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Polyps and Polypectomy Surveillance—Role of the Histopathologist

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The traditional roles of the pathologist are those of diagnostician, and being able to communicate these diagnoses back to the clinician in a clear unambiguous form so that subsequent therapy can be planned. Important findings may require more direct communication, particularly when the implications involve a choice between therapeutic options. Some diagnoses have implications that require an educational role for the pathologist; these in turn may evolve into a research role, based on clinico-pathological correlation, active basic science research or simply supplying tissue for research. Clinicians must also be aware that the same biopsy can be interpreted in numerous ways, depending upon the clinical situation.

Key words: pathology, pathologist, polyp, dysplasia, interpretation
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TRADITIONAL ROLES of the pathologist include diagnosis, education, research and, of course, communication (as well as the increasing administrative roles that all of us face). There is marked variation between pathologists' involvement in any of these areas, which is to a large extent dependent on the interest of the parties concerned, the patient population and intrinsic biases. Thus, a large, tertiary, referral centre in an academic environment will have different problems to those of a large, community hospital with interested physicians who are also on call for internal medicine. All this impacts on the role of the pathologist when dealing with colorectal polyps, and basic expectations are outlined as follows.

The role of the pathologist is to ensure that the correct diagnosis is made, and that any implications of that diagnosis are conveyed to the clinician in a form that is unambiguous. Sometimes this may require direct communication or use of a biopsy conference or rounds.

Polyps occur throughout the entire gastrointestinal tract (Table 1). Increasingly, the means are becoming available to suggest on clinical or research grounds that a particular patient may be at increased risk of developing tumours at other sites, both within or beyond the gastrointestinal tract or of having other underlying disease within the large bowel.

The process of making a diagnosis has two distinct phases. The first is that of observation, and the second is interpretation in the light of the clinical problem. Failure to state this clearly results in an inability to carry out this function. Increasingly, pathologists are becoming aware of the role that expectation bias plays in their diagnosis, so that observation and a morphological diagnosis (e.g. adenoma) precedes the correlation. Thus, a biopsy that has all of the morphological appearances of a typical 4-mm tubular adenoma histologically (Figure 1) may have different implications in different situations. This also illustrates the educational role of the pathologist. For example:

(a) If this was from a 4-mm polyp in the sigmoid colon of a 55-year-old woman, the diagnosis would be that of a tubular adenoma.
(b) If one of several mucosal nodules in the rectum of a 12-year-old child, although still a tubular adenoma, it would be highly suggestive of adenomatous polyposis coli. Implications are to confirm the diagnosis, surgical excision, and also investigate other family members.
(c) If one of many polyps in the rectum of a 40-year-old

Table 1. Polyps that occur within the large bowel

Non-neoplastic polyps	
Hyperplastic	
Hamartomatous	Peutz-Jegher type (solitary, multiple)
	Juvenile type (solitary, multiple, adult type)
Inflammatory	In IBD, infection, ischaemia
	Postiatrogenic injury (drugs, resection)
	Prolapse, e.g. solitary rectal ulcer syndrome
Endometriotic	
Neoplastic polyps	
Adenomas	Tubular, tubulo-villous, villous
	Polypoid, broad-based, sessile, flat, depressed with misplaced glands
Dysplasia	In IBD e.g. DALMs
	In other non-neoplastic polyps serrated adenomas/mixed polyps
Invasive carcinomas	Typical, in other polyps, *de novo*
Other	Lymphoid/lymphoma, carcinoid, metastatic, mesenchymal

DALM, dysplasia-associated lesion or mass; IBD, inflammatory bowel disease.

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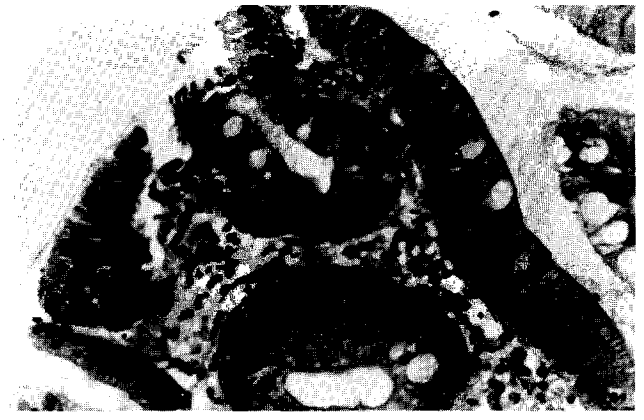

Figure 1. Fragment of a biopsy with mucin depletion, hyperchromatic stratified nuclei typical of low grade dysplasia/adenoma.

immigrant, who says he had his colon removed 20 years ago elsewhere, this is also likely to be APC with implications not only for local therapy, but also for upper endoscopy, particularly looking for duodenal/ampullary neoplasia. Investigation of first-degree family members at risk is also indicated.

(d) If part of an ulcerating mass in the sigmoid colon, this is likely to be the adenomatous edge of a carcinoma. As the mass (assuming the biopsy to be representative) is demonstrably neoplastic, then resection is indicated. A definitive diagnosis of invasion is not required unless atypical or other features are present, suggesting this is not the correct diagnosis.

