

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:**

PLEASE DO NOT R...

MAN
S
OF C

Ame

AICC
Canc



American J

ajcc
Canc
Mar
Sixth Edi

Springer

J. B. Lippincott Company

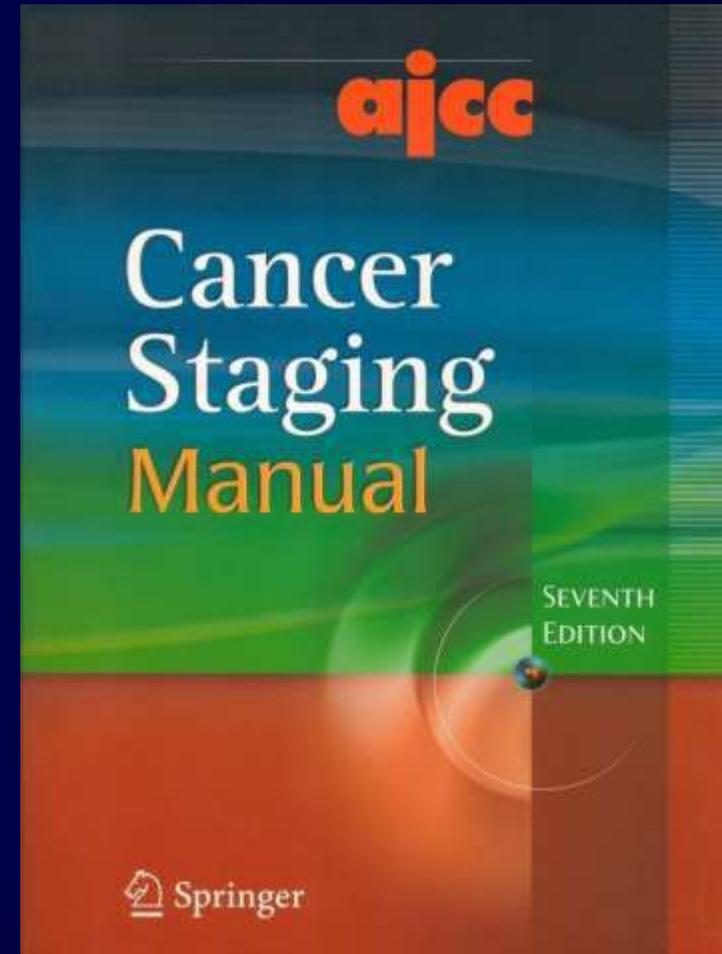
ajcc

Cancer
Staging
Manual

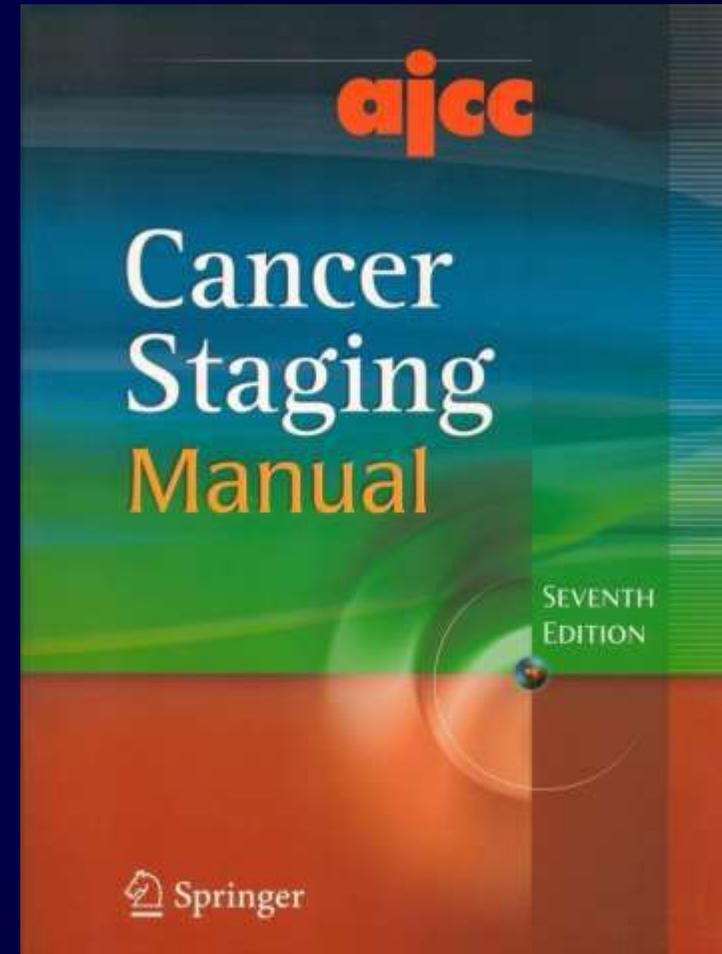
SEVENTH
EDITION

Springer

**My only conflict
of interest is that
I was on the site
task force for the
esophageal chapter**

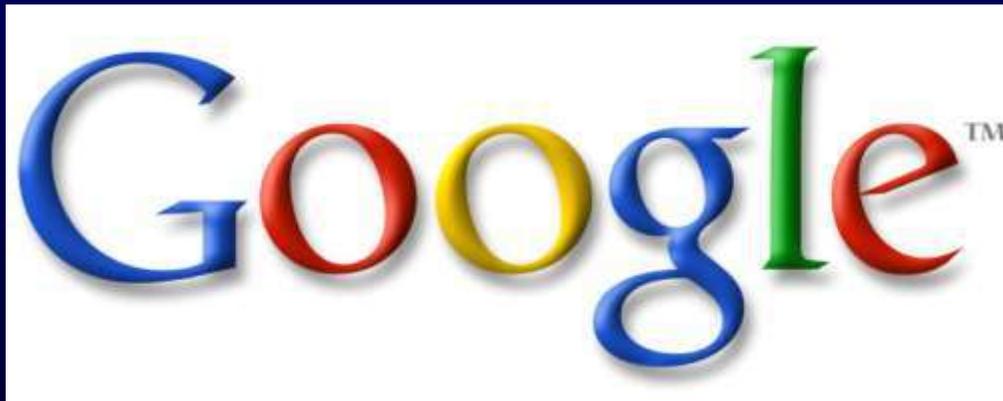


**With a bunch of
surgeons and
oncologists who
ignored me
completely.....**



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 equipment companies, other 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.

**Mod Pathol,
Supplement 1,
2015;28:S95-S108**

MODERN PATHOLOGY (2015) 28, S95–S108

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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.**

Histopathology 2015, 66, 102–111. DOI: 10.1111/his.12563

**Histopathol,
2015;66:102-111**

REVIEW

Current concepts of colorectal cancer resection pathology

Iris D Nagtegaal

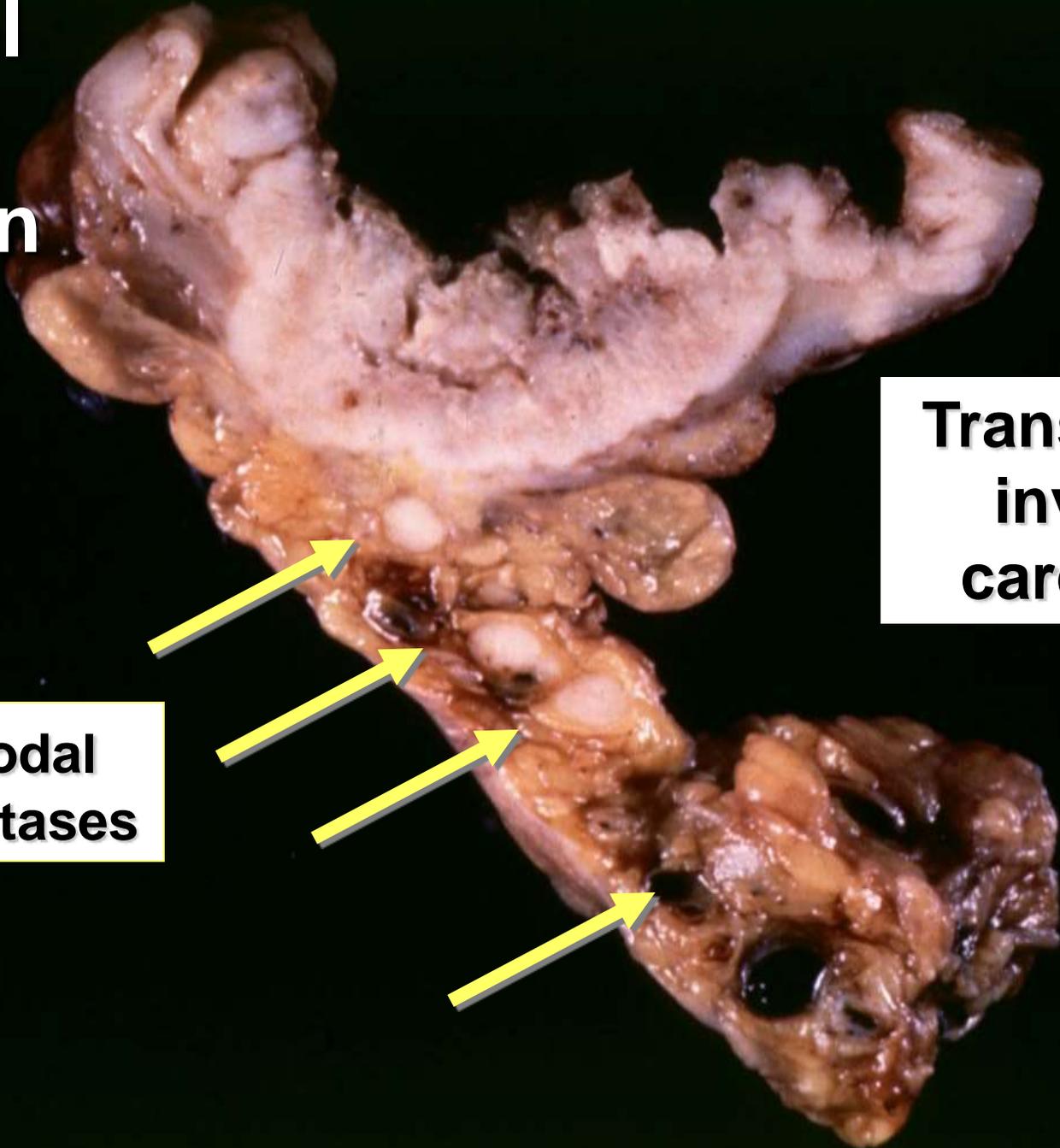
Department of Pathology, Radboud University Medical Centre, Nijmegen, The Netherlands

**Another erudite, informative
paper, far more insightful and
sophisticated than this lecture.**

Staging colorectal carcinomas:

Historical perspective

**The model
for this
discussion**



**Transmurally
invasive
carcinoma**

**4 Nodal
metastases**

The first staging system for this carcinoma??

