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DOCTORAL CANDIDATE

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***ABSTRACT***

***DOCTORALE THESIS***

***PARTICULAR ASPECTS in GASTRIC (NONEPITHELIAL) TUMORS. PROBLEMS  
of DIAGNOSIS and THERAPY***

**SCIENTIFIC COORDINATOR:  
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**2011**

Particular aspects in gastric (nonepithelial) tumors. Problems of Diagnosis and Therapy. To obtain the title of Doctor of Medicine, Surgical Pathology specialization, developed by DRAGOȘ OVIDIU HORȘIA, to obtain the scientific title of Doctor of Medical Sciences, Medical.

## PART I (NORMAL STOMACH)

In **Chapter I**, called the *anatomy of the stomach*, are exposed to aspects of classical descriptive anatomy gastric, body positioning, components, data about the arterial and venous vasculature of the stomach, innervation stomach problems with three nervous pedicle of particular importance in gastric surgery and lymphatics stomach with four main areas of drainage and lymph nodes involved. Thus, for a primary tumor is necessary to investigate specific areas of draining lymph nodes of the respective area. In conclusion, this chapter the thesis author conducted a study and appreciation of worthy synthesis of present knowledge of functional anatomy integrated physiological role.

In **Chapter II**, entitled *stomach histology* are analyzed particular aspects of classical microscopy and electron microscopy occurred in the stomach and eso-gastric junction. All these data are accompanied by microscopic images that come to fill this vast chapter.

In **Chapter III**, which is reserved for *stomach physiology*, modern exploration techniques are presented: pH- meters for 24 hours (circadian), manometers, electrical impedance, analysis of three-dimensional vector in

the volume, scan and ultra-fast computed tomography.

Each chapter is accompanied by selective bibliography.

## PART II (SURGICAL STOMACH)

Comprises two distinct parts:

a) The problem of benign and malignant tumors of the stomach, epithelial and nonepithelial, gastroesophageal reflux disease (GERD), Barrett esophagus, intestinal metaplasia, adenocarcinoma postreflux, macroscopic and endoscopic classification.

b) Resection and reconstruction in benign and malignant tumors.

*Types of gastric resection* (subtotal gastrectomy and total, antrectomy, hemigastrectomy, pyloroplasty with vagotomy).

*Types of vagotomy*: total, partial. Enlarged gastric resections; reresections (after Pean), degastrogastrectomy (after Reichel-Poly), subtotal and total esogastrectomy with lymphadenectomy type R1, R2 and R3. Lesions were analyzed at the gastric and eso-gastric junction, recourse to complementary examination. Of these, the diagnostic value biopsy and histopathological examination are final. Examination of the classic X-ray examination can remember, ultrasound, computer tomography, nuclear magnetic resonance structural details giving the location and expansion. Also, these procedures will be used for staging and assessment of the occurrence of postoperative recurrence. Currently there is a consensus that

all diseases are treated surgically. The introduction of antisecretory medication (proton pump inhibitors) resulted in the exclusion wrongly gastric resection. Long-term treatment leads to gynecomastia or gastric anaciditate which is likely to degenerate into cancer especially if asymptomatic. A growing number of doctors, comment that medical error, considering that if a major complication for a commission shall be composed of the surgeon and gastroenterologist to decide at surgery.

*Types of surgical reconstruction:* Gastric reconstruction Reichel-Polya type and Pean type , the Roux Y reconstruction (with variants), other types of reconstruction: „Ulm pouch" and Lygidakis-Popovici; classification.

#### The personal part

Statistics are based on a clinical material of 116 cases operated by Academician Dr. Zeno Popovici in Emergency Hospital of Bucharest (1962-1986) and Department of Surgery Hospital in Sibiu County (1986-2003). During the 1992-2010, operating in Faculty of Medicine „Victor Papilian”, Sibiu, University „Lucian Blaga”. Postoperative complications were related to anastomotic fistulas (5), intestinal occlusions (3), haemoperitoneum (1). Intestinal obstruction was determined by agglutination of intestinal loops and required laparotomy. Haemoperitoneum was caused by slippage of ligatures pressure. Immediate postoperative mortality was 10 deaths per 116 cases (10.5%): 5 were from medical causes, pulmonary thromboembolic (1), intraoperative heart attack (1), intraoperative

fibrinolysis (1), cataclysmic HDS by portal hypertension (1) and myocytic infarction. The remaining five deaths occurred in patients in stage 4 after palliative surgery necessary. Types of surgery are analyzed in the stomach, mostly resection of the Roux Y with or without stomach pylorus preservation. The types of surgical reconstruction (more than 64 operations) were reduced to two major types,, Ulm Pouch "(Cuschieri) and tank-type Lygidakis Popovici (representing the majority). The Lygidakis procedure is based on the reintroduction of duodenum in circuit making two additional anastomosis with creation of a gastric reservoir. Amendment to the Dr. Popovici is based on longitudinal incisions jejunal replacement, sectioning the circular muscle, stomach turning in a atonic reservoir. In version Lygidakis-Popovici, is performed a cross section that saves muscles and peristalsis.

