The Rodger C. Haggitt Memorial Lecture
I got an email on 4/22/14 from Hala El Zamaity inviting me to give this lecture and giving me this topic:

“The ever changing TNM classification and its implication”

To me, colon cancer is annoying. But an assignment for the Haggitt lecture is sacrosanct.
My primary sources of information for this lecture include:
My only conflict of interest is that I was on the site task force for the esophageal chapter.
With a bunch of surgeons and oncologists who ignored me completely.... just like my children
I also used the 2 premier reference sites for practicing surgical pathologists when all other options fail.
Disclaimer:
I really wish that I could be supported by 10 equipment companies and another 10 reagent companies, but they have ignored my requests.
There is a massive amount of published data covering everything I will discuss. I cannot deal with most of it, since my assignment was to concentrate on the AJCC classification.
Serosal surfaces, mucin pools, and deposits, Oh my: challenges in staging colorectal carcinoma

Wendy L Frankel and Ming Jin

Department of Pathology, The Ohio State University Wexner Medical Center, Columbus, OH, USA

An erudite, informative paper, far more insightful and sophisticated than this lecture.
Another erudite, informative paper, far more insightful and sophisticated than this lecture.
Staging colorectal carcinomas:

Historical perspective
The model for this discussion

4 Nodal metastases

Transmurally invasive carcinoma
The first staging system for this carcinoma?

THE CLASSIFICATION OF CANCER OF THE RECTUM.

CUTHBERT E. DUKES.

Pathologist to St Mark’s Hospital, London.

Journal of Pathology and Bacteriology 1932;35:323
Dukes’ staging system was only for the rectum.

Had 2 components:
1. The extent of the primary tumor when there were no nodal metastases
2. Nodal metastases.
The A stage had no subsets based on depth.
The C stage was nodal metastases regardless of depth of invasion.
Distant metastases were not included, nor would they be for 45 years.
Depth: extension into extra rectal tissues

Dukes, 1932

+ nodes

Depth limited to wall of rectum.

Extension of growth to extra rectal tissues but no metastases in regional lymph nodes.

Metastases in regional lymph nodes.

Extent of spread of cancer of rectum.
Dukes stages and survival were related

5 year survival with Dukes’ classification

A - 97%
B - 81%
C1 - 51%
C2 - 16.5%
C3 - 4%
Mayo Clinic modification, 1949


The site now included the **sigmoid colon**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Limited to mucosa</td>
</tr>
<tr>
<td>B1</td>
<td>Extending into muscularis propria</td>
</tr>
<tr>
<td>B2</td>
<td>Penetrating muscularis propria</td>
</tr>
<tr>
<td>C</td>
<td>B1 or B2 with nodal metastasis</td>
</tr>
</tbody>
</table>

The A stage, carcinoma limited to the mucosa, is really an **adenoma**
Comparison of Dukes and Kirklin et al

Dukes rectum

Kirklin et al sig-rectum

A -> A

B -> B-1

B-2

C -> C
Kirklin et al Staging of a colorectal cancer

Depth: B2 penetrating muscularis

+ Nodes
From the U of Michigan. They got help from an esteemed pathologist, Carl V. Weller, but they did not make him a co-author.
Astler-Coller Staging

The whole colon was now included

A  Mucosal only, nodes negative
B-1  Submucosa to muscularis propria nodes negative
B-2  Beyond muscularis propria nodes negative
C-1  B-1 with + nodes
C-2  B-2 with + nodes

the A stage is still an adenoma
Astler-Coller modified Kirklin et al which modified Dukes

<table>
<thead>
<tr>
<th>Dukes rectum</th>
<th>Kirklin et al sig-rectum</th>
<th>Astler-Coller colorectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>B-1</td>
<td>B-1</td>
</tr>
<tr>
<td>B</td>
<td>B-2</td>
<td>B-2</td>
</tr>
<tr>
<td>C</td>
<td>C</td>
<td>C-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C-2</td>
</tr>
</tbody>
</table>
Astler-Coller Staging of a colorectal cancer