616.351—006.46

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**

Cuthbert Esquire Dukes



CUTHBERT ESQUIRE DUKES O.B.E.
M.D., F.R.C.S., F.R.C.PATH., D.P.M.
Pioneer of the staging of cancer
Pathologist to St. Marks Hospital 1922-1956
Funded by
FRANCIS ROSE
President of the Medical Art Society
1971

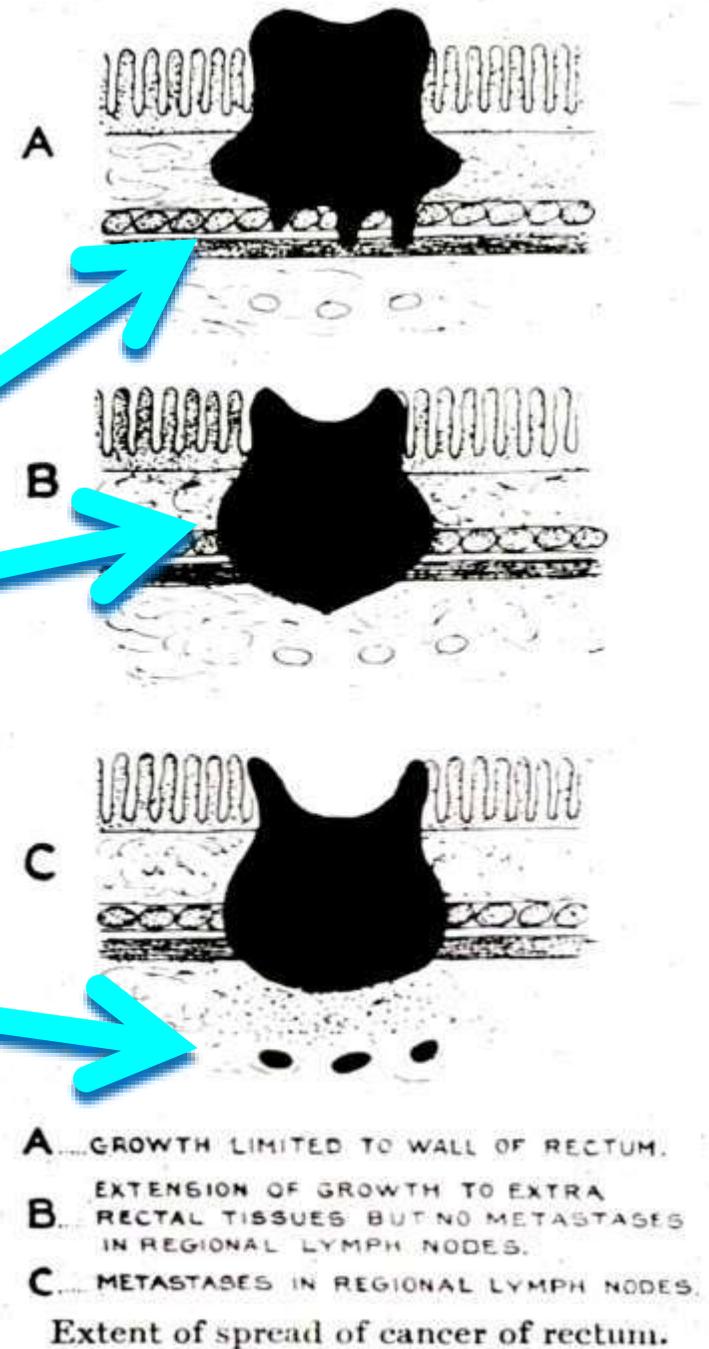
St. Mark's Hospital,
City Road.



Dukes' staging system was only for the rectum.

Had 2 components:

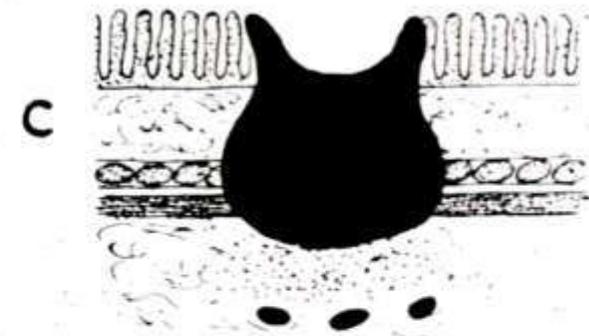
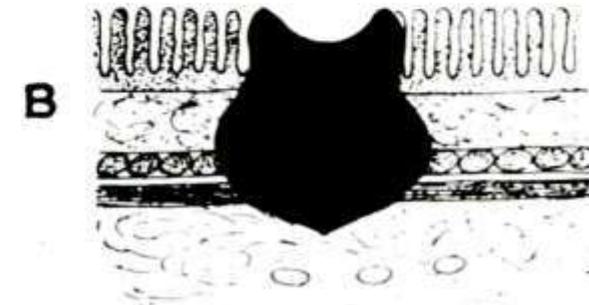
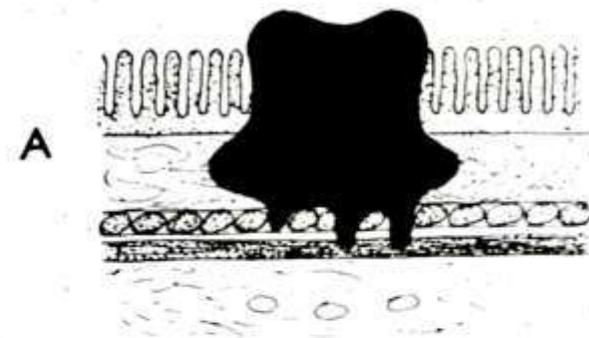
1. The extent of the primary tumor when there were no nodal metastases
2. Nodal metastases.



The A stage had no subsets based on depth

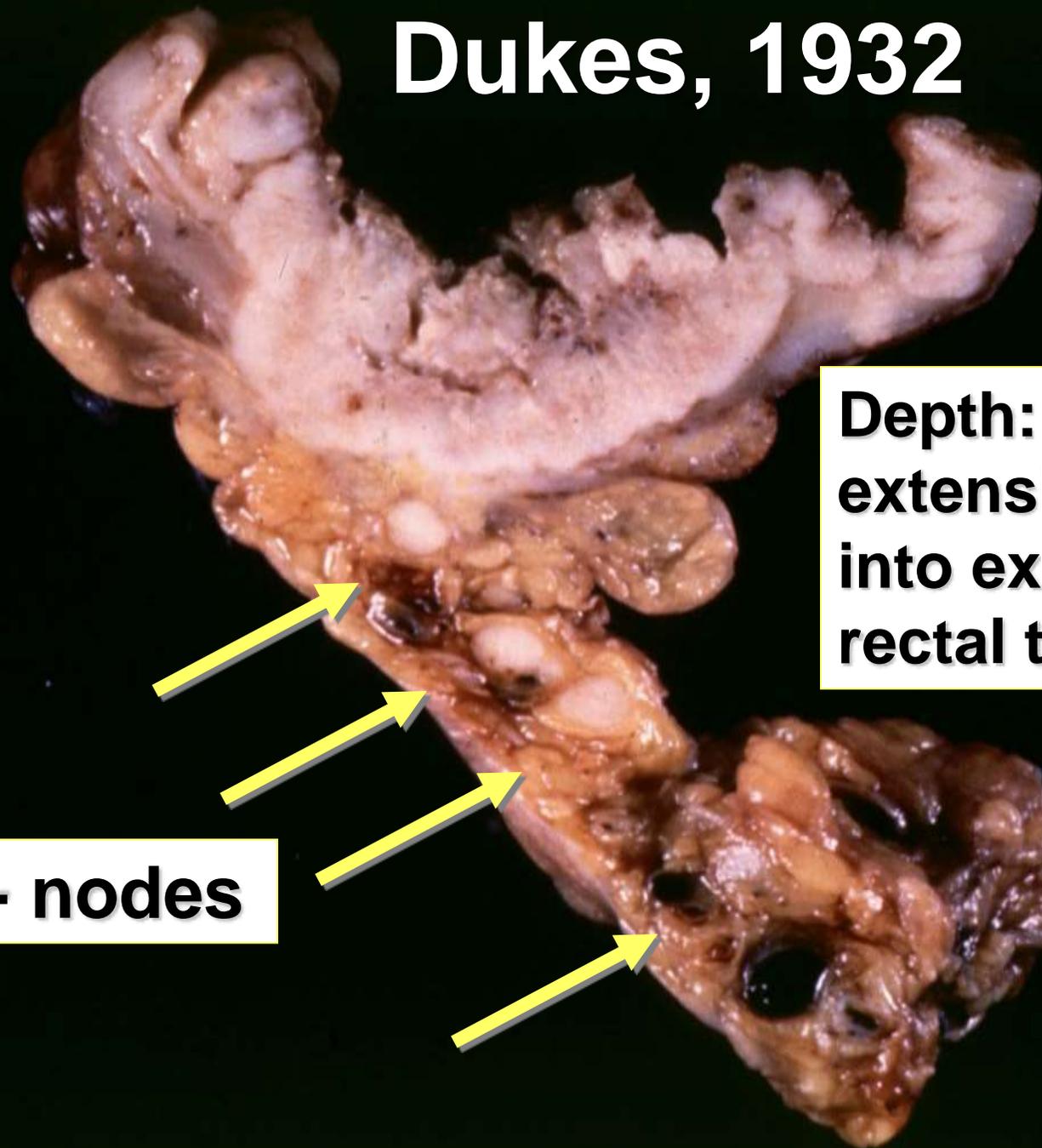
The C stage was nodal metastases regardless of depth of invasion.

Distant metastases were not included, nor would they be for 45 years.



