МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

MODERN PRACTICE OF INTERNAL MEDICINE WITH EMERGENCY CONDITIONS

Management of patients with melena and haematemesis

Guidelines for students and interns

СУЧАСНА ПРАКТИКА ВНУТРІШНЬОЇ МЕДИЦИНИ З НЕВІДКЛАДНИМИ СТАНАМИ

Ведення хворих з блювотою кров'ю та меленою

Методичні вказівки для студентів та лікарів-інтернів

Затверджено вченою радою ХНМУ.
Протокол № 1 від 21.01.16.

ХАРКІВ
ХНМУ
2016

Modern practice of internal medicine with emergency conditions. Management of patients with melena and haematemesis : guidelines for students and interns / comp. O. Ya. Babak, K. A. Lapshyna, N. M. Zhelezniakova et al. – Kharkiv : KNMU, 2016. – 16 p.

Compilers O. Ya. Babak
K. A. Lapshyna
N. M. Zhelezniakova
O. E. Zaichenko
K. O. Prosolenko
I. I. Zelena
A. O. Andrieieva
E. Yu. Frolova-Romaniuk
O. V. Goptsii
K. O. Sytnyk

Сучасна практика внутрішньої медицини з невідкладними станами. Ведення хворих з блювотою кров'ю та меленою : метод. вказ. для студентів та лікарів-інтернів / упоряд. О. Я. Бабак, К. А. Лапшина, Н. М. Железнякова та ін. – Харків : ХНМУ, 2016. – 16 с.

Упорядники О. Я. Бабак
К. А. Лапшина
Н. М. Железнякова
О. Є. Зайчєнко
К. О. Просоленко
І. І. Зелена
А. О. Андрєєва
Е. Ю. Фролова-Романюк
О. В. Гопцій
К. О. Ситник

Management of patients with melena and haematemesis

General Outcome

The students should be able to describe main causes, links of pathogenesis, clinical features, diagnostic and treatment of melena and haematemesis.

The aim of this topic is to provide the student with an opportunity to:

- Provide a basic overview of the pathophysiology, diagnosis, and classification of upper gastrointestinal bleeding.
- Discuss the role of endoscopic diagnostic and treatment in patients with upper gastrointestinal bleeding.
- Evaluate guideline-based management strategies for the treatment of upper gastrointestinal bleeding.
- Provide a basic overview of the pathophysiology, diagnosis, classification, signs, diagnostic and treatment of lower gastrointestinal bleeding.

Specific Learning Outcomes:

Upon successful completion of this unit, the students should be able to:

1. Describe the upper and lower gastrointestinal bleeding classifications.
2. Describe the main causes of gastrointestinal bleeding.
3. Describe the main clinical features of gastrointestinal bleeding.
4. List and describe the methods and groups of drugs that are used in the treatment of gastrointestinal bleeding and give specific examples of each.
5. Make a treatment plan of patient with gastrointestinal bleeding.

Specification of the theoretical question for training of "Management of the patients with hepatic encephalopathy"

Student must know:

1. What is the definition of hematemesis, melena and hematochezia?
2. What are the main types of upper gastrointestinal bleeding?
3. What are the main causes of upper gastrointestinal bleeding?
4. What are the risk assessments of upper gastrointestinal bleeding?
5. What are the management of upper gastrointestinal bleeding?
6. What are the main types of direct endoscopic treatments?
7. What the drug treatments are used in patients with upper gastrointestinal bleeding?
8. What are the main causes of lower gastrointestinal bleeding?
9. What treatment methods and drugs are used for treatment of lower gastrointestinal bleeding?

DEFINITION

Hematemesis is the vomiting of blood, which may be obviously red or have an appearance similar to coffee grounds.

Melena is the passage of black, tarry stools.

Hematochezia is the passage of fresh blood per anus, usually in or with stools.