C2

Depth: B2
Beyond Muscularis

+ Nodes
5 year survival using the Astler-Coller staging based on 352 resected cases at the University of Michigan, 1940-1944

<table>
<thead>
<tr>
<th>Stage</th>
<th>#cases</th>
<th>5-yr surv</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>B-1</td>
<td>48</td>
<td>67%</td>
</tr>
<tr>
<td>B-2</td>
<td>164</td>
<td>47%</td>
</tr>
<tr>
<td>C-1</td>
<td>14</td>
<td>43%</td>
</tr>
<tr>
<td>C-2</td>
<td>125</td>
<td>22%</td>
</tr>
</tbody>
</table>
Finally, the **TNM** staging system was introduced to the general public, including the pathologist public.
A TNM system was originally proposed in the 1950s for the clinical staging of malignant tumors in general by the International Union Against Cancer (UICC).

In the 1960s the American Joint Committee for Cancer Staging and End Result Reporting (AJCCSERR) established a task force to come up with a postoperative staging system, so this is where we pathologists got into the TNM staging business.

This postoperative staging system was developed, and the AJCCSERR published it in the first edition of the Staging Manual in 1977.

The A and B of previous systems is T C is N M finally

The AJCC 1\textsuperscript{st} Ed Colorectal TNM

Primary Tumor (T)

\textbf{Tis} Carcinoma in situ (no penetration of lamina propria)

\textbf{T1} Clinically benign lesion or lesion confined to the mucosa or submucosa

\textbf{T2} Involvement of muscular wall or serosa, no extension beyond
Primary Tumor (T)

T3  Involvement of all layers of colon or rectum with extension to immediately adjacent structures or organs or both, no fistula

T4  Fistula present along with any of the above degrees of tumor penetration

T5  Tumor has spread by direct extension beyond the immediately adjacent organs or tissues
The AJCC 1<sup>st</sup> Ed Colorectal TNM

**Nodal Involvement (N)**

**NX** Nodes not assessed or involvement not recorded

**N0** Nodes *not believed to be involved*

**N1** Regional nodes involved (distal to inferior mesenteric artery)
Nodal Involvement (N)

NX  Nodes not assessed or involvement not recorded

N0  Nodes not believed to be involved

N1  Regional nodes involved (distal to inferior mesenteric artery)
The AJCC 1<sup>st</sup> Ed Colorectal TNM

**Nodal Involvement (N)**

- **NX** Nodes not assessed or involvement not recorded
- **N0** Nodes not believed to be involved
- **N1** Regional nodes involved (distal to inferior mesenteric artery)

Separation of church and staging?
Distant Metastasis (M)

**MX** Not assessed

**M0** No (known) distant metastasis

**M1** Distant metastases present
The 2nd Edition was published in 1983
At Last—Worldwide Agreement on the Staging of Cancer

Presidential Address

Robert V. P. Hutter, MD

The current TNM system for classification and staging of cancer approved by both the American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer (UICC/TNM) is designed primarily for patient care and, in this context, is equally applicable to patients in clinical research. It is built in general to the AJCC therefore it does not follow the UICC in the anatomic extent of disease derived from the TNM classification: T, extent of primary tumor; N, absence or presence and extent of regional lymph node metastasis; and M, absence or presence of distant metastasis. Later, in 1959, the AJCC (formerly the American Joint Committee on Cancer: Staging and End Results Reporting) was formed...
The T and N changed in the 2nd (1983) and 3rd (1988) editions with no change in M. By the 3rd edition,

Fistulas were not mentioned for T

T3 was limited to pericolic adipose

T4 was extension beyond pericolic adipose

T5 disappeared

N1 was separated into N1 and N2 based on number of positive nodes

N3 was any + node along a major vessel
DEFINITIONS as of 4th and 5th editions

Tis Carcinoma in situ: intraepithelial or invasion of LP

T1 invasion of submucosa

T4 Direct invasion of other organs or structures and/or perforates visceral peritoneum

