

Cullen Sign and Grey Turner Sign Revisited

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Financial Disclosures:

None reported.

Support: None reported.

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Submitted

January 7, 2016;

revision received

March 8, 2016;

accepted

March 30, 2016.

Cullen sign and Grey Turner sign, named after Thomas Stephen Cullen, MB, and George Grey Turner, MBBS, respectively, are signs of abdominal wall hemorrhage and are generally associated with acute pancreatitis. However, the research from which these signs arose was documented long before Cullen and Grey Turner made their contributions. The present article examines the history, pathologic mechanisms, and clinical application of these signs in relation to acute pancreatitis and ectopic pregnancy.

J Am Osteopath Assoc. 2016;116(6):398-401

doi:10.7556/jaoa.2016.081

Given the prominence of Thomas Stephen Cullen, MB, and George Grey Turner, MBBS, in the history of clinical medicine, one is inclined to believe that the 2 principal physical examination signs (*Figure 1*) that bear their names—periumbilical ecchymosis (Cullen sign) and flank ecchymosis (Grey Turner sign)—were identified solely by these 2 men. However, the ideas from which these signs arose were documented by others long before Cullen and Grey Turner made their contributions. Cullen and Grey Turner are names for common physical examination signs of abdominal wall hemorrhage, also known as *rectus abdominis subfascial bleeding*. To provide appropriate and timely interventions, it is important that health care providers—particularly primary care and emergency physicians, general and colorectal surgeons, obstetricians, and gastroenterologists—have a thorough, evidenced-based understanding of these signs in terms of historical evolution, anatomy, pathophysiologic and epidemiologic processes, and associated medical conditions.

Early Historical Concepts of Abdominal Wall Hemorrhage

One might assume that Cullen sign and Grey Turner sign emerged not long after clinicians recognized that physical examination findings could be used to ferret out disease among the many aches and minor perturbations of otherwise healthy existence. But, in fact, such observations seem to have been used as a means of distinguishing health from disease for as long as humans have committed thoughts to writing. There are, for example, written accounts of spontaneous rectus abdominis subfascial bleeding traced as far back as the writings of Hippocrates, Claudius Galen, and Leonardo da Vinci.²⁻⁴ The earliest published account of this condition in the United States was written by Samuel Bainbridge Richardson⁴ in 1857 in his description of a healthy 28-year-old man. In 1882, Czechoslovakian surgeon Karl Maydl provided accurate descriptions of this condition, as well as an extensive review of literature covering 14 cases between 1809 and 1880.⁶

Since that time, many cases of abdominal wall bleeding have been described using terms such as *spontaneous hematoma of the abdominal wall*, *spontaneous hematoma of the rectus sheath*, and *spontaneous rupture of the epigastric artery*.⁷ Spontaneous abdominal wall hemorrhage offers the best example of early notions of abdominal wall bleeding;

however, this clinical finding is distinct from Cullen sign and Grey Turner sign, which also indicate abdominal wall bleeding. An important distinction is that neither Cullen nor Grey Turner intended these signs to be indicators of intra-abdominal pathology.

Abdominal Wall Hemorrhage Associated With Intra-abdominal Pathology

Abdominal wall hemorrhage has been reported after trauma, subcutaneous drug injection, and paracentesis, and it has been reported to occur spontaneously during pregnancy and biliary tract disease. However, the first description of isolated periumbilical discoloration as a result of intra-abdominal pathology was made by American surgeon Joseph Louis Ransohoff in 1906 in his account of a 53-year-old man with a ruptured common bile duct and bile peritonitis.⁸ Ransohoff wrote,

On inspection of the abdomen, attention was called to a marked jaundice of the umbilicus. The navel was of distinct saffron-yellow color in strong contrast with the rest of the skin over the abdomen.⁸

Six years later, Grey Turner reported the observation of “a bluish color appearance of the abdominal wall surrounding the umbilicus” in a 54-year-old woman with acute pancreatitis.⁹ He later described abdominal wall discoloration of the flanks in a 53-year-old man with acute pancreatitis, as follows⁹:

The tenderness over the gall-bladder region was very marked, and I now noticed two large discolored areas in the loins. They were about the size of the palm of the hand, slightly raised above the surface, and of a dirty-greenish color. There was a little edema, with pitting on pressure, but there was no pain or tenderness.

In 1918, Cullen presented a paper entitled, “A new sign in ruptured extrauterine pregnancy,”¹⁰ in which he reported periumbilical “bluish-black” discoloration

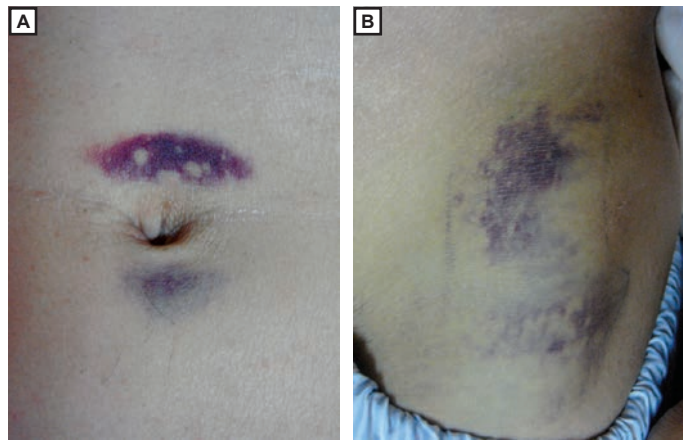


Figure 1.
(A) Periumbilical ecchymosis (Cullen sign) and
(B) flank ecchymosis (Grey Turner sign). Published
with permission from Chung and Chuang.¹

in a 38-year-old woman in association with a ruptured ectopic pregnancy. Although it is historically associated with ruptured ectopic pregnancy, Cullen sign has also been described in association with acute pancreatitis and other clinical conditions such as rectus sheath hematoma,¹¹ splenic rupture in infectious mononucleosis,¹² portal hypertension,¹³ amoebic liver abscess,¹⁴ metastatic thyroid cancer,¹⁵ metastatic esophageal cancer,¹⁶ and non-Hodgkin lymphoma.¹⁷ Current prominent clinical manuals such as *Harrison's Principles of Internal Medicine* and *Cecil's Textbook of Internal Medicine* describe both Cullen sign and Grey Turner sign in association with severe acute pancreatitis, and it is now customary for medical students, resident physicians, and attending physicians to associate one with the other.