Hematemesis, melena, and hematochezia are symptoms of acute gastrointestinal bleeding. Acute gastrointestinal bleeding is a common medical emergency which carries hospital mortality in excess of 10 %. Bleeding that brings the patient to the physician is a potential emergency and must be considered as such until its seriousness can be evaluated. The goals in managing a major acute gastrointestinal hemorrhage are to treat hypovolemia by restoring the blood volume to normal, to make a diagnosis of the bleeding site and its underlying cause, and to treat the cause of the bleeding as definitively as possible.

CLASSIFICATION

The classification of gastrointestinal bleeding include:

- Upper gastrointestinal hemorrhage=bleeding above Ligament of Treitz.
- Lower gastrointestinal hemorrhage=bleeding below Ligament of Treitz.

CAUSES

The most important cause of major life threatening acute gastrointestinal bleeding is peptic ulcer. Significant haemorrhage is due to erosion of an underlying artery and the magnitude of bleeding is related to the size of the arterial defect and the diameter of the artery; consequently bleeding from a large posterior duodenal ulcer which may erode the gastroduodenal artery and high, lesser curve gastric ulcers involving branches of the left gastric artery can be particularly severe. The majority of cases present with little or no history of dyspepsia, while a history of aspirin or non-steroidal anti-inflammatory drug (NSAID) consumption is common.

Oesophagogastric varices are a less common cause but because the patient often has other features of decompensated cirrhosis and because bleeding is often high volume the impact on hospital resources is high. Prognosis is related to the severity of liver disease rather than to the magnitude of bleeding.

Mallory-Weiss tears are usually associated with alcohol abuse but other causes of vomiting including drugs (chemotherapy, digoxin toxicity, etc.), renal failure, or advanced malignancy may be responsible. Bleeding usually stops spontaneously and endoscopic therapy only required in rare severe cases.

Oesophagitis is a common finding in elderly patients who present with "coffee ground" haematemesis. Bleeding is never life threatening and conservative supportive therapy combined with the use of proton pump acid inhibitor drugs is all that is necessary.

Table 1

Causes of acute upper gastrointestinal bleeding

Cause	Frequency (%)
Peptic ulcer	35–50
Varices	5–12
Mallory-Weiss tear	2–5
Oesophagitis	20–30
Duodenitis/gastritis/erosions	10–20
Vascular	2–3
Tumours	2–5
Aortoduodenal fistula	< 1

Gastritis, duodenitis, and gastroduodenal erosions are often linked to NSAID use and to Helicobacter pylori infection. Circulatory support, stopping NSAIDs, and H pylori eradication are required.

A range of vascular anomalies may be responsible:

- Large or multiple arteriovenous malformations (AVMs) usually present with iron deficiency anaemia but occasionally cause major acute haemorrhage. Most AVMs have no obvious cause and present in elderly patients, but in younger patients they are sometimes due to hereditary haemorrhagic telangiectasia. Other patients have valvular heart disease, or artificial heart valves, and bleeding may be exacerbated by anticoagulant drugs.
- Gastric antral vascular ectasia (GAVE) is an uncommon vascular anomaly characterised by linear, readily bleeding red streaks radiating from the pyloris into the gastric antrum; it is sometimes associated with liver disease.
- Portal hypertensive gastropathy is due to venous congestion of the gastric mucosa from portal hypertension.
- Dieulafoy's lesion is an unusual cause of severe and recurrent bleeding in which a superficial submucosal artery is eroded by a small strategic ulcer. The commonest site is the gastric fundus, although it can occur in the duodenum and other parts of the stomach.

Oesophagogastric tumours are a relatively uncommon cause of acute upper gastrointestinal haemorrhage. The most important benign type is gastrointestinal stromal cell tumour. Carcinomas and lymphomas of the stomach tend to present with other upper gastrointestinal symptoms and with iron deficiency anaemia rather than acute bleeding.