Clinical material comprises two parts: a) gastric cancers (38 cases) and b) nonepithelial tumors (78 cases), randomized to be analyzed statistically. The two parts (gastric neoplasms and nonepithelial tumors) are analyzed separately, because they have distinct morbidity and mortality and the results are not comparable.

a) **In the first group**, which includes *gastric neoplasms* (38 cases) were noted five clinical types, namely: the majority of patients had a esocardio-tuberozitar cancer (10 cases) followed in descending order of vertical portion neoplasms of the stomach (8 cases) , linitis plastica (8 cases), blunt gastric neoplasms (5 cases) and antropyloric neoplasms (5 cases). We have created two distinct types: giant gastric neoplasm (1 case) and malignant gastric polyposis colitis (1 case). In the latter case is difficult

differential diagnosis with "hypertrophic gastritis of Ménétrier". Also, an intraoperative surprise may be multicentric neoplasm of lymphoma, after gastrectomy. Patients have suffered subtotal or total gastric resection associated with a gastric reconstruction of the Roux Y loop. In total gastrectomy, a change in the standard process of anastomosis of jejunum to the esophagus is the Rankin-Lawrence-Rodino Hunt which was later renamed the J-pouch by Herfarth and which is considered to offer the following advantages: (1) perform a function that slows progression of pseudo-pyloric tank ingested food into the small intestine and reduce dumping syndrome, (2) providing a reservoir for digestion and absorption and (3) reduce the requirement for frequent meals. The most sensitive technique used to determine the subtle abnormalities emptying "stomach" is a test using solid food. This technique uses a gamma-emitting radionuclide  $^{99m}\text{Tc}$  evidence in addition to lunch.

In contrast, Pellegrini et al. have shown that small bowel transit rate is slowed by esojunal anastomosis Roux-en-Y in total gastrectomy.

Series of Mc Alley in Belfast based on 19 patients treated with total gastrectomy, compared to 11 with J pouch. Weight gain was better in J-Pouch, compared with esojunal standard anastomosis may be caused by slowing orocecal time. Roux-en-Y reconstruction has become the most common method used in the world, and the results of gastric resection has become a European experience.

### Why resection in Y?

Resection in Y was introduced by Roux in Switzerland (Lausanne) in 1905 as the third variant of gastric reconstruction after Pean-Billroth I and Reichel-Polya. Reichel-Polya technique found to cause an increased frequency of blunt gastric cancer, which led to a restriction in using this method. American authors (Capusotti, Bombeck, Llynwood-Herrington) showed that if Pean resection is not possible, is preferable to be used in the resection of the Roux Y-loop, even in emergency conditions (i.e., perforated ulcer). With the introduction of fibroscopy, demonstration of gastro-oesophageal reflux disease (GERD) and ineffective Nissen antireflux surgery technique, have reached to re-resection in Y, which was considered ideal GERD surgery after a long period of disregard of this procedure. After total gastrectomy resection it was suggested introduction the Y, to facilitate reconstruction.

Digestive disorders in patients without stomach have led to gastric reservoir (64 types), which can be reduced to two basic types: (a) gastrojejuno-plasty type "ULM Pouch", perfected by Alfredo Cuschieri and (b) Lygidakis tank, as amended by Prof. Dr. Z. Popovici with jejunal transverse incisions through the practice floor that prevents an atonic "neogaster". So I called this tank Lygidakis-Popovici. In conclusion, in our statistics, gastric resections Y gastric tank were divided into two categories: (a) duodenum reintegration in the digestive circuit (26 patients) and tank-Popovici Lygidakis (10 patients); (b) in one case we used tank "Ulm-Pouch".

Pean resection is contraindicated in cancer, being a non-cancer surgery, because it allows removal of retropyloric lymph early postoperative recurrence and cause. Should be excluded "a priori" of surgical cancer arsenal.

b) Since the doctoral candidate is a specialist in pathology and no surgeon was suggested to highlight the second group of "*nonepithelial tumors*" and not so much technical surgical procedures that will be the subject of another thesis.

Nonepithelial tumors are classified into:

a) benign tumors, muscle tumors (leiomyomas and rhabdomyomas), granular cell tumors, lymphomas, plasmacytomas, schwannomas, apudoma and neuroendocrine tumors (pheochromocytoma, vipoma, Zollinger-Ellison syndrome).

b) malignant tumors: leiomyosarcoma, rhabdomyosarcoma, lymphosarcoma, Hodgkin lymphoma and non-Hodgkin's lymphoma, malignant fibrous histiocytomas, reticulosarcoma, malignant venereum limfogramuloma.