N3 disappeared
DEFINITIONS

Primary Tumor (T)
- TX  Primary tumor cannot be assessed
- T0  No evidence of primary tumor
- Tis Carcinoma in situ: intraepithelial or invasion of lamina propria
- T1  Tumor invades submucosa
- T2  Tumor invades muscularis propria
- T3  Tumor invades through the muscularis propria into the subserosa, or into non-peritonealized pericolic or perirectal tissues
- T4  Tumor directly invades other organs or structures, and/or perforates visceral peritoneum

Regional Lymph Nodes (N)
- NX  Regional lymph nodes cannot be assessed
- N0  No regional lymph node metastasis
- N1  Metastasis in 1 to 3 regional lymph nodes
- N2  Metastasis in 4 or more regional lymph nodes

Total nodes examined = _______

Distant Metastasis (M)
- MX  Distant metastasis cannot be assessed
- M0  No distant metastasis
- M1  Distant metastasis

Biopsy of metastatic site performed..... □Y ...... □N
Source of pathologic metastatic specimen ____
DEFINITIONS

Primary Tumor (T)

- TX: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- Tis: Carcinoma in situ: intraepithelial or invasion of lamina propria
- T1: Tumor invades submucosa
- T2: Tumor invades muscularis propria
- T3: Tumor invades through the muscularis propria into the subserosa, or into non-peritonealized pericolic or perirectal tissues
- T4: Tumor directly invades other organs or structures, and/or perforates visceral peritoneum

Regional Lymph Nodes (N)

- NX: Regional lymph nodes cannot be assessed
- N0: No regional lymph node metastasis
- N1: Metastasis in 1 to 3 regional lymph nodes
- N2: Metastasis in 4 or more regional lymph nodes

Distant Metastasis (M)

- MX: Distant metastasis cannot be assessed
- M0: No distant metastasis
- M1: Distant metastasis

Biopsy of metastatic site performed..... □ Y .... □ N

Source of pathologic metastatic specimen
Starting with the 6th edition, big changes were summarized at the beginning of the chapter.
The 7th edition from 2010 is what we all use now. Cancer registries require it.
The rest of my comments, both snide and nit-picking deal mainly with the 7th edition.
PRIMARY TUMOR (T) 7th Edition

Tis Carcinoma *in situ*: intraepithelial or invasion of lamina propria

T1 invasion of submucosa
T2 invasion of muscularis propria
T3 invasion through the muscularis propria into pericolorectal tissues
T4a penetrates to the surface of the visceral peritoneum
T4b direct invasion or adherence to other organs or structures
The Evolution of Tis and T1

1st and 2nd Editions:
Tis = carcinoma in situ
T1 = tumor confined to mucosa or submucosa

3rd Edition
Tis = carcinoma in situ
T1 = tumor invades submucosa
No mention of LP invasion

4th Edition
Tis = carcinoma in situ: intraepithelial or invasion of LP
T1 = tumor invades submucosa
The Tis saga, courtesy of the 7th edition, AJCC Staging Manual

Carcinoma in situ, by definition, is a non-invasive epithelium.

However, in the manual, carcinoma in situ includes invasion as well as non-invasion.
The Tis saga, courtesy of the 7th edition, AJCC Staging Manual

*Note: Tis includes cancer cells confined within the glandular basement membrane (intraepithelial) or mucosal lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa.

What is required to prove that the basement membrane is not breached? Laminin? Collagen IV? Light microscopy is notoriously inept
The Tis saga, courtesy of the 7th edition, AJCC Staging Manual

*Note: Tis includes cancer cells confined within the glandular basement membrane (intraepithelial) or mucosal lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa.

Nit-Picking stuff:

The colon has crypts, not glands!