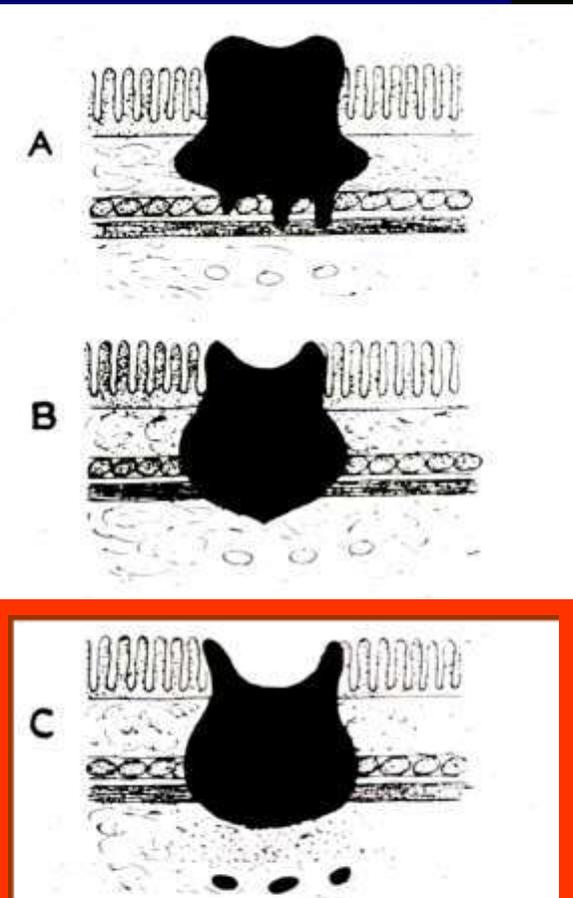
- A...GROWTH LIMITED TO WALL OF RECTUM.
B...EXTENSION OF GROWTH TO EXTRA-RECTAL TISSUES BUT NO METASTASES IN REGIONAL LYMPH NODES.
C...METASTASES IN REGIONAL LYMPH NODES.
- Extent of spread of cancer of rectum.

Dukes, 1932

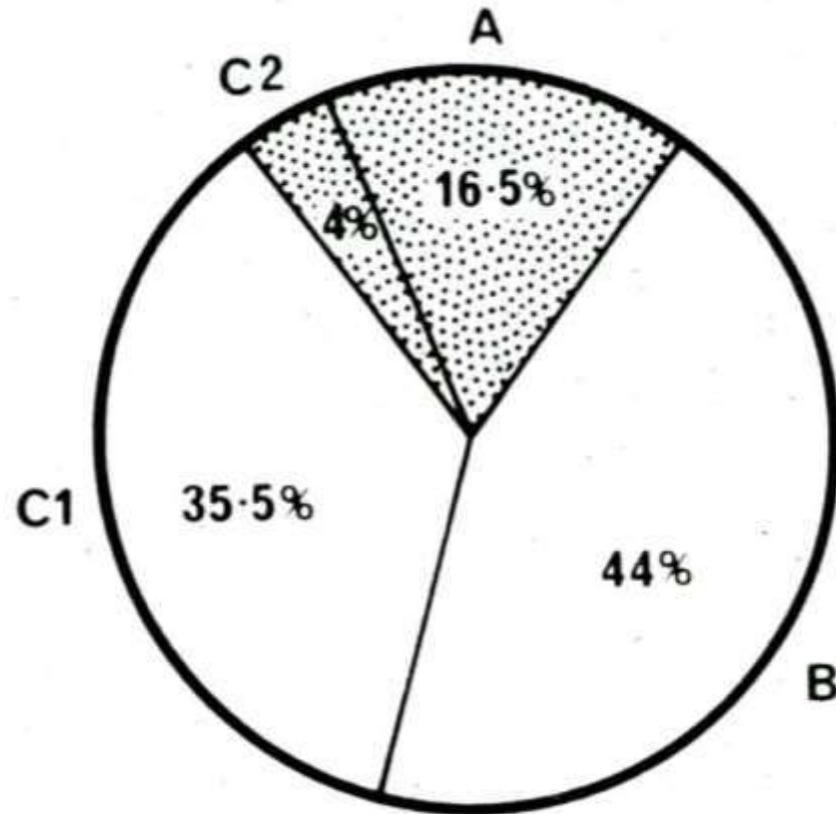
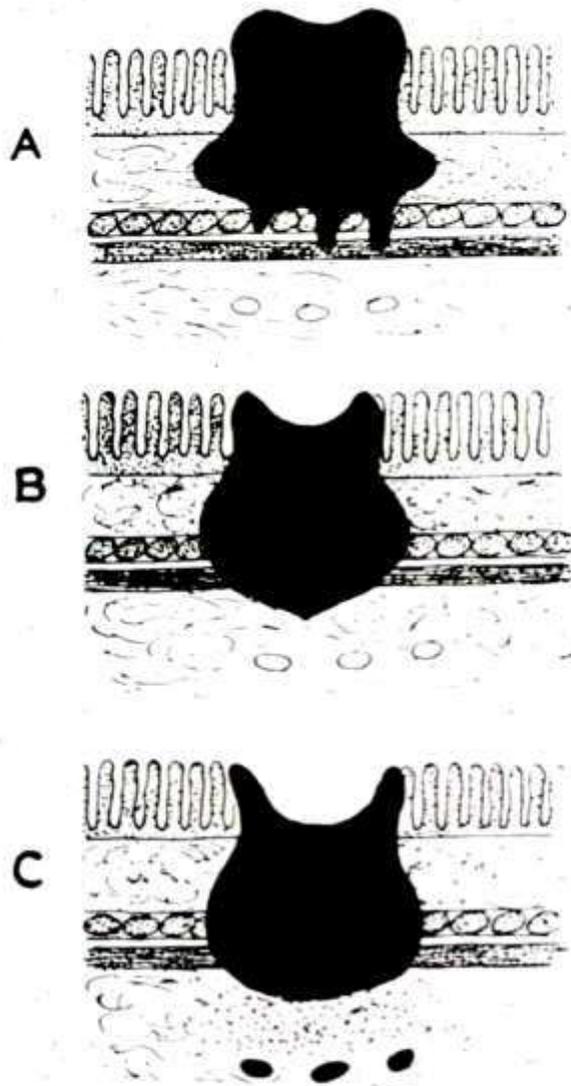


**Depth:
extension
into extra
rectal tissues**

+ nodes



A ...GROWTH LIMITED TO WALL OF RECTUM.
B EXTENSION OF GROWTH TO EXTRA-RECTAL TISSUES BUT NO METASTASES IN REGIONAL LYMPH NODES.
C METASTASES IN REGIONAL LYMPH NODES.
Extent of spread of cancer of rectum.



5 year survival with
Dukes' classification

A - 97%

B - 81%

C1 - 51%

Dukes stages and survival were related

Mayo Clinic modification, 1949

Kirklin JW, Dockerty MB, Waugh JW: The role of the peritoneal reflection in the prognosis of carcinoma of the rectum and sigmoid colon. Surg Gynec & Obst, 88:326, 1949

The site now included the sigmoid colon

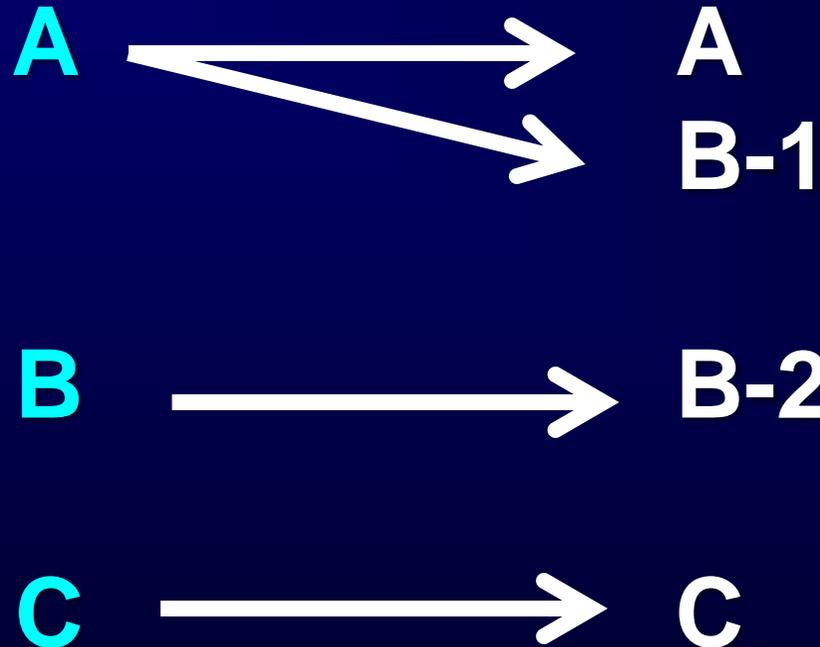
- A Limited to mucosa
- B1 extending into muscularis propria
- B2 penetrating muscularis propria
- C B1 or B2 with nodal metastasis

