molecular characteristics, and patient-specific risk factors. A comprehensive diagnostic approach combining clinical assessment, colonoscopy, histopathology, laboratory investigation, molecular testing, and appropriate imaging is essential for accurate classification and risk assessment. Colonoscopic removal remains the cornerstone of treatment for most clinically significant lesions, while advanced techniques such as EMR and ESD provide options for larger or technically complex polyps. Surgical and transanal approaches remain important for selected malignant, unresectable, recurrent, or hereditary disease. Recognition of hereditary syndromes is particularly important because affected patients require individualized surveillance and genetic evaluation of relatives. Overall, multidisciplinary coordination among gastroenterology, pathology, radiology, laboratory medicine, genetics, pharmacy, surgery, and rehabilitation professionals can improve diagnostic accuracy, therapeutic decision-making, cancer prevention, and long-term patient outcomes.

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