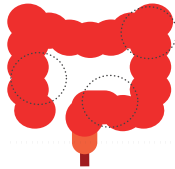


THE COMPLICATIONS OF CROHN'S DISEASE

WHAT IS CROHN'S DISEASE?

Crohn's disease is a **CHRONIC INFLAMMATORY DISEASE OF THE DIGESTIVE SYSTEM**¹



SYMPTOMS of the disease most commonly include:



DIARRHEA



ABDOMINAL PAIN



WEIGHT LOSS



FATIGUE

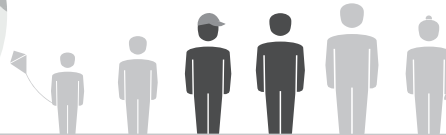


BLOOD IN THE FECES²

IN THE EUROPEAN UNION, CROHN'S DISEASE IS ESTIMATED TO AFFECT UP TO



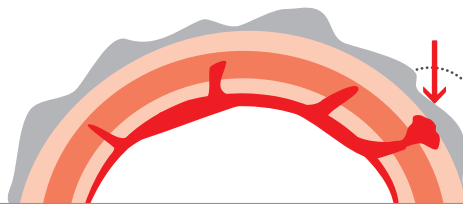
It can affect people of all ages, though onset is most common in **late adolescence** or **early adulthood**⁴



CROHN'S DISEASE IS CHARACTERIZED BY **FLARES AND REMISSION**¹ IT IS A **LIFE-LONG DISEASE WITH NO CURE**⁵

Complications of Crohn's disease can include **bleeding, abscesses, obstruction, perforation or stricture (narrowing) of the intestine**, and increase the risk of other complications, such as **malnutrition** and developing **colorectal** or **small bowel cancers**⁶

ANOTHER COMPLICATION CAN BE THE DEVELOPMENT OF **FISTULAS**⁷



Fistulas develop from **deep ulcers into 'tunnels'** running from one part of the digestive system to another^{8,9}

They are defined as a **pathologic tract connecting two hollow organs**, or one hollow organ and the skin^{8,9}

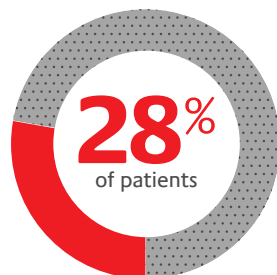
PERIANAL FISTULAS ARE WHERE THE FISTULA DEVELOPS BETWEEN THE RECTUM AND THE SKIN NEAR THE ANUS¹⁰

COMPLEX ANAL FISTULAS ARE THOSE FISTULAS WITH TRACKS EXTENDING ABOVE THE LEVEL OF THE MID-ANAL CANAL, WITH **MULTIPLE TRACKS** OR **ABSCESSSES**^{8,11}

IMPACT OF FISTULAS ON PATIENT QUALITY OF LIFE

PERIANAL FISTULAS ARE '**ONE OF THE MOST DISABLING COMPLICATIONS**' OF CROHN'S DISEASE¹²

They are estimated to affect up to 28% of patients in the first **two decades** after Crohn's disease diagnosis^{13,14}



People with perianal fistulas suffer **SIGNIFICANT NEGATIVE IMPACTS** on their quality of life across **PHYSICAL, FUNCTIONAL, & PSYCHOSOCIAL** domains¹⁵



ONE STUDY ASKING PATIENTS TO RATE THE **MOST SIGNIFICANT** QUALITY OF LIFE FACTORS FOR THEM FOUND THAT THE KEY **IMPAIRMENTS** WERE:¹⁵

- ✓ Anal pain
- ✓ Anal discharge
- ✓ Physical activity restriction
- ✓ Sleep interference
- ✓ Feeling unclean