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

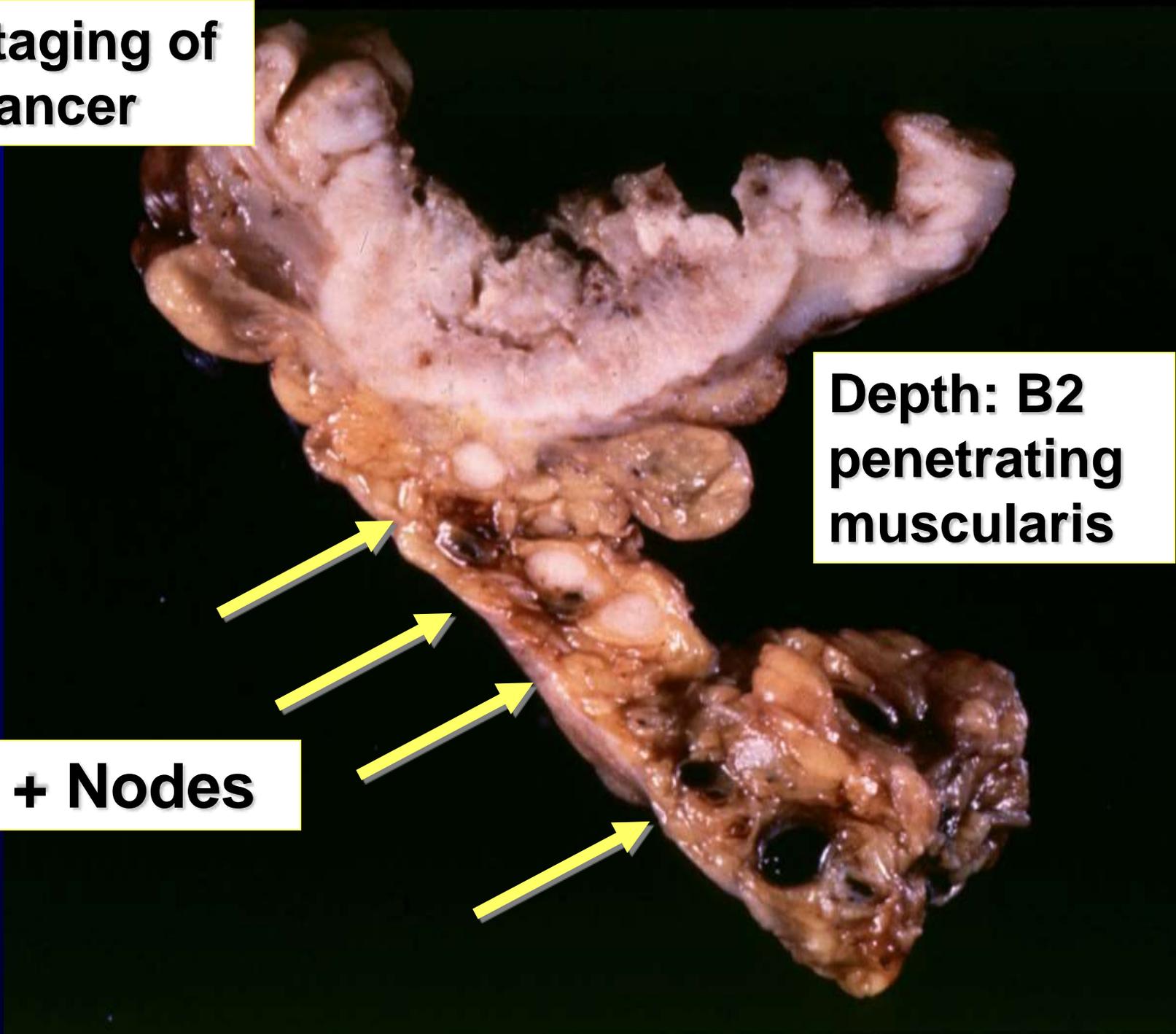


Kirklin et al Staging of a colorectal cancer

C

+ Nodes

**Depth: B2
penetrating
muscularis**



top 1/2
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Vol. 139

JUNE, 1954

No. 6

Copyright, 1954, by J. B. Lippincott Company.

THE PROGNOSTIC SIGNIFICANCE OF
DIRECT EXTENSION OF CARCINOMA OF THE COLON AND RECTUM*

VERNON B. ASTLER, M.D. AND FREDERICK A. COLLER, M.D.

ANN ARBOR, MICHIGAN

FROM THE DEPARTMENTS OF SURGERY AND PATHOLOGY, MEDICAL SCHOOL, UNIVERSITY OF MICHIGAN

THE PROGNOSIS OF a patient with cancer of the large bowel is dependent upon the cancer cells has been less emphasized, but the important influence of direct extension

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

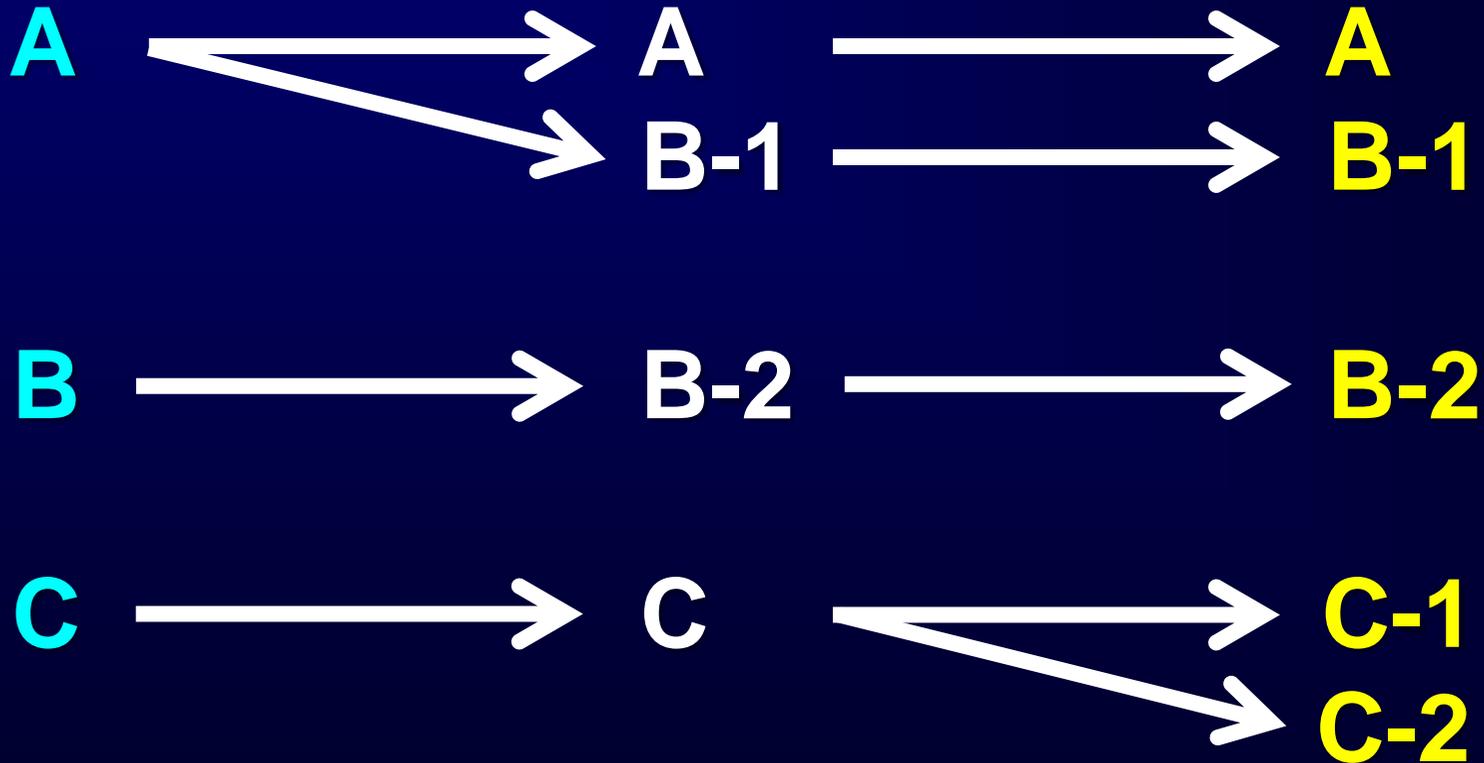
the A stage is still an adenoma

Astler-Coller modified Kirklin et al which modified Dukes

Dukes
rectum

Kirklin et al
sig-rectum

Astler-Coller
colorectum

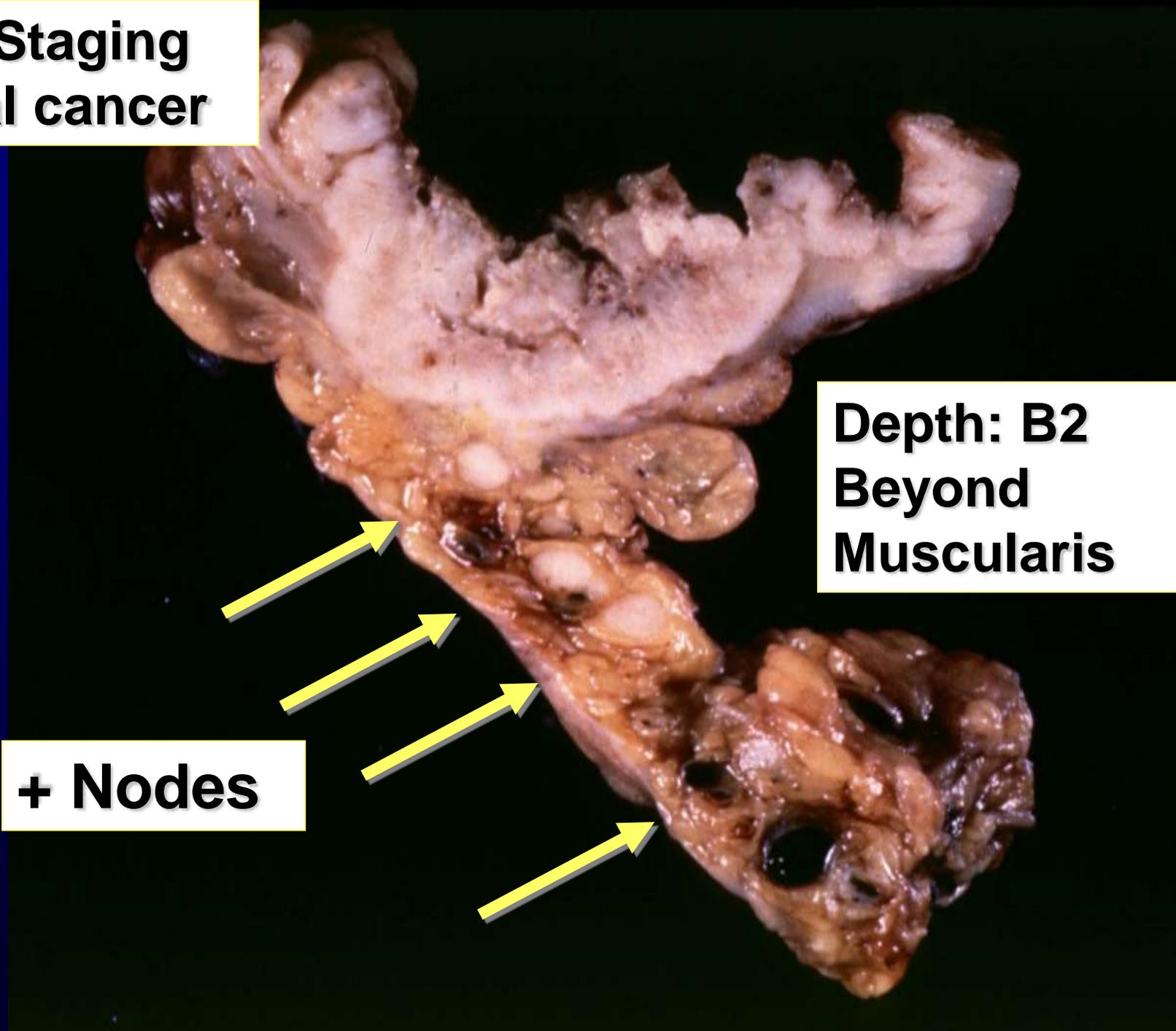


Astler-Coller Staging of a colorectal cancer

C2

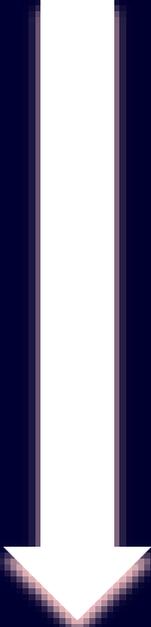
+ Nodes

**Depth: B2
Beyond
Muscularis**



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

| <u>Stage</u> | <u>#cases</u> | <u>5-yr surv</u> |
|---------------------|----------------------|-------------------------|
| A | 1 | 100% |
| B-1 | 48 | 67% |
| B-2 | 164 | 47% |
| C-1 | 14 | 43% |
| C-2 | 125 | 22% |