**Leiomyomas** is a large group of tumors characterized histologically by the appearance point of view crossed sheaves of smooth muscle cells associated with variable fibrosis producing a characteristic appearance.



**Gastrointestinal stromal tumors (GIST)** are the most common mesenchymal tumors of the digestive tract and are defined as c-KIT (CD 34 and CD 117, stem factor receptor) positive marker for epitheloid or fusiform mesenchymal cells. The differential diagnosis of GIST is essential not only because this group has a high risk of malignancy, but also because it responds to treatment target recently discovered, STI-571 (imatinib mesylate), an inhibitor of tyrosine-kinase receptor protein of KIT. GIST, is today considered a particular tumor that originates in interstitial cells of Cajal. This is the most important chapter of pathology, including nonepithelial tumors group which has recently been differentiated epithelial tumors as they progress and survive much longer, even in case of metastases for which resection is mandatory. In epithelial tumors, the only treatment of metastases is their way of hepatic artery necrosis. Also, a special feature presents an endocrine tumors whose prognosis is determined by the appearance of multiple endocrine neoplasia (MEN I and MEN II). In this last category, tumors are associated with each of them requiring multiple determination. A special category is the hyperparathyroidism which is associated in most endocrine tumors. Therefore, removal of the parathyroid gland subtotal or total to be associated with autotransplant (strenocleidomastoidian muscles). In establishing this diagnosis, determination of calcitonin is required. There are also links with pituitary tumors (pituitary) and tumors in the adrenal (Cushing). In this category enter and Zollinger-Ellison syndrome (gastrinomas) both the home and the pseudo pancreatic Zollinger-Ellison tumors characterized by the presence of localization in the antral and

duodenal level. Remote monitoring is required of these tumors („follow-up“). A special place is occupied by pheochromocytomas that may occur away from the adrenal glands (extrarenale forms, mediastinum, heart). The most important and personal work is the histopathological analysis and discussion especially immunohistochemistry and electron modern stain that helps definitive diagnosis of these diseases, especially since they discovered guanidine compounds with double aspect: diagnosis and treatment. A particular aspect is studied in cases of benign or malignant gastric schwannomas with a better outcome after tumor ablation. On the other hand, fibrosarcomas are quite frequent location in retrogastric and retroperitoneal spaces away from the pylorus, which can preserve. The paper also emphasizes presenting some cases (5) of carcinoid appendiculare more common in children and are usually associated with generalized erythematous reaction („flush“). These tumors appendiculare, if they exceed 1-2 cm, must be associated with certain types of resection (right hemicolectomy). As long as they are limited to appendix and especially if the basis of appendix are not interested, have two major advantages: are diagnosed with acute appendicitis easier and has a very favorable prognosis without recurrence. They often remain undiagnosed because the part operator is not sent for histopathological examination. A bizarre aspect, reported in the literature shows that sometimes, after a longer period of time, the patient may be hospitalized for colic adenocarcinoma. Today no longer allows a definite diagnosis of nonepithelial tumor not be supported by immunohistochemistry and electronmicroscopy. In this kaleidoscopic mosaic occupies a special place Hodgkin's disease or non-Hodgkin

lymphoma to be associated with various locations especially in the digestive system as well as other diseases (Crohn's). A special place certain rare diseases as Sezary syndrome, mycosis fungoides, pemphigus vulgaris, pemphigoid scar or Behçet's disease.

<b><i>Nonepithelial tumors</i></b>	Number of cases
Lymphomas	12
Plasmacytoma	1
Malignant fibrous histiocytomas	2
Leiomyomas and rhabdomyomas	7
Schwannomas	8
Lymphosarcomas	6
Reticulosarcomas	11
Malignant venereum limfogr anuloma	2
Pheochromocytoma	1
Apudoma	5
<b><i>Other mesenchymal tumors</i></b>	23
<b><i>Gastric neoplasms</i></b>	38
<b>Total</b>	116

## CONCLUSIONS

1. Stomach surgery is a surgical border, involving several specialties.
2. The major objective in reconstructive surgery of the stomach, is the quality of life.
3. Immunohistochemistry is a „new "decisive in formulating the diagnosis of these types of gastric neoplasms.
4. Multimodal treatment of cancer is key to success in the pathology of malignant tumors.
5. Prevention of malignant phenomenon will result in fewer illnesses.
6. Percentage of 5 year survival in patients with gastric malignancy depends on the stage it was diagnosed.
7. Creation of new specialties stomach cancer surgery beneficial to patients.