DIFFICULTY OF TREATING FISTULAS

FEW PHARMACOLOGICAL TREATMENTS for complex perianal fistulas exist and **REPEATED SURGICAL PROCEDURES** are usually required,¹⁶⁻²⁰ which are generally associated with **MORBIDITY** (e.g. incontinence)²⁰



and an increased **RISK OF PERMANENT STOMA** (surgically created opening on the surface of the abdomen)²¹

Treatments that do exist, such as



ANTIBIOTICS

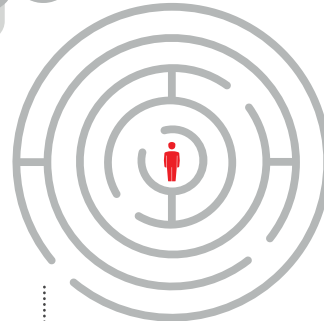


THIOPURINES
(immunosuppressive treatments)



ANTI-TUMOUR NECROSIS FACTOR TREATMENTS

are generally associated with **moderate efficacy** and **high rates of relapse upon discontinuation**²⁰⁻²⁸



THE TREATMENT PATHWAY IS COMPLEX



and a **MULTIDISCIPLINARY TEAM IS REQUIRED TO MANAGE THE COMPLICATION**²⁸

To **heal** a complex perianal fistula, it commonly takes six surgical procedures²⁹

In a study of 232 patients with perianal fistulizing Crohn's disease, patients with previously healed complex fistula had a **RELAPSE RATE OF 41.9%** after a median follow up time of **10 YEARS**²⁷