Finally, the TNM staging system was introduced to the general public, including the pathologist public

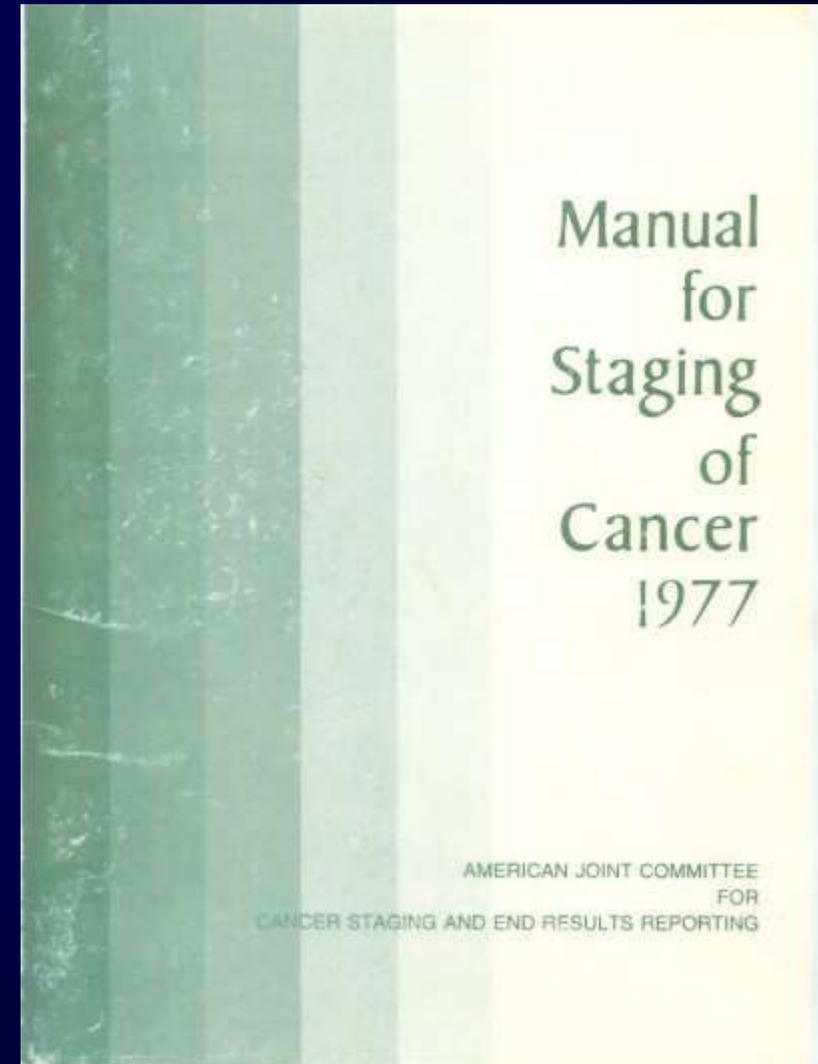
A TNM system was originally proposed in the 1950s for the clinical staging of malignant tumors in general by the International Union Against Cancer (UICC).

Wood, et al. Staging of cancer of the colon and cancer of the rectum. *Cancer*. 1979;43:961-968

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.

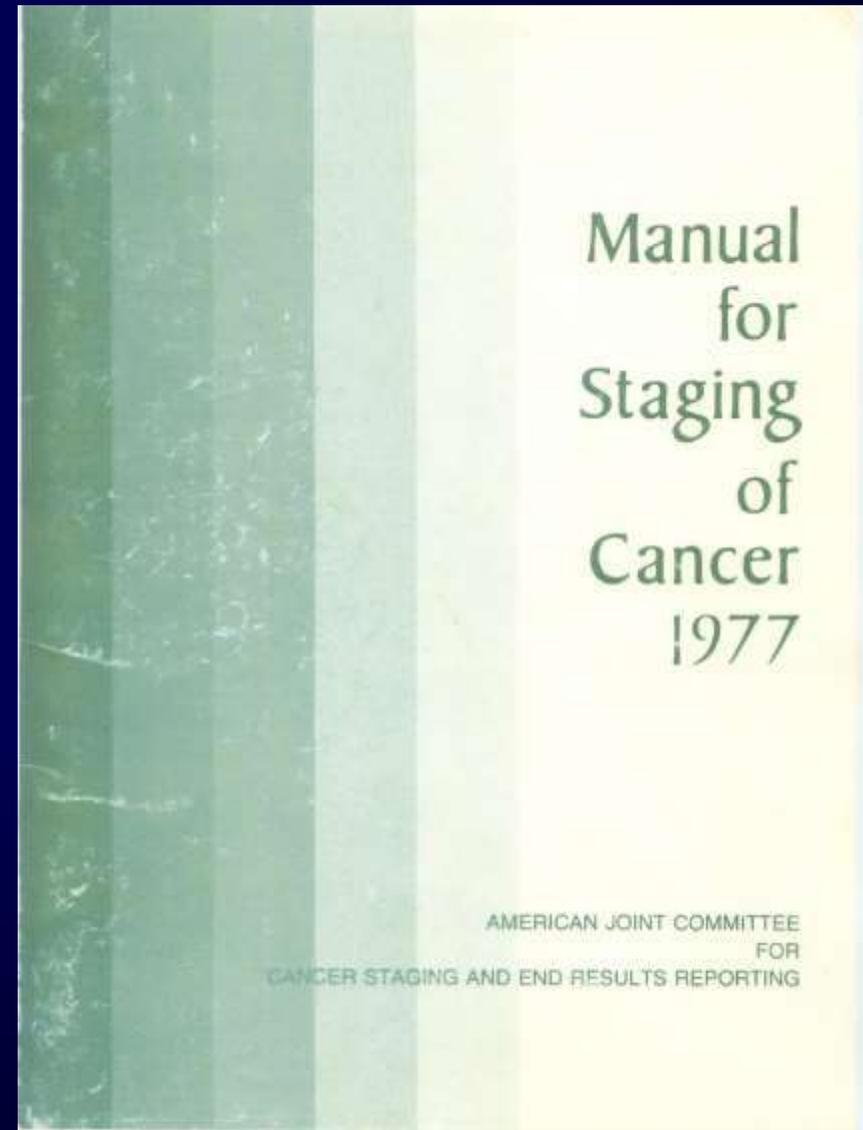
Wood, et al. Staging of cancer of the colon and cancer of the rectum. Cancer. 1979;43:961-968

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



Wood, et al. Staging of cancer of the colon and cancer of the rectum. Cancer. 1979;43:961-968

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



Wood, et al. Staging of cancer of the colon and cancer of the rectum. Cancer. 1979;43:961-968

The AJCC 1st Ed Colorectal TNM

Primary Tumor (T)

- Tis** Carcinoma in situ (no penetration of lamina propria)
- T1** Clinically benign lesion or lesion confined to the mucosa or submucosa
- T2** Involvement of muscular wall or serosa, no extension beyond

The AJCC 1st Ed Colorectal TNM

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 1st 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)

The AJCC 1st Ed Colorectal TNM

Nodal Involvement (N)

NX Nodes not assessed or
involvement not recorded

N0 Nodes not believed to be
involved ← **Faith? Religion?**

N1 Regional nodes involved
(distal to inferior mesenteric
artery)

The AJCC 1st Ed Colorectal TNM

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Separation of church and staging?