Aortoduodenal fistula should be considered in patients who present with major upper gastrointestinal bleeding after aortic graft insertion. Bleeding occurs from the second part of the duodenum, is massive, and may recur over hours or days. Small bowel or right sided colonic diseases sometimes present as melaena and rarely as haematemesis. Colonoscopy, barium radiology, and enteroscopy may identify the underlying tumour or vascular anomaly when upper gastrointestinal endoscopy fails to identify a bleeding source. In young patients a bleeding Meckel's diverticulum should be considered.

RISK ASSESSMENT

The best risk assessment tool is the Rockall score, developed from a large prospective audit of patients who were managed for acute upper gastrointestinal bleeding in England. Multivariant analysis identified age, shock, medical co-morbidity, and specific endoscopic findings as independent variables which predicted re-bleeding and death (*tables 2 and 3*). Others have confirmed that the Rockall score accurately predicts mortality but is less good at predicting re-bleeding.

Table 2

The Rockall scoring system

Variable	Score 0	Score 1	Score 2	Score 3
SRH, stigmata of recent haemorrhage.				
Age (years)	< 60	60–79	> 80	–
Shock	None	Pulse > 100 beats/min; normal blood pressure	Pulse > 100 beats/min; systolic blood pressure < 100 mmHg	–
Co-morbidity	None	–	Cardiac; gastrointestinal cancer; other major co-morbidity	Renal failure; liver failure; disseminated malignancy
Diagnosis	Mallory-Weiss tear; no lesion, no SRH	All other diagnoses	Malignancy of the upper gastrointestinal tract	–
Major SRH	None or dark spots	–	Blood in the upper gastrointestinal tract, adherent blood clot, visible or spurting vessel	–

Endoscopy provides very important prognostic information. The presence of blood within the upper gastrointestinal tract, active spurting haemorrhage, and a "non-bleeding visible vessel" are signs of poor prognosis. Active ulcer bleeding implies an 80–90 % risk of continuing haemorrhage or re-bleeding, while the visible vessel (representing adherent blood clot or

a pseudoaneurysm over the arterial defect) is associated with a 50 % chance of re-bleeding during that hospital admission. Re-bleeding is associated with a 10-fold increase in hospital mortality.

Table 3

Rockall score, re-bleeding, and mortality

Risk score	No	% Re-bleed	% Mortality
0	144	5	0
1	281	3	0
2	337	5	0.2
3	444	11	3
4	528	14	5
5	455	24	11
6	312	33	17
7	267	44	27
>8	190	42	41

A formal risk assessment should always be done. It focuses the mind and identifies high risk patients, who should be energetically resuscitated and monitored, and low risk patients, who can be "fast tracked" towards early discharge from hospital. Risk assessment is essential for the audit process.

MANAGEMENT: RESUSCITATION

The principles of "airway, breathing, and circulation" apply. Patients who present with major bleeding are frequently elderly and have significant cardiorespiratory, renal, and cerebrovascular co-morbidity. It is crucial that this is recognised and supported since most deaths are due to decompensation of general medical diseases precipitated either by the bleed itself or postoperative complications which are much more likely when medical co-morbidity is present. Central venous pressure monitoring is useful in the elderly and in patients with cardiac disease to optimise decisions concerning fluid replacement. Intravenous fluids should be given through a large cannula inserted in an anticubital vein. Crystalloids (principally normal saline) are used to normalise blood pressure and urine output; colloids (such as gelefusin) are often employed in the presence of major hypotension. Saline should be used with care in patients with liver disease.

Blood transfusion is administered to patients who are shocked and are actively bleeding. Blood is also transfused when the haemoglobin concentration is less than 100 g/l. The evidence base for this transfusion threshold is rather poor, but it is known in the intensive care setting that a haemoglobin concentration of less than 70 g/l has significant adverse cardiac effects and

it is reasonable to pre-empt this by employing a value of 100 g/l in bleeding patients.

Appropriate monitoring includes measurement of pulse, blood pressure, urine output (through an indwelling catheter), and central venous pressure. Actively bleeding, shocked patients are managed in a high dependency environment.