TREATMENT GOALS FOR FISTULAS

SHORT-TERM:²⁸



ABSCESS DRAINAGE



REDUCTION OF SYMPTOMS

LONG-TERM:²⁸



RESOLUTION OF FISTULA DISCHARGE



IMPROVEMENT IN QUALITY OF LIFE



FISTULA HEALING



PRESERVATION OF CONTINENCE



AVOIDANCE OF PROCTECTOMY WITH STOMA

REFERENCES 1. Xavier RJ and Podolsky DK. Unravelling the pathogenesis of inflammatory bowel disease. *Nature*. 2007; 448(7152): 427-434. 2. Mayo Clinic. Crohn's disease symptoms. Available at: <http://www.mayoclinic.org/diseases-conditions/crohns-disease/basics/symptoms/con-20032061>. Accessed September 28, 2017. 3. Burisch J, Jess T, Martinato M and Lakatos P, on behalf of ECCO – EpiCom. The burden of inflammatory bowel disease in Europe. *J Crohns Colitis*. 2013; 7: 322-337. 4. NICE Clinical Knowledge Summaries – Crohn's disease – Suspecting Crohn's disease. Available at: <https://cks.nice.org.uk/crohns-disease#diagnosis>. Accessed September 28, 2017. 5. Klionsky DJ. Crohn's Disease, Autophagy, and the Paneth Cell. *N Engl J Med*. 2009; 360(17): 1785-1786. 6. NICE Clinical Knowledge Summaries – Crohn's disease – Complications. Available at: <https://cks.nice.org.uk/crohns-disease#backgroundsub:4>. Accessed September 28, 2017. 7. Rankin GB, Watts HD, Melnyk CS, et al., National Cooperative Crohn's Disease Study: extraintestinal manifestations and perianal complications. *Gastroenterology*. 1979; 77: 914-920. 8. Torkzad MR and Karlbom U. MRI for assessment of anal fistula. *Insights Imaging*. 2010; 1(2): 62-71. 9. Edmunds LH, Williams GM and Welch CE. External Fistulas Arising From the Gastro-intestinal Tract. *Ann Surg*. 1960; 152(3): 445-469. 10. de Miguel Criado J, del Salto LG, Rivas PF, et al., MR imaging evaluation of perianal fistulas: spectrum of imaging features. *Radiographics*. 2012; 32(1): 175-194. 11. Stitz R. Surgery for complex anal fistulae. Proceedings of the International Colorectal Disease Symposium. 2002; 43: 93-94. Available at: http://www.gastrohep.com/conreports/hong_kong/hkstitzurgical.pdf. Accessed September 28, 2017. 12. Marzo M, Felice C, Pugliese D, et al., Management of perianal fistulas in Crohn's disease: An up-to-date review. *World J Gastroenterol*. 2015; 21(5): 1394-1395. 13. Schwartz DA, Loftus EV Jr, Tremaine WJ, et al., The natural history of fistulizing Crohn's disease in Olmsted County, Minnesota. *Gastroenterology*. 2002; 122: 875-880. 14. Eglinton TW, Barclay ML, Garry RB, et al., The spectrum of perianal Crohn's disease in a population-based cohort. *Dis Colon Rectum*. 2012; 55(7): 773-777. 15. Mahadev S, Young JM, Selby W, et al., Quality of life in perianal Crohn's disease: what do patients consider important? *Dis Colon Rectum*. 2011; 54(5): 579-585. 16. Sands BE, Anderson FH, Bernstein CN, et al., Infliximab maintenance therapy for fistulizing Crohn's disease. *N Engl J Med*. 2004; 350(7): 876-885. 17. Thia KT, Mahadevan U, Feagan BG, et al., Ciprofloxacin or metronidazole for the treatment of perianal fistulas in patients with Crohn's disease: a randomized, double-blind, placebo-controlled pilot study. *Inflamm Bowel Dis*. 2009; 15(1): 17-24. 18. Present DH, Korelitz BI, Wisch N, Glass JL, Sachar DB, Pasternack BS. Treatment of Crohn's disease with 6-mercaptopurine. A long-term, randomized, double-blind study. *N Engl J Med*. 1980; 302(18): 981-987. 19. Present DH, Rutgeerts P, Targan S, et al., Infliximab for the treatment of fistulas in patients with Crohn's disease. *N Engl J Med*. 1999; 340(18): 1398-1405. 20. Panés J, Garcia-Olmo D, Van Assche G, et al., Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomized, double-blind controlled trial. *The Lancet*. 2016; 388(10051): 1281-1290. 21. Gecke K, Khanna R, Stroker J, et al., Fistulizing Crohn's disease: diagnosis and management. *United European Gastroenterol J*. 2013; 1(3): 206-213. 22. Domenech E, Hinojosa J, Nos P, et al., Clinical evolution of luminal and perianal Crohn's disease after inducing remission with infliximab: how long should patients be treated? *Aliment Pharmacol Ther*. 2005; 22: 1107-1113. 23. Goldstein ES, Marion JF, Present DH. 6-mercaptopurine is effective in Crohn's disease without concomitant steroids. *Inflamm Bowel Dis*. 2004; 10(2): 79-84. 24. Korelitz BI and Present DH. Favorable effect of 6-mercaptopurine on fistulae of Crohn's disease. *Dig Dis Sci*. 1985; 30(1): 58-64. 25. Brandt L, Bernstein LH, Boley SJ, et al., Metronidazole therapy for perineal Crohn's disease: a follow up study. *Gastroenterology*. 1982; 83(2): 383-387. 26. Solomon MJ, McLeod RS, O'Connor BI, et al., Combination ciprofloxacin and metronidazole in severe perianal Crohn's disease. *Can J Gastroenterol*. 1993; 7: 571-573. 27. Molendijk I, Nuij VJ, van der Meulen-de Jong AE, et al., Disappointing durable remission rates in complex Crohn's disease fistula. *Inflamm Bowel Dis*. 2014; 20(11): 2022-2028. 28. Gecke KB, Bemelman W, Kamm MA, et al., A global consensus on the classification, diagnosis and multidisciplinary treatment of perianal fistulizing Crohn's disease. *Gut*. 2014; 63: 1381-1392. 29. Geltzeiler B, Wieghard N and Vassiliki T. Recent developments in the surgical management of perianal fistula for Crohn's disease. *Ann Gastroenterol*. 2014; 27(4): 320-330.