(e) If part of a mucosal irregularity in a patient with a 20-year history of ulcerative colitis, this is likely to be a DALM (dysplasia-associated lesion or mass) or possibly the superficial part of a carcinoma [1]. Colectomy would be recommended.

(f) If a random biopsy of a patient with a long history of extensive colitis, this would almost certainly be indicative of an increased risk of carcinoma [2]. Colectomy would be recommended irrespective of the grade of dysplasia. Confirmation of the diagnosis by a second opinion may be required.

(g) If a 4-mm polyp in the sigmoid colon of a 55-year-old woman with a long history of extensive colitis, then this is likely to be a tubular adenoma [3]. Verification that local excision was complete, that dysplasia did not extend into the adjacent mucosa, and that no other dysplastic lesions were identifiable elsewhere in the large bowel is required.

(h) If a reddish lesion in the ascending colon of a 35-year-old man, then this may be part of a flat adenoma. Association with Lynch syndromes would need to be considered seriously. A careful family history would be required, and if available, DNA could be taken from the formalin-fixed material to determine the presence of replication errors (microsatellite instability), which strongly support the diagnosis.

Further guidance regarding clinical management may be offered under specific circumstances. For example, in a sigmoid colon adenoma with a focus of invasive carcinoma in the submucosa, it is reasonable for the pathologist to comment on the presence or absence of criteria that impact on the likelihood of the carcinoma metastasising to regional nodes [4, 5]. If this is clearly low, e.g. a well differentiated carcinoma in a polyp with no invasion of the adjacent submucosa or endothelial-lined channels and completely excised, then this should be stated, with the appropriate comment regarding the negligible risk of metastases [4–6]. If some of these features are present, then the risks of metastases and subsequent death need to be weighed against the morbidity and mortality of resection. Increasingly, lack of histological completeness of resection is not an automatic indication for excision, but for endoscopic re-examination to determine whether the diathermy burn in fact caused necrosis of all residual tumours.

Similar situations occur for non-neoplastic polyps. For example, the presence of multiple juvenile polyps should also raise the question of juvenile polyposis, which might require colectomy for both symptom control and cancer risk, as well as an understanding that similar polyps may be present in other organs, such as the stomach. However, juvenile polyps may also be morphologically indistinguishable from inflammatory polyps and may, therefore, indicate underlying inflammatory bowel disease [5].

In the upper gastrointestinal tract, the presence of gastric fundic gland polyps, although usually harmless, and only rarely accompanied by dysplasia/adenomatous change, the additional presence of adenomas in the antrum, or particularly in the duodenum/ampulla, raises the possibility of underlying familial polyposis.

It should be appreciated that some pathologists have been taught that their role is not as a consultant in patient management, but to simply render a diagnosis and leave the interpretation and implications to the clinician. It is an extremely knowledgeable (or arrogant) person who believes they never require advice, and a poor reflection on pathology training, or the pathologist to deliberately withhold it.

The academic role of the pathologist is increasingly changing as tests which were originally purely research-based rapidly evolve to the routine level. Nowhere is this exemplified as in the exploding molecular biology field, particularly as applied to large bowel neoplasia. It is increasingly recognised that approximately 10% of colorectal cancers may occur due to inherited disposition, and that this is linked to at least four genes involved in DNA repair. While probes for these are not yet currently available, the result of the lack of one of these genes is failure of DNA repair, which results in replication errors (RERs) within these tumours. Because these can be readily detected by appropriate DNA probes to microsatellite DNA (inherited repetitive sequences), the use of simple PCR techniques can readily be used to screen tumours, and to detect which are likely to be the result of an inherited defect, with the implication that other first-degree family members may also be at risk.

A further academic role for the histopathologist is for quality, and therefore reproducibility of the diagnoses rendered and the suitability of the terminology used. In the large bowel, this is becoming increasingly problematic as increasing numbers of papers from Asia, and particularly Japan, challenge our notions regarding aetiopathogenesis of neoplasms (e.g. flat adenomas, *de novo* carcinoma), but use terminology that is unfamiliar, being derived primarily from gastric carcinoma and reapplied to large bowel neoplasia. The converse is also happening as the role of *H. pylori* in gastric cancers causes the use of terms typically used for large bowel neoplasia to gastric cancers. Both of these trends cause confusion, and sometimes an inability to comprehend the underlying message for want of clear and unambiguous terminology. This is increasingly important as molecular techniques are used, for pathology remains the gold standard in

pathogenesis. This may be the time to re-examine the differing terminologies used, with an attempt to define precisely all terms. In particular, the spectrum of changes encompassed by high-grade dysplasia (which in the large bowel includes *in situ* carcinoma) and carcinoma (which can be used at the cytological level, architectural level or for invasive carcinoma) is not only unhelpful, but may be causing loss of information in defining precisely the morphological correlates of molecular abnormalities. The relative lack of inter- and intra-observer variability studies as a basis for corrective studies is increasingly important.

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