Key points:

• Optimum resuscitation must be done before endoscopy is undertaken. Endoscopy is dangerous in the haemodynamically compromised or hypoxic patient.

• Take great care with sedation in the critically ill patients. Unstable patients are best managed with the help of an anaesthetist.

• Patients must be supported by trained assistants at the time of endoscopy.

ENDOSCOPIC THERAPY

Endoscopy is the primary diagnostic modality and is undertaken after optimum resuscitation has been achieved.

At least 80 % of patients admitted to hospital because of acute bleeding have an excellent prognosis; bleeding stops spontaneously and circulatory supportive therapy is all that is required.

Endoscopic therapy is indicated in the following situations:

1. Bleeding oesophageal varices.

2. Peptic ulcer with major stigmata of recent haemorrhage (active spurting bleeding, non-bleeding visible vessel or non-adherent blood clot).

3. Vascular malformations including actively bleeding AVMs, GAVE, and the Dieulafoy malformation.

4. Rarely for active bleeding from a Mallory-Weiss tear.

The evidence base of endoscopic therapy for non-variceal therapy is principally based upon clinical trials for peptic ulcer haemorrhage. Three types of direct endoscopic treatments have been evaluated; each is designed to seal the arterial defect created by the ulcer. It is necessary to remove as much overlying blood clot as possible during endoscopy (using washing devices and snares) in order that therapy can be accurately given. This risks further active bleeding but this can almost always be stopped by the endoscopist.

Injection

Direct injection of fluids into the bleeding ulcer using disposable needles is technically straightforward. The efficacy of therapy has been demonstrated by several clinical trials, although mechanism are uncertain; tamponade, vasoconstriction from adrenaline, endarteritis after sclerosant,

or alcohol injection and a direct effect upon blood clot formation from fibrin glue or thrombin may all be relevant.

The most widely used injection fluid is 1:10 000 adrenaline. This stops active bleeding in more than 90 % of cases but 15–20 % of cases will re-bleed. The addition of sclerosants (polidocanol, STD, or ethanolamine) or alcohol does not reduce the risk of re-bleeding and risks causing life threatening necrosis of the injected area and should not be used. Fibrin glue (a mixture of thrombin and fibrinogen) and human thrombin are probably the most effective injection materials and have few complications.

Heat energy

Devices are applied directly to the bleeding point to cause coagulation and thrombosis.

The heater probe is pushed firmly on to the bleeding lesion to apply tamponade and deliver defined pulses of heat energy. Clinical trials have shown the device to be as effective and as safe as injection therapy. Multipolar coagulation (BICAP), in which electrical energy is conducted between multiple probes on the tip of an endoscopically positioned catheter and the argon plasma coagulator have comparable efficacy.

Mechanical devices

"Endoclips" can be applied to visible vessel and although they may be difficult deploy on to awkwardly positioned ulcers, they may represent the best option for major bleeding ulcers. It is known that arterial defects greater than 1 mm in diameter do not usually respond to injection or thermal therapies, while an adequately positioned clip can stop bleeding from relatively large arteries.

Combinations of endoscopic therapy

Although the exact modes of action of these endoscopic therapies are largely speculative, it is clear that each achieve haemostasis by different mechanisms and several groups have examined the hypothesis that combinations of endoscopic therapies are better than single modalities.

DRUG THERAPY

Three groups of drugs have been used in an attempt to reduce the risk of further bleeding in high risk patients:

- Acid suppressing drugs.
- Somatostatin and its analogue octreotide.
- Tranexamic acid.

Gastric acid lowering drugs

The stability of a blood clot is low in an acid environment and powerful gastric acid suppressing drugs therefore have the potential to optimise clot formation, thereby reducing the re-bleeding risk. It is crucial that the gastric

pH does not fall below 6 and the only practical way that this can be achieved is by constant infusion of a proton pump inhibitor (PPI).23 Only patients at high risk of re-bleeding should receive a PPI infusion since the prognosis of the remainder, who comprise the majority of cases, is good without their use. It follows that patients with major stigmata of recent haemorrhage who have undergone endoscopic therapy should be treated by PPIs. Clinical trials have shown that an 80 mg bolus of omeprazole followed by a 72 hour infusion of 8 mg/hour significantly reduces the risk of re-bleeding and need for emergency surgery.

