IN BRIEF

COLORECTAL CANCER

A trial of deep-learning detection in colonoscopy

A double-blind randomized trial in China has assessed the effect of operational bias in the use of computer-aided detection (CAD) systems for polyp detection. A total of 962 patients presenting for diagnostic and screening colonoscopy were randomly allocated to colonoscopy with a CAD or a sham system; both patient and operator were unaware of the assigned group. The adenoma detection rate was significantly greater in the CAD group than the sham group ($P = 0.03$). Polyps detected by the CAD system but not the endoscopist had difficult-to-recognise characteristics (small, flat, isochromatic and unclear boundaries).

ORIGINAL ARTICLE Wan, P. et al. Effect of a deep-learning computer-aided detection system on adenoma detection during colonoscopy (CADe-DB trial): a double-blind randomised study. *Lancet Gastroenterol. Hepatol.* https://doi.org/10.1016/S2468-1253(19)30411-X (2020)

COLORECTAL CANCER

Perioperative cetuximab plus chemotherapy reduces overall survival in metastatic disease

The phase III New EPOC trial examined the addition of cetuximab to perioperative systemic chemotherapy versus chemotherapy alone for patients with resectable colorectal liver metastasis. The trial was stopped in 2012 after progression-free survival was found to be reduced in those treated with cetuximab. Now, an analysis performed after long-term follow-up (median 66.7 months) has found that overall survival was also significantly reduced in the chemotherapy plus cetuximab group (median 55.4 months versus 81.0 months; $P = 0.036$), confirming that cetuximab should not be used in the perioperative setting.

ORIGINAL ARTICLE Bridgewater, J. A. et al. Systemic chemotherapy with or without cetuximab in patients with resectable colorectal liver metastasis (New EPOC): long-term results of a multicentre, randomised, controlled, phase 3 trial. *Lancet Oncol.* https://doi.org/10.1016/S1470-2045(19)30798-3 (2020)

GASTRIC CANCER

H. pylori elimination reduces gastric cancer risk

Although family history and *Helicobacter pylori* infection are the two main risk factors for gastric cancer, whether eradication of *H. pylori* benefits those with a family history of gastric cancer was unknown. In a single-centre study in South Korea, 1,676 first-degree relatives of patients with gastric cancer were randomly assigned to receive *H. pylori* eradication therapy or placebo. After a median follow-up of 9.2 years, gastric cancer developed in 10 individuals in the treatment group versus 23 in the placebo group ($P = 0.03$), suggesting that *H. pylori* eradication reduced the risk of gastric cancer in those with a familial risk.

ORIGINAL ARTICLE Choi, I. J. et al. Family history of gastric cancer and *Helicobacter pylori* treatment. *N. Engl. J. Med.* **382**, 427–436 (2020)

NONALCOHOLIC STEATOHEPATITIS

FAST identification of NASH progression

A new algorithm has been developed to non-invasively identify patients with nonalcoholic steatohepatitis (NASH) at risk of progression to cirrhosis. Using a derivation cohort of 350 patients with suspected nonalcoholic fatty liver disease, the best-fitting multivariable logistic regression model predicting NASH was established, using measurements of liver stiffness by FibroScan and serum aspartate aminotransferase (AST) levels. This score, named FAST (FibroScan–AST), performed well in both the derivation dataset as well as in external validation cohorts ($n = 1,026$), and could reduce unnecessary liver biopsies.

ORIGINAL ARTICLE Newsome, P. N. et al. FibroScan-AST (FAST) score for the non-invasive identification of patients with non-alcoholic steatohepatitis with significant activity and fibrosis: a prospective derivation and global validation study. *Lancet Gastroenterol. Hepatol.* https://doi.org/10.1016/S2468-1253(19)30383-8 (2020)

MOTILITY

Enteric neuron regulation of gut motility by the microbiota

The gut microbiota regulates neural programmes of intestinal motility, but the mechanisms remain unknown. A new study shows that the transcription factor aryl hydrocarbon receptor (AHR) acts as a biosensor that links the intestinal luminal environment to intestinal motility programmes of the enteric nervous system (ENS).

"We hypothesized that molecular mechanisms that link the microbiota to intestinal motor behaviour are likely to be encoded by genetic programs that operate predominantly in neural circuits of the colon, the intestinal segment with the heaviest load of microorganisms," write the authors. First, RNA sequencing identified genes that were upregulated in colonic enteric neurons of specific-pathogen-free (SPF) mice and germ-free mice. By comparing the nuclear transcriptomes of colonic neurons from SPF with those of germ-free mice, they identified microbiota-dependent genes, one of which was *Ahr*, which encodes a transcription factor known to be involved in intestinal homeostasis. The researchers used immunostaining to confirm that expression of AHR in enteric neurons was commensurate with the gut microbial load. Next, transcriptome analysis experiments suggested that specific genes regulating AHR signalling or enteric excitability are activated by microbiota-dependent induction of *Ahr* in colonic neurons.

The intestinal transit time of mice with deletion of *Ahr* specifically in enteric neurons was higher than that of control mice, suggesting that AHR signalling in enteric neurons regulates gut motility. Furthermore, ex vivo observations indicated that the activity of specific colonic motility programmes was reduced in the conditional *Ahr*-knockout mice. Thus, enteric-neuron-specific deletion of *Ahr* reduced colonic peristaltic activity.

COELIAC DISEASE

Mimicking coeliac disease in mice

A pathophysiological mouse model of coeliac disease that mimics the intestinal tissue destruction observed upon ingestion of gluten in humans has been reported in *Nature*. The new model reflects the complexities of the interactions between gluten, genetics and the immune response that drive disease development.

"It is now well-recognized that a gluten-free diet does not allow tissue healing in all patients with coeliac disease and has a negative impact on the lives and well-being of many patients," explains author Bana Jabri, which has prompted the search for new treatment options. However, what was lacking was an experimental model that developed the main feature observed in patients with coeliac disease: intestinal tissue destruction (villous atrophy) after exposure to dietary gluten in genetically susceptible individuals (either HLA-DQ8 or HLA-DQ2 haplotypes). IL-15 upregulation is associated with organ-specific autoimmune disorders and coeliac disease. Work by Jabri and colleagues in mice and humans had previously highlighted the importance of IL-15 overexpression in the lamina propria and the intestinal epithelium to promote loss of oral tolerance to gluten and licensing of cytotoxic T cells to kill tissue cells.

The researchers generated mice expressing HLA-DQ8 in which IL-15 was upregulated in both intestinal epithelial cells and the lamina propria. After 30 days of gluten feeding, 75% of these mice developed small intestinal tissue destruction. Importantly, the villous architecture was restored once the mice had been fed a gluten-free diet for 30 days. Cytotoxic intraepithelial lymphocytes were observed to be the