Pathophysiologic Process of Cullen Sign and Grey Turner Sign

The notion of blood within the abdominal wall as a result of pancreatic inflammatory products has been promulgated to account for the development of Cullen sign and Grey Turner sign. In 1953, surgeons Elbert T. Phelps and Richard A. Lemmer described a case of hemorrhagic

pancreatitis in a 34-year-old man who developed Grey Turner sign on the left flank.¹⁸ A biopsy of the left flank lesion demonstrating the greatest discoloration was taken on hospital day 7 and revealed...

... edema of the subcutaneous tissue with a moderate amount of perivascular infiltration of lymphocytes around some of the smaller vessels, but there was no evidence of vascular lesions or tissue necrosis.¹⁸

In 1958, nationally known academic obstetrician James A. Merrill reported the histologic findings of a 43-year-old woman with Cullen sign.¹⁹ Microscopic examination of the biopsy demonstrated intact erythrocytes within all tissue planes and most pronounced in the striated muscles, superficial adipose tissue, and surrounding dermal sweat glands. Erythrocytes were not found filling lymphatics. While hemosiderin deposition occurred within the dermis, vascular endothelial components were intact.

In another case report, Meyers et al²⁰ used computed tomographic images of 4 patients presenting with acute pancreatitis to posit pathways leading to the development of Cullen sign and Grey Turner sign in 1989. According to their findings, Grey Turner sign may result from anatomical defects of the transversalis fascia, which may serve as a structural predisposition allowing direct extension of hemorrhagic fluid from the anterior pararenal space (via the 2 leaves of the posterior renal fascia) to the lateral edge of the quadratus lumborum muscle. Cullen sign may develop secondary to an inflamed gastrohepatic ligament allowing direct extension of hemorrhagic fluid across the falciform ligament to the periumbilical anterior abdominal wall.

Based on these findings, it is thought that both signs occur as a result of hemorrhagic fluid tracking from retroperitoneal regions along fascial planes, thus permitting access to the abdominal wall musculature and subsequent periumbilical or flank tissues.¹⁸⁻²⁰ Skin discoloration results from the accumulation of blood within the subcutaneous fascial planes.¹⁸⁻²⁰ Variation of color between green, yellow, and purple is based on the stage of red blood cell breakdown.¹⁸⁻²⁰

Evidence of the Accuracy of Cullen Sign and Grey Turner Sign

Despite their long history, Cullen sign and Grey Turner sign are considered to be relatively uncommon. In a collective review of 6063 patients with ectopic pregnancy between 1941 and 1955, Merrill¹⁹ reported Cullen sign was observed in only 4 patients (0.06%). In a retrospective study to examine the clinical spectrum of acute pancreatitis and identify factors related to life-threatening complications, Jacobs et al²¹ reported that of 519 patients from December 1963 through April 1969, Grey Turner sign occurred in 5 (0.96%) and Cullen sign occurred in 4 (0.77%). The associated mortality rate of patients presenting with these signs was reported between 50% to 60%. In a randomized, double-blinded trial involving 257 patients evaluating the effects of aprotinin and glucagon on the course of acute pancreatitis, it was reported that Grey Turner sign was observed in only 2 patients (0.78%).²² Finally, in a prospective evaluation of 770 patients admitted to the Glasgow Royal Infirmary for acute pancreatitis between January 1971 and March 1983, Dickson and Imrie²³ reported 9 patients (1.17%) with Grey Turner sign, 9 patients (1.17%) with Cullen sign, and 5 patients (0.65%) with both signs. In this cohort, these signs most commonly appeared on hospital day 4 and had a female to male ratio of 3:1, with an associated mortality rate of 37%.²³

Conclusion

Based on the review of the literature, it is evident that Cullen sign and Grey Turner sign are neither sensitive nor specific for acute pancreatitis. Further, Cullen sign is neither sensitive nor specific for ectopic pregnancy, for which it was originally ascribed. Therefore, it may be best to revise the teaching of these signs from cardinal manifestations of acute pancreatitis and ectopic pregnancy to conditions associated with abdominal pathology and retroperitoneal hemorrhage (*Figure 2*). This revised teaching would be best given with con-

Acute hemorrhagic pancreatitis
Amoebic liver abscess
Common bile duct rupture and biliary peritonitis
Idiopathic perirenal hemorrhage
Infectious mononucleosis with splenic rupture
Metastatic esophageal cancer
Metastatic thyroid cancer
Non-Hodgkin lymphoma
Portal hypertension
Rectus abdominal sheath hematoma
Retroperitoneal hemorrhage
Ruptured ectopic pregnancy

Figure 2.

Conditions associated with both Cullen sign and Grey Turner sign.^{1,8,11-18}

tinued emphasis on the bedside examination of patients through all years of training and beyond. The medical profession should continue to refine its understanding of Cullen sign and Grey Turner sign, along with other physical signs, and carefully examine their operating characteristics. Medical educators must also urge their trainees to do the same.

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