Somatostatin

This drug and its analogue octreotide are theoretically attractive because they reduce mesenteric arterial flow and suppress gastric acid secretion. A meta-analysis has shown significant reduction in re-bleeding and need for emergency surgery in somatostatin treated ulcer bleeding patients compared with those receiving placebo infusions. The quality of some of the trials is relatively weak and octreotide appears ineffective. The efficacy of somatostatin in endoscopically treated patients has not been evaluated and the drug is not widely used in clinical practice.

Tranexamic acid

This antifibrinolytic agent has the potential to improve the stability of the clot and reduce the risk of re-bleeding. Although one trial showed benefit in treated patients, tranexamic acid is not often used, possibly because of a fear that its use could lead to the development of venous thrombosis.

SURGICAL INTERVENTION

Emergency surgery is done when endoscopic therapy combined with pharmacological intervention fails to secure permanent haemostasis:

1. Active bleeding which cannot be controlled by endoscopic therapy either because torrential haemorrhage obscures the bleeding point or when active bleeding continues despite successful application of endoscopic therapy.
2. Re-bleeding after initially successful endoscopic treatment. As previously discussed, it is reasonable to repeat endoscopic therapy on one occasion after re-bleeding providing local expertise is available and only after discussion between endoscopist and surgeon.

The type of operation depends upon the site of the ulcer. Bleeding duodenal ulcers are treated by under-running the ulcer, sometimes with pyloroplaty. Gastric ulcers are treated by partial gastrectomy of simple ulcer excision. Vagotomy is no longer undertaken since PPIs abolish acid secretion.

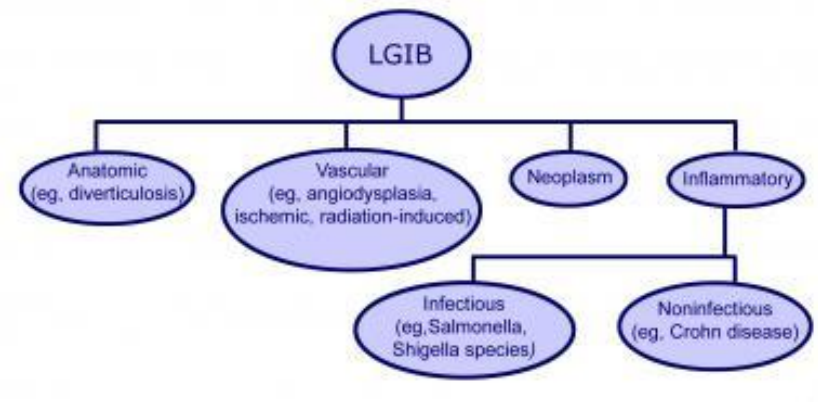
SECONDARY PROPHYLAXIS

After haemostasis has been achieved it is important to prevent late recurrent ulcer haemorrhage. *H pylori* eradication virtually abolishes the risk of late re-bleeding. When a patient needs for good reason to continue NSAID therapy the following should be considered:

- Use the least toxic NSAID which controls the arthritic symptoms.
- Co-prescribe a PPI with the NSAID.
- Consider use of a cyclo-oxygenase-2 specific anti-inflammatory drug. These are associated with significantly fewer recurrent ulcer related adverse events than occur with non-selective NSAIDs.
- Treatment in patients who have *H pylori* and need to continue a NSAID remains controversial. Gastritis, which is an inevitable consequence of *H pylori* infection, induces prostaglandin production and this may protect the gastroduodenal mucosa from the harmful effects of NSAIDs. Current studies suggest, however, that the magnitude of prostaglandin production is unlikely to outweigh the deleterious effects of *H pylori* and that eradication therapy is indicated in patients who have developed ulcer bleeding, are *H pylori* positive, and require long term NSAID therapy.