The AJCC 1st Ed Colorectal TNM

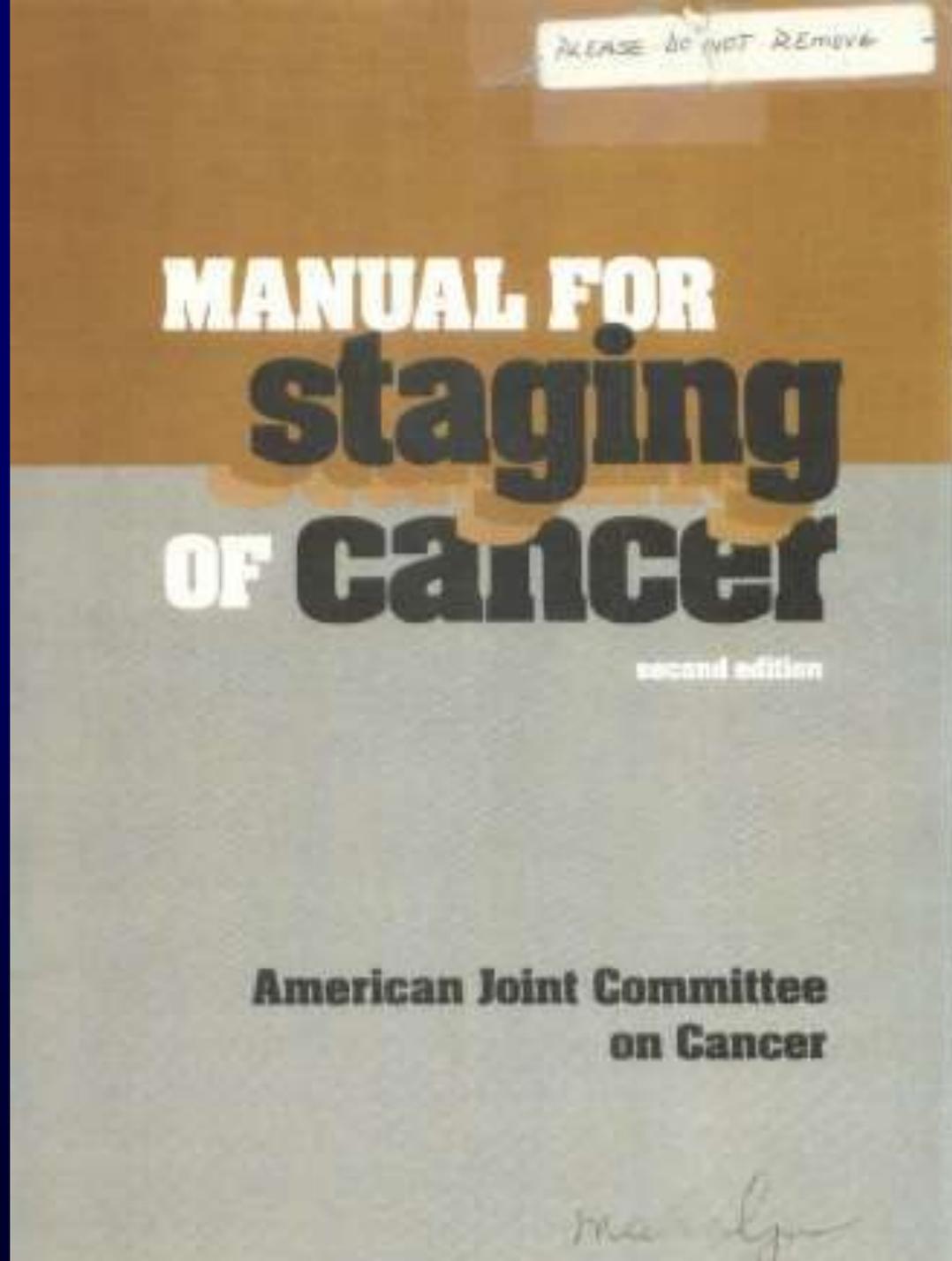
Distant Metastasis (M)

MX Not assessed

M0 No (known) distant
metastasis

M1 Distant metastases
present

**The 2nd
Edition was
published
in 1983**



Papers Read Before the 39th Annual Meeting of the
Society of Surgical Oncology, London,
April 27 to April 30, 1987—Part I

1987
Why?

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/TNM Committee (UICC/TNMC) is designed primarily for patient care and, in this context, is equally

based on 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 Point Registration) formally

The T and N changed in the 2nd (1983) and 3rd (1988) editions with no change in M.

By the 3rd edition,

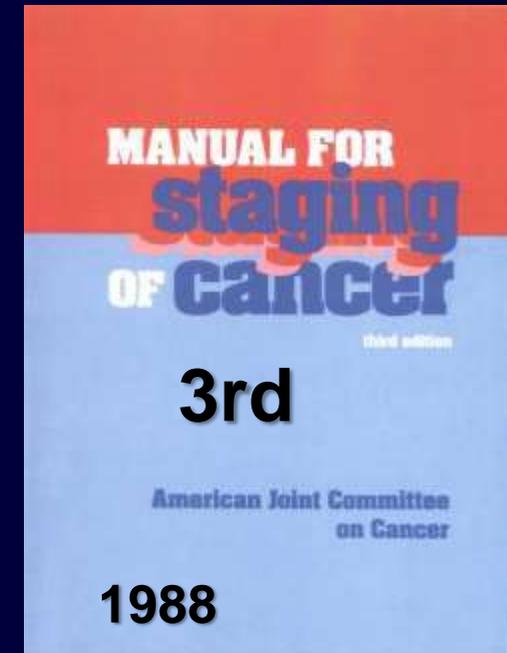
Fistulas were not mentioned for T
T3 was limited to pericolic adipose
T4 was extension beyond pericolic
adipose

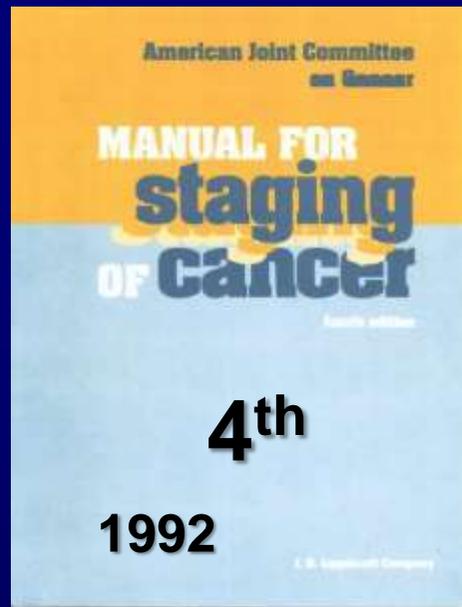
T5 disappeared

N1 was separated into N1 and N2

based on number of positive nodes

N3 was any + node along a major vessel





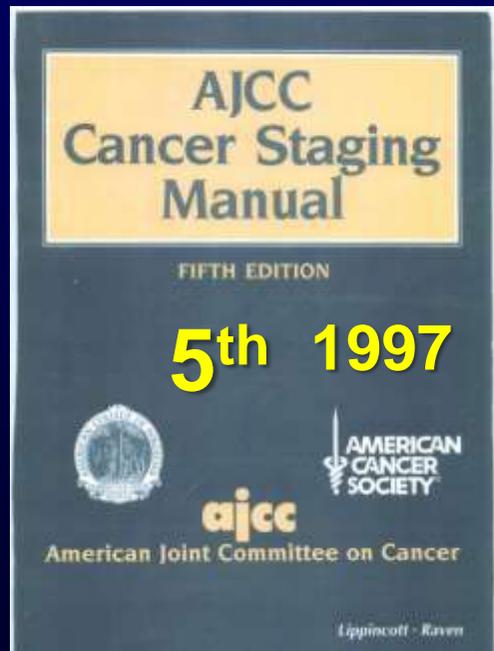
DEFINITIONS as of 4th and 5th editions

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⁽¹⁻³⁾
- 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⁽²⁻³⁾

Regional Lymph Nodes (N)

- NX Regional lymph nodes cannot be assessed⁽⁴⁾
- 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 _____

ajcc

Cancer Staging Manual

Sixth Edition

6th

Springer

2002

DEFINITIONS

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- T0 No evidence of primary tumor
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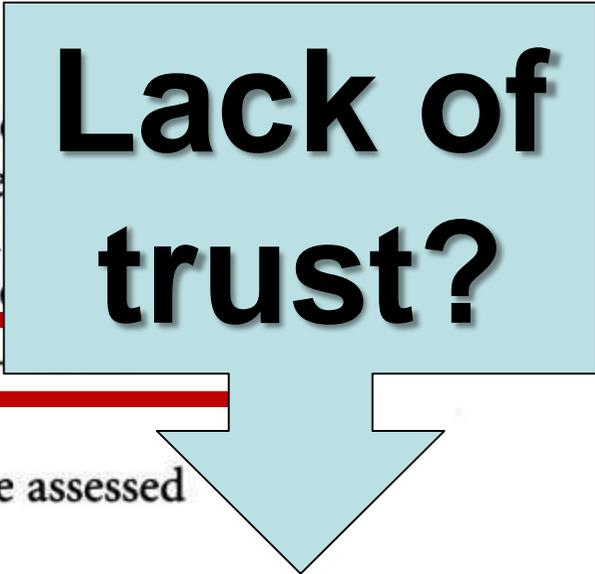
Distant Metastasis (M)

- 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 _____

Lack of trust?



ajcc

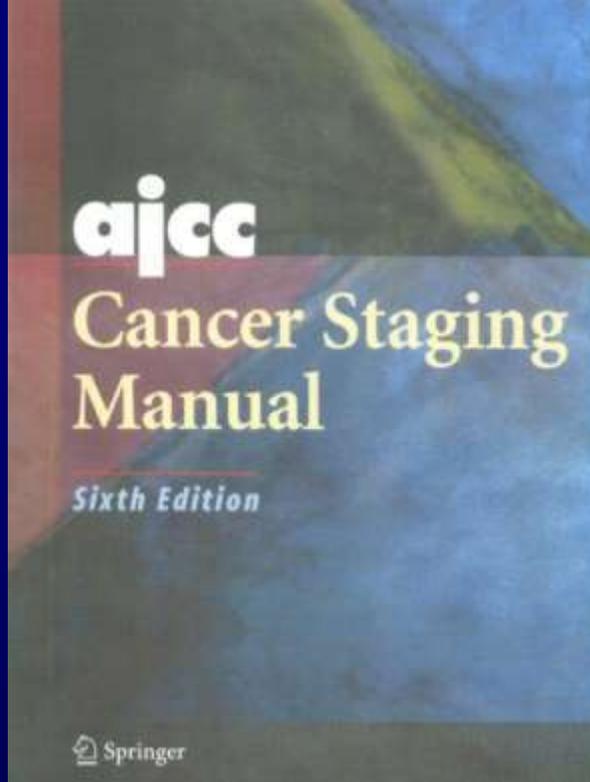
Cancer Staging
Manual

Sixth Edition

6th

Springer

2002



SUMMARY OF CHANGES

- A revised description of the anatomy of the colon and rectum better delineates the data concerning the boundaries between colon, rectum, and anal canal. Adenocarcinomas of the vermiform appendix are classified according to the TNM staging system but should be recorded separately, whereas cancers that occur in the anal canal are staged according to the classification used for the anus.
- Smooth metastatic nodules in the pericolic or perirectal fat are considered lymph node metastases and will be counted in the N staging. In contrast, irregularly contoured metastatic nodules in the peritumoral fat are considered vascular invasion and will be coded as an extension of the T category as either a V1 (microscopic vascular invasion) if only microscopically visible or a V2 (macroscopic vascular invasion) if grossly visible.
- Stage Group II is subdivided into IIA and IIB on the basis of whether the primary tumor is T3 or T4, respectively.
- Stage Group III is subdivided into IIIA (T1–2N1M0), IIIB (T3–4N1M0) or IIIC (any TN2M0).