Is there another lamina propria that differs from the one in the mucosa?
malignant looking cribriform stuff
Looks even worse at high power
Should we call this a Tis?
Has it breached the glandular basement membrane?
Complex proliferation limited to the mucosa
The stroma is pure lamina propria.
Should we call this a Tis?
I bet this has breached the glandular basement membrane.
If we do call this Tis, then we have to fill out a template, right?
Hardly anyone calls this Tis; HGD instead and no template
In the esophagus
Tis = HGD

In the stomach
Tis = intraepithelial without invasion of LP

In the colon
Tis = intraepithelial or invasion of LP

Regardless of the definition
Tis doesn’t metastasize
In the esophagus
Tis = HGD

In the stomach
Tis = intraepithelial without invasion of LP

In the colon
Tis = intraepithelial or invasion of LP

Maybe, Tis should die!
Kill this!

PRIMAR Y TUMOR (T) 7th Edition

Tis Carcinoma *in situ*: intraepithelial or invasion of lamina propria

T1 Tumor invades submucosa
T2 Tumor invades muscularis propria
T3 Tumor invades through the muscularis propria into pericolorectal tissues
T4a Tumor penetrates to the surface of the visceral peritoneum
T4b Tumor directly invades or is adherent to other organs or structures
 PRIMARY TUMOR (T) 7th Edition

Tis Carcinoma *in situ*: intraepithelial or invasion of lamina propria

T1 Tumor invades submucosa

T2 Tumor invades muscularis propria

T3 Tumor invades through the muscularis propria into pericolorectal tissues

T4a Tumor penetrates to the surface of the visceral peritoneum

T4b Tumor directly invades or is adherent to other organs or structures
T4 history: fistula time

T3 involves all layers with extension to immediately adjacent structures or organs, no fistula

T4 Fistula with any depth of invasion

T5 further extension

T3 invades all layers including serosa with or without extension to adjacent or contiguous tissues +/- fistula

T4 direct extension beyond contiguous tissue or immediately adjacent organs
T4 history: forgotten fistulae
A time of great stability

T4: 2 components combined
Invasion of other organs or structures
Perforation of visceral peritoneum
<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ: intraepithelial or invasion of lamina propria*</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades muscularis propria</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades through the muscularis propria into pericolectal tissues</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor penetrates to the surface of the visceral peritoneum**</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor directly invades or is adherent to other organs or structures^,**</td>
</tr>
</tbody>
</table>

In the 7th edition, T4 is split into 2 parts.
The T4a mess

T4a
tumor penetrates to the surface of the visceral peritoneum
On the surface and growing along it
On the surface T4a
Not on the surface and covered by exudate.

T4a?
T4a?

Not on the surface and covered by exudate
Various definitions of a T4a tumor:
Tumor actually on the peritoneal surface
Tumor close to the surface with overlying mesothelial hyperplasia
Tumor close to the surface with overlying inflammation and exudate.

The AJCC Staging Manual does not give us guidelines, thus leaving it for the pathologist community to fight it out.
On the surface!!!

Close to the surface with reaction!!!
The T4b mess

Tumor directly invades or is adherent to other organs or structures
pT4b

Urinary bladder muscularis

Sigmoid carcinoma
T4b : Tumor directly invades or is adherent to other organs or structures

Tumor that is adherent to other organs or structures, grossly, is classified as cT4b. (Presumably, grossly means clinically, since the c prefix is used.)

It seems logical that if tumor is found microscopically to be in the adhesion, then it should be classified as pT4b, but that is not clarified.
T4b: Tumor directly invades or is adherent to other organs or structures.

It does say: However, if no tumor is present in the adhesion, microscopically, the classification should be pT1-4a depending on the anatomic depth of wall invasion.

How can a T1 or T2 tumor (confined to the wall) adhere to another organ or structure?