LOWER GASTROINTESTINAL BLEEDING

Lower gastrointestinal bleeding (LGIB) is a frequent cause of hospital admission and is a factor in hospital morbidity and mortality. LGIB is distinct from upper GI bleeding in epidemiology, management, and prognosis. The image below illustrates types of LGIB.



Types of lower gastrointestinal bleeding (LGIB)

SIGNS AND SYMPTOMS

The clinical presentation of LGIB varies with the anatomical source of the bleeding, as follows:

- Maroon stools, with LGIB from the right side of the colon.
- Bright red blood per rectum with LGIB from the left side of the colon.
- Melena with cecal bleeding.

In practice, however, patients with upper GI bleeding and right-sided colonic bleeding may also present with bright red blood per rectum if the bleeding is brisk and massive.

The presentation of LGIB can also vary depending on the etiology. A young patient with infectious or noninfectious (idiopathic) colitis may present with the following:

- Fever.
- Dehydration.
- Abdominal cramps.
- Hematochezia.

An older patient with diverticular bleeding or angiodysplasia may present with painless bleeding and minimal symptoms. Ischemic colitis, abdominal pain, and varying degrees of bleeding are usually observed in patients with multiple comorbidities such as congestive heart failure, atrial fibrillation, or chronic renal failure. LGIB can be mild and intermittent, as often is the case of angiodysplasia and colon carcinoma, or moderate or severe, as may be the situation in diverticula-related bleeding. Colon carcinoma rarely causes significant LGIB.

Massive lower GI bleeding usually occurs in patients aged 65 years and older who have multiple medical problems, and produces the following manifestations:

- Systolic blood pressure of less than 90 mmHg.
- Hemoglobin (Hb) level of 6 g/dL or less.
- The passage of maroon stools or bright red blood from the rectum.

DIAGNOSIS

Nonsurgical modalities used to diagnose LGIB include the following:

- Colonoscopy.
- Radionuclide scans.
- Angiography.

Fiberoptic flexible colonoscopy is the initial diagnostic method of choice in most patients who are hemodynamically stable. Colonoscopy should be performed following a rapid bowel preparation ("prep") with volume cathartic agents. Rapid bowel prep colonoscopy has higher diagnostic and therapeutic

yields compared to unprepped colonoscopic evaluation. In hemodynamically unstable patients and in those with brisk ongoing LGIB, angiography with or without a preceding radionuclide scan can be performed. Angiography is also performed if colonoscopy has failed to identify a bleeding site. Rarely, exploratory laparotomy and intraoperative push enteroscopy can be performed in truly hemodynamically unstable patients owing to the speed and the volume of the bleeding.

Appropriate routine blood tests include the following:

- Complete blood cell (CBC) count.
- Serum electrolytes levels (eg, sequential multiple analysis 7).
- Coagulation profile, including activated partial thromboplastin time (aPTT), prothrombin time (PT), platelet count, and/or bleeding time (bleeding time is only recommended in patients with bleeding disorders and use of antiplatelet agents)

Helical CT scanning of the abdomen and pelvis can be used when a routine workup fails to determine the cause of active GI bleeding. Multiple criteria are used for establishing the bleeding site, including the following:

- Vascular extravasation of the contrast medium.
- Contrast enhancement of the bowel wall.
- Thickening of the bowel wall.
- Spontaneous hyperdensity of the peri-intestinal fat.
- Vascular dilatations.

MANAGEMENT

Resuscitation and initial assessment

Initial resuscitation involves establishing large-bore IV access and administration of normal saline. The patient's blood loss and hemodynamic status should be ascertained, and in cases of severe bleeding, the patient may require invasive hemodynamic monitoring to direct therapy.