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.**

ajcc

Cancer Staging Manual

SEVENTH
EDITION

 Springer

**The rest of my
comments, both
snide and nit-picking
deal mainly with the
7th edition**

Tis

T1

PRIMARY TUMOR (T) 7th Edition

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

T1 invasion of submucosa

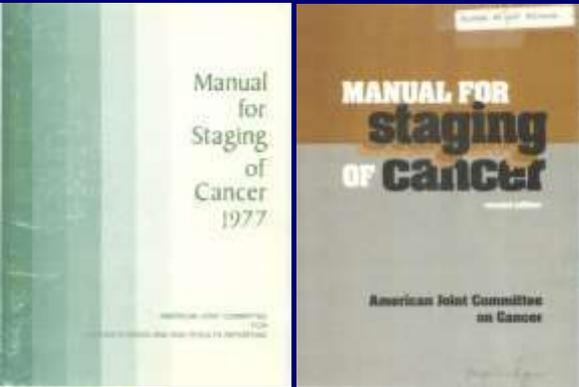
T2 invasion of muscularis propria

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

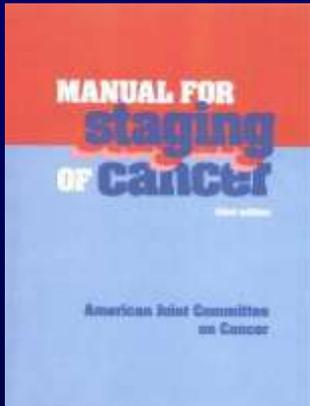
The Evolution of Tis and T1



1st and 2nd Editions:

Tis = carcinoma in situ

T1 = tumor confined to mucosa or submucosa

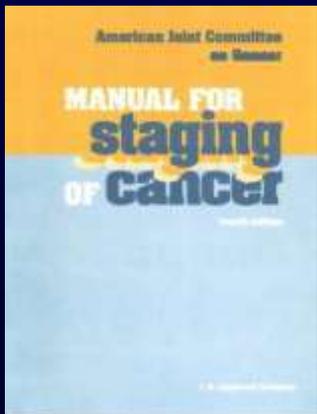


3rd Edition

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*: intraepithelial or **invasion** of lamina propria*

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**

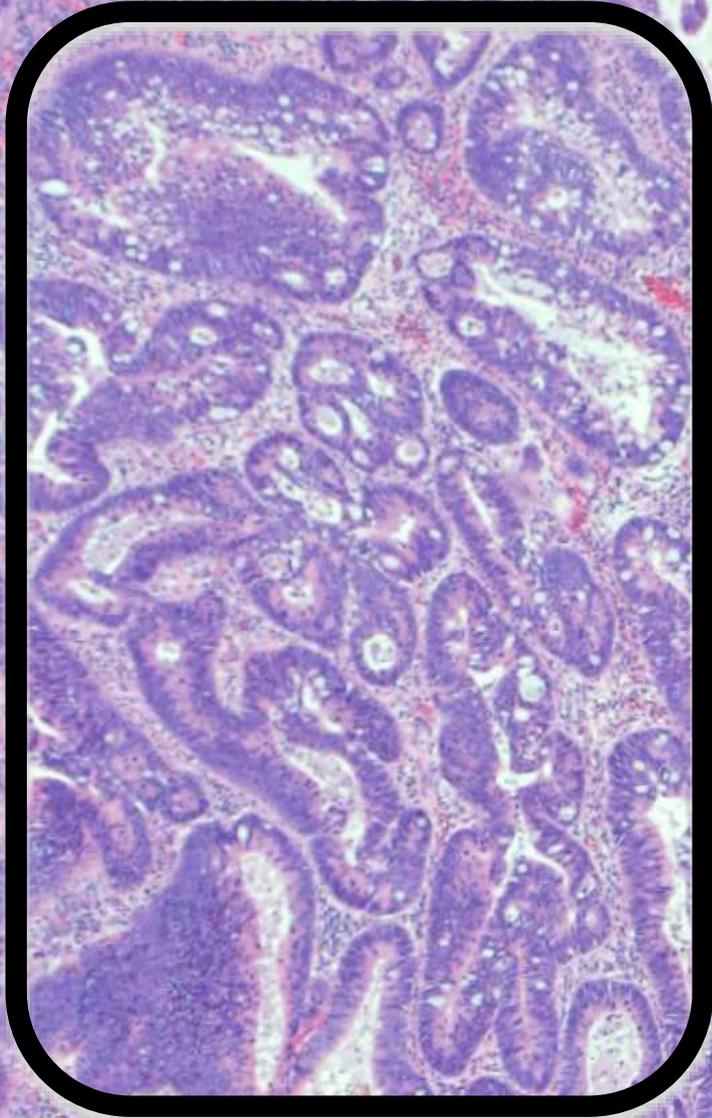
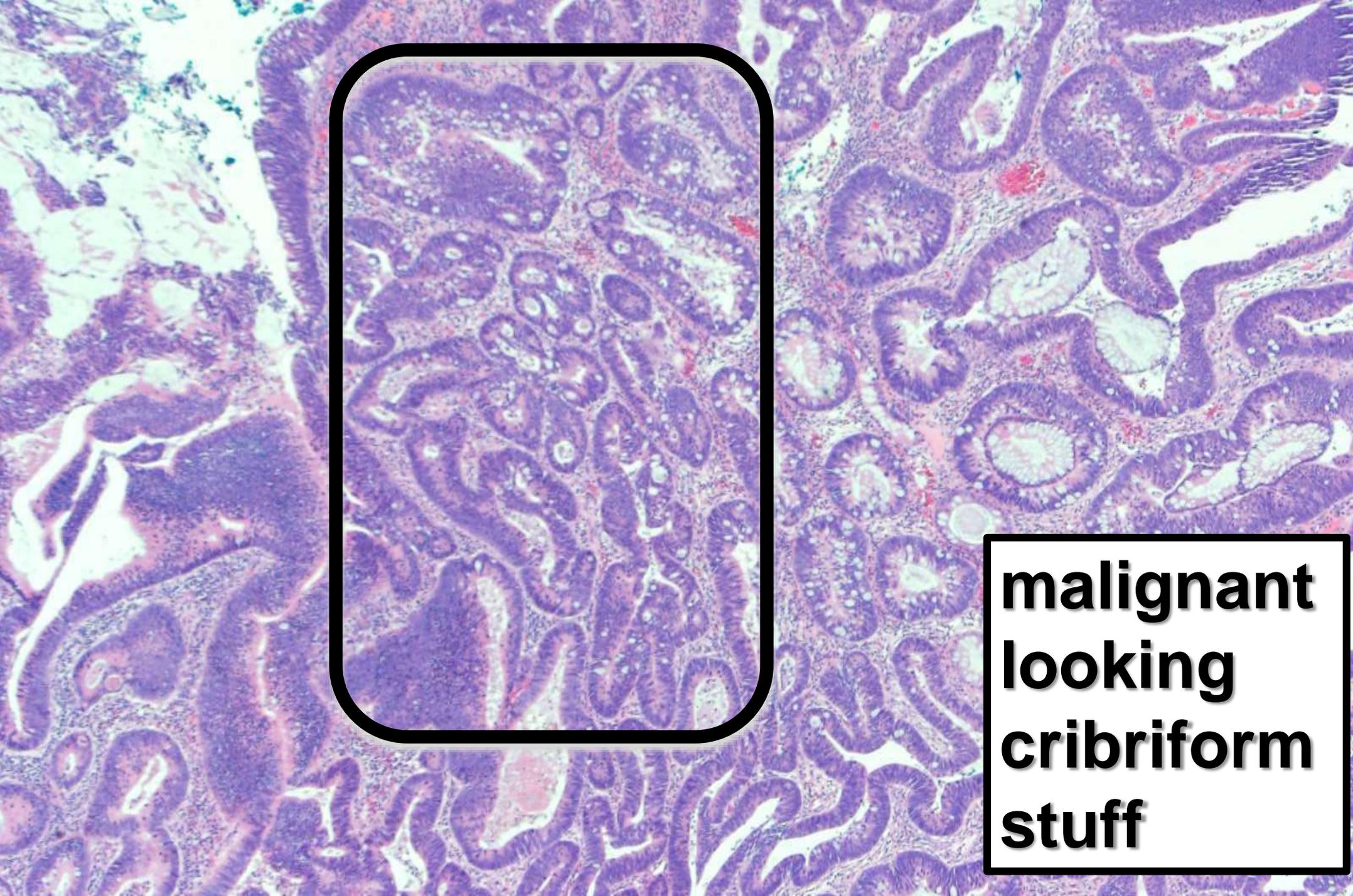
The Tis saga, courtesy of the 7th edition, AJCC Staging Manual

*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.