Only with perseverance and speed.
Enough of the T stuff!
Let’s explore N....
Are you exhausted yet?
I can stop here, and you can rest....go drinking
But then we would lose the chance to fight the battle of TUMOR DEPOSITS!!
Things nodal were pretty stable from the 1st through the 6th editions
### Nodal Involvement (N) 1st Edition

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Nodes not assessed or involvement not recorded</td>
</tr>
<tr>
<td>N0</td>
<td>Nodes not believed to be involved</td>
</tr>
<tr>
<td>N1</td>
<td>Regional nodes involved (distal to inferior mesenteric artery)</td>
</tr>
</tbody>
</table>

### Regional Lymph Nodes (N) 2nd through 6th Edition

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in 1 to 3 regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in 4 or more regional lymph nodes</td>
</tr>
</tbody>
</table>
In the 6th edition, a new twist:

<table>
<thead>
<tr>
<th>Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Tumor (T)</strong></td>
</tr>
<tr>
<td>TX</td>
</tr>
<tr>
<td>T0</td>
</tr>
<tr>
<td>Tis</td>
</tr>
<tr>
<td>T1</td>
</tr>
<tr>
<td>T2</td>
</tr>
<tr>
<td>T3</td>
</tr>
<tr>
<td>T4</td>
</tr>
<tr>
<td><strong>Regional Lymph Nodes (N)</strong></td>
</tr>
<tr>
<td>NX</td>
</tr>
<tr>
<td>N0</td>
</tr>
<tr>
<td>N1</td>
</tr>
<tr>
<td>N2</td>
</tr>
<tr>
<td>Total nodes examined = ...</td>
</tr>
<tr>
<td><strong>Distant Metastasis (M)</strong></td>
</tr>
<tr>
<td>MX</td>
</tr>
<tr>
<td>M0</td>
</tr>
<tr>
<td>M1</td>
</tr>
<tr>
<td>Biopsy of metastatic site performed..... □ Y ...... □ N</td>
</tr>
<tr>
<td>Source of pathologic metastatic specimen</td>
</tr>
</tbody>
</table>
**Regional Lymph Nodes (N)**

<table>
<thead>
<tr>
<th>N</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed[^4]</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in 1 to 3 regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in 4 or more regional lymph nodes</td>
</tr>
</tbody>
</table>

Total nodes examined = ________

[^4]: This appears in the staging check list at the end of the chapter, but there is no explanation in the text for why it is included. The number of total nodes must be important!
However, it was not important for long, because this was dropped from the 7th edition, only 8 years later.

<table>
<thead>
<tr>
<th>Regional Lymph Nodes (N)</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed(^4)</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in 1 to 3 regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in 4 or more regional lymph nodes</td>
</tr>
</tbody>
</table>

Total nodes examined = ________
The 7th edition went ballistic!

N1 was split into 3 parts
N2 was split into 2 parts
REGIONAL LYMPH NODES (N) 7th Edition

N1 1 to 3 positive nodes
   N1a 1 positive node
   N1b 2-3 positive nodes
   N1c Tumor deposit(s) in the subserosa, mesentery, or non-peritonealized pericolic or perirectal tissues without regional nodal metastasis

N2 4 or more positive nodes
   N2a 4 to 6 positive nodes
   N2b 7 or more positive nodes
How many nodes are enough?

The first to deal with this was the 5th edition: “it is desirable to obtain at least 12 lymph nodes ….”
How many nodes are enough?

The 6th edition “it is important to obtain at least 7-14 lymph nodes…”
How many nodes are enough?

The 7th edition: “it is important to obtain at least 10-14 lymph nodes ....”
at least 12 lymph nodes

at least 7-14 lymph nodes

at least 10-14 lymph nodes
Are they serious?
at least 7-14 nodes!
Is it 7? Or is it 14?

at least 10-14 nodes!
Is it 10? Or is it 14?
The lymph node saga

How many is enough lymph nodes?

The 12 rule

There are studies that say that tumors for which fewer than 12 nodes are found do worse than tumors for which 12 or more nodes are found.

3rd party payers are legislating 12 nodes.

The Dutch only need 10, a 16.7% difference.
Theoretically, finding more nodes should find more nodal metastases. So, there should be significant upstaging of tumors with fewer nodes found initially that have more nodes found on re-evaluation. If more nodes are found over time, there should be a trend toward upstaging.
Using SEER data, 1995-2005: The number of lymph nodes hospitals examine …is not associated with staging, use of adjuvant chemotherapy, or patient survival. Efforts by payers and professional organizations to increase node examination rates may have limited value as a public health intervention.