Hemostasis

Once the bleeding site is localized, nonsurgical therapeutic options that may be considered include the following:

- Diverticular bleeding: Colonoscopy with bipolar probe coagulation, epinephrine injection, or metallic clips.
- Recurrent bleeding: Resection of the affected bowel segment.
- Angiodysplasia: Thermal therapy (eg, electrocoagulation, argon plasma coagulation).
- Conservative management, including nothing by mouth (NPO) and intravenous (IV) hydration in patients with ischemic colitis.

In patients in whom the bleeding site cannot be determined, vasoconstrictive agents such as vasopressin (Pitressin) can be used. If vasopressin is unsuccessful or contraindicated, superselective embolization is useful.

Surgery

The indications for surgery include the following:

- Active persistent bleeding with hemodynamic instability that is refractory to aggressive resuscitation
- Persistent, recurrent bleeding
- Transfusion of more than 4 units packed red blood cells in a 24-hour period, with active or recurrent bleeding
- Transfusion of more than 6 units of packed red blood cells during the same hospitalization

MAIN REFERENCES

1. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding / A. N. Barkun, M. Bardou, E. J. Kuipers et al. // Ann Intern Med. – 2010. – Jan. 19. – № 152 (2). – P. 101–13.

2. Management of acute upper and lower gastrointestinal bleeding. A national clinical guideline / Scottish Intercollegiate Guidelines Network (SIGN): Scottish Intercollegiate Guidelines Network (SIGN). – Edinburgh, 2008. – Sep. (SIGN publication; no. 105).

ADDITIONAL REFERENCES

1. Fallah M. A. Acute gastrointestinal bleeding / M. A. Fallah, C. Prakash, S. Edmundowicz // Med. Clin. North. Am. – 2000. – Sep., N 84 (5). – P. 11, 83–208.

2. Risk stratification of upper GI bleeding with an esophageal capsule / S. Chandran, A. Testro, P. Urquhart et al. // Gastrointest Endosc. – 2013. – Feb., N 26.

3. Vargas H. E. Management of portal hypertension-related bleeding / H. E. Vargas, D. Gerber, K. Abu-Elmagd // Surg. Clin. North. Am. – 1999. – Feb., N 79 (1). – P. 1–22.

4. Pezzulo G. Assessing upper gastrointestinal bleeding in adults / G. Pezzulo, D. Kruger // Journal of the American Academy of Physician Assistants. – 2014. – Т. 27, № 9. – С. 19–25.

5. Multidisciplinary management strategies for acute non- variceal upper gastrointestinal bleeding / Lu Y. et al. // British Journal of Surgery. – 2014. – Т. 101, № 1. – С. e34–e50.

Навчальне видання

Сучасна практика внутрішньої медицини з невідкладними станами

Ведення хворих з блювотою кров'ю та меленою

Методичні вказівки для студентів та лікарів-інтернів

Упорядники Бабак Олег Якович
Лапшина Катерина Аркадіївна
Железнякова Наталя Мерабівна
Зайчєнко Ольга Євгеніївна
Просоленко Костянтин Олександрович
Зелена Ірина Іванівна
Андрєєва Анастасія Олександрівна
Фролова-Романюк Еліна Юріївна
Гопцій Олена Вікторівна
Ситник Ксенія Олександрівна

Відповідальний за випуск О. Я. Бабак

Комп'ютерний набір К. А. Лапшина
Комп'ютерна верстка Н. І. Дубська

Формат 60×84/16. Умов. друк. арк. 1,0. Зам. № 16-33139.

Редакційно-видавничий відділ ХНМУ,
пр. Науки, 4, м. Харків, 61022
izdatknmu@mail.ua

Свідоцтво про внесення суб'єкта видавничої справи до Державного реєстру видавництв, виготівників і розповсюджувачів видавничої продукції серії ДК № 3242 від 18.07.2008 р.

MODERN PRACTICE OF INTERNAL MEDICINE WITH EMERGENCY CONDITIONS

Management of patients with melena and haematemesis

Guidelines for students and interns