Using SEER data from 1988-2008

“The number of lymph nodes evaluated for colon CA has markedly increased in the past 2 decades, but was not associated with an overall shift toward higher-staged cancers, questioning the upstaging mechanism as the primary basis for improved survival in patients with more lymph nodes evaluated.”

Parsons, et al, JAMA, 2011;306:1089-1097
These two important epidemiologic studies appeared in the JAMA.

Do cancer people ever read the JAMA?

Maybe that is why they pay no attention to the results.
Other studies dispute this and hold on to 12 or some other number.
In the 7th edition, the AJCC says 10-14 nodes, and "when fewer than the number of nodes recommended by the CAP have been found, it is important that the pathologist report the degree of diligence of their efforts to find lymph nodes...."
In the 7th edition, the AJCC says 10-14 nodes, and "when fewer than the number of nodes recommended by the CAP have been found, it is important that the pathologist report the degree of diligence of their efforts to find lymph nodes..."

CAP: Where in the hell did those guys come from? They are everywhere!
In the 7th edition, the AJCC says 10-14 nodes, and “when fewer than the number of nodes recommended by the CAP have been found, it is important that the pathologist report the degree of diligence of their efforts to find lymph nodes....”
In the 7th edition, the AJCC says 10-14 nodes, and "when fewer than the number of nodes recommended by the CAP have been found, it is important that the pathologist report the degree of diligence of their efforts to find lymph nodes..." This is an insulting demand!
Example

**Diagnosis:** Sigmoid colon: Transmurally invasive adenocarcinoma. Metastases in one of 7 nodes.

**Comment:** I looked through the sigmoid mesocolon 3 times, trying to find 5 more nodes, but there were none. I even sent through 7 blocks of the mesocolon hoping for some tiny nodes, but there were none. I truly apologize for my inadequacies, and I promise to do better in the future.
I have a better suggestion:

“when fewer than the number of nodes recommended by the CAP have been removed, it is important that the surgeon report the degree of diligence of her/his efforts to remove enough lymph nodes....”
TNM Staging a colorectal cancer: have to count + nodes

200 nodes recovered

T3
N2a
M not used

Depth: T3 invades through muscularis

4+ Nodes N2a
<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>5-Yr Surv</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>T1-2</td>
<td>N0</td>
<td>M0</td>
<td>74-79%</td>
</tr>
<tr>
<td>IIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>67%</td>
</tr>
<tr>
<td>IIIB</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
<td>61%</td>
</tr>
<tr>
<td>IIC</td>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
<td>46%</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1-2</td>
<td>N1/N1c</td>
<td>M0</td>
<td>67-74%</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2a</td>
<td>M0</td>
<td>65%</td>
</tr>
<tr>
<td>IIIB</td>
<td>T3-4a</td>
<td>N1/N1c</td>
<td>M0</td>
<td>52-58%</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N2a</td>
<td>M0</td>
<td>43%</td>
</tr>
<tr>
<td>IIC</td>
<td>T4a</td>
<td>N2a</td>
<td>M0</td>
<td>33%</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>N2b</td>
<td>M0</td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>N1</td>
<td>M0</td>
<td>30%</td>
</tr>
<tr>
<td>IVA</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
<td>~6%</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1b</td>
<td>~5%</td>
</tr>
</tbody>
</table>
What about M: Distant Metastasis?

1st through 6th editions:
- **MX**: cannot be assessed
- **M0**: No distant metastasis
- **M1**: Distant metastasis
M in the 7th edition: Major changes

MX omitted

M0 No distant metastasis

\textit{no pathologic M0}; use \textit{clinical M}

to complete stage group

M1 Distant metastasis split

M1a Metastasis confined to one organ or site

M1b Metastases in more than one organ/site or the \textit{peritoneum}