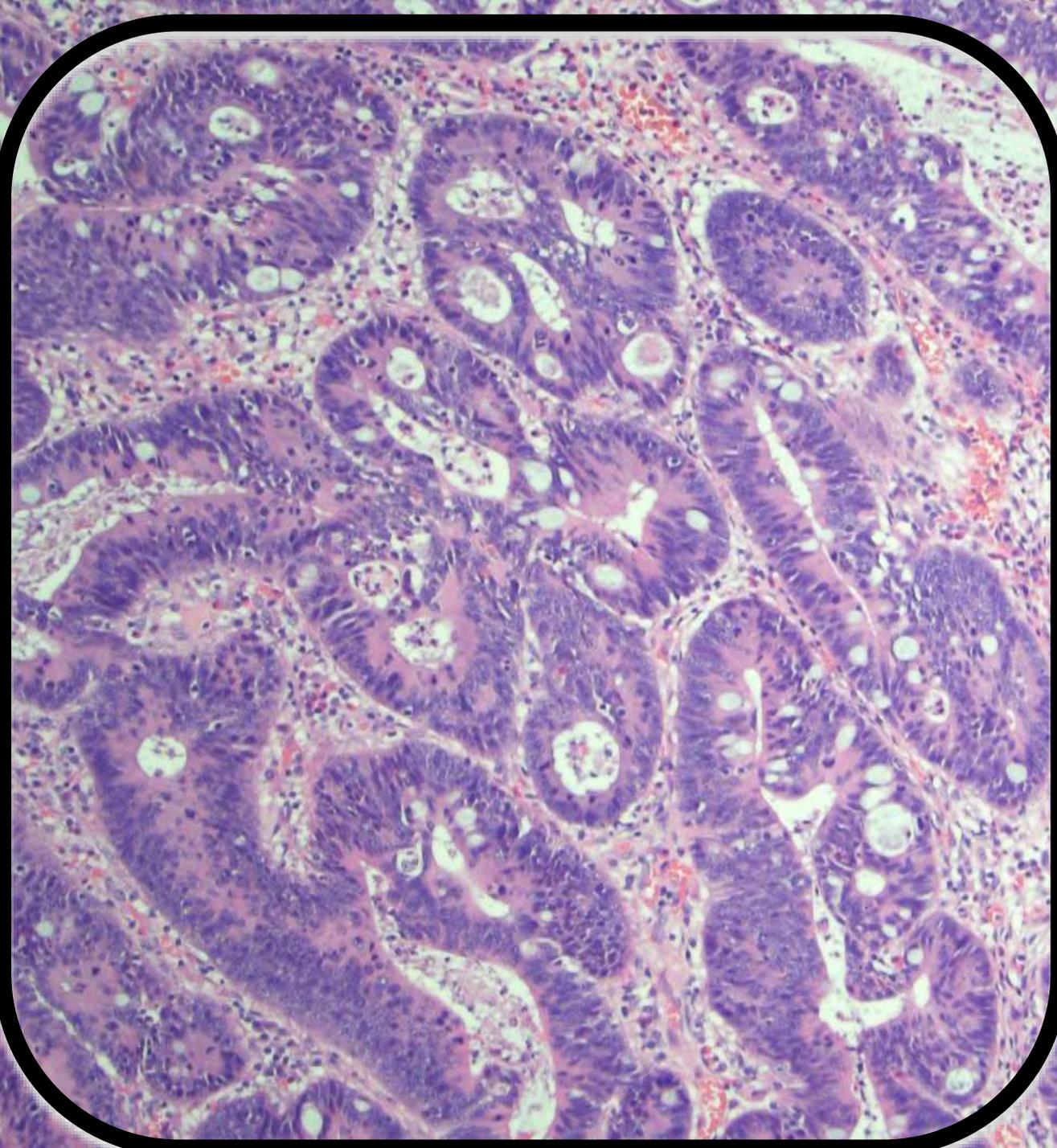
Nit-Picking stuff:

The colon has crypts, not glands!

Is there another lamina propria that differs from the one in the mucosa?



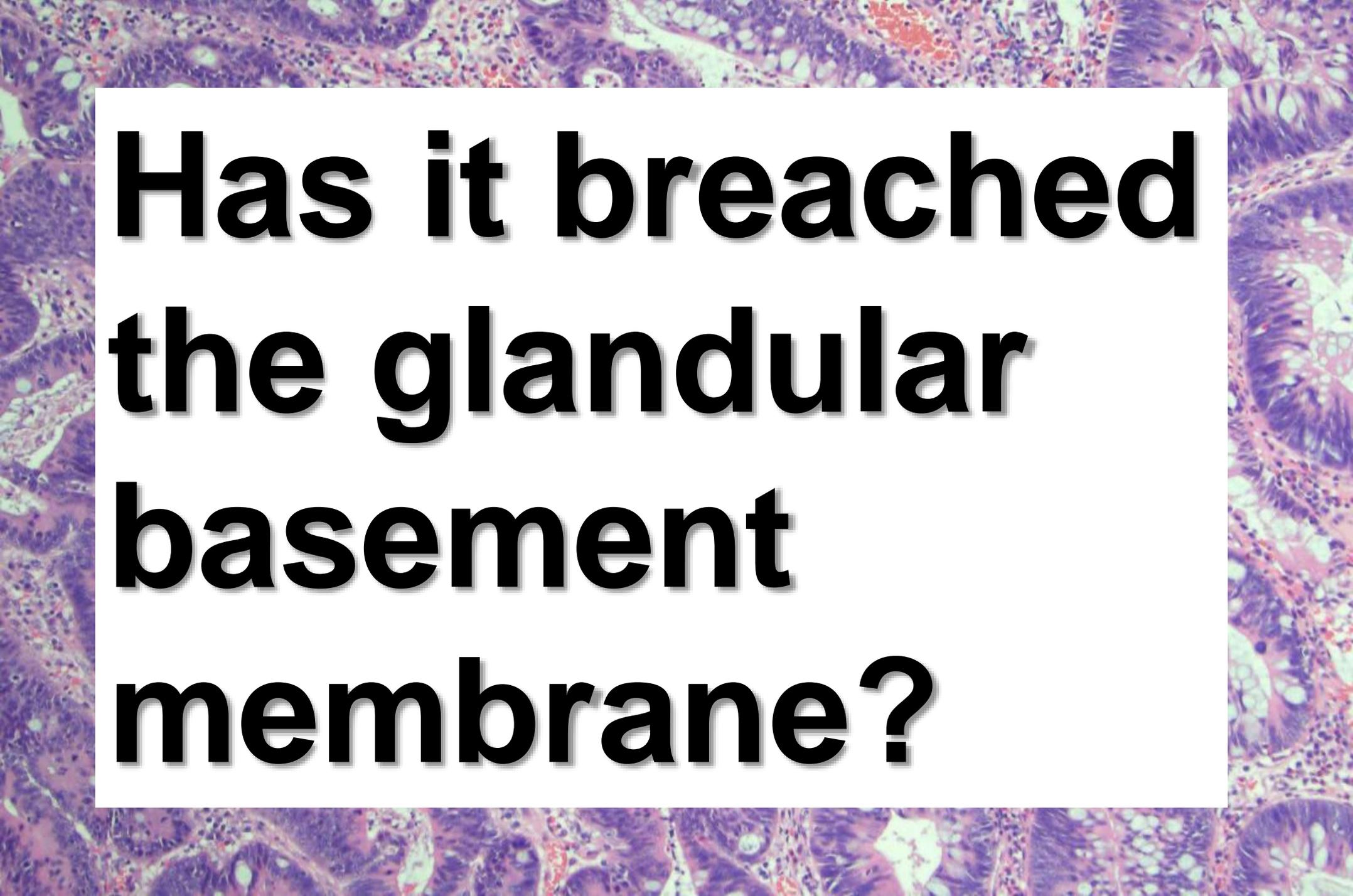
**malignant
looking
cribriform
stuff**



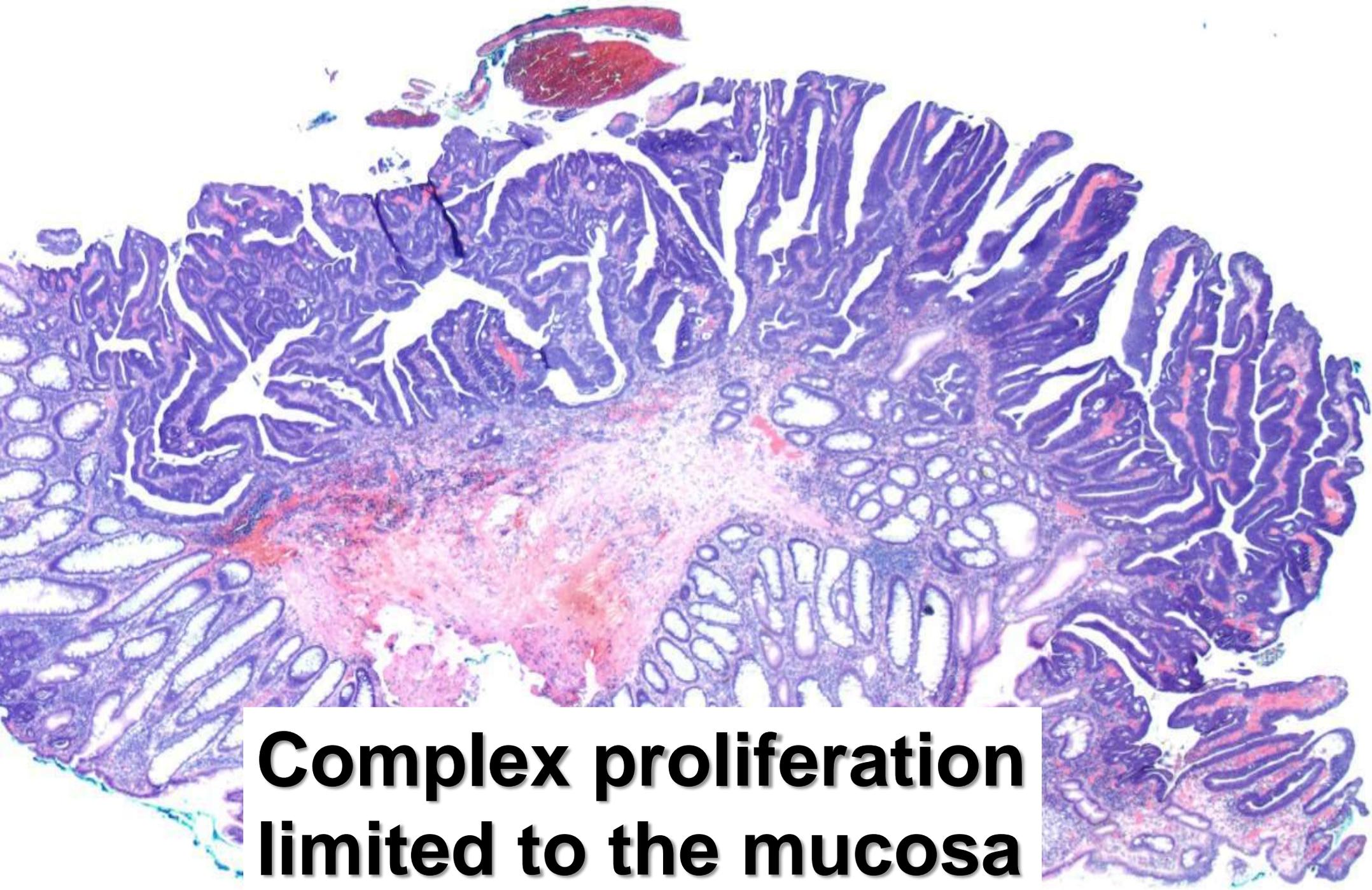
Looks even worse at high power

A histological section of the prostate gland, stained with hematoxylin and eosin (H&E). The image shows numerous glandular units of varying sizes, some with prominent nucleoli and hyperchromatic nuclei, suggesting a neoplastic process. The glands are separated by thin layers of stroma. The overall architecture is disorganized, with some glands appearing crowded and fused, which is characteristic of prostatic adenocarcinoma.

**Should we
call this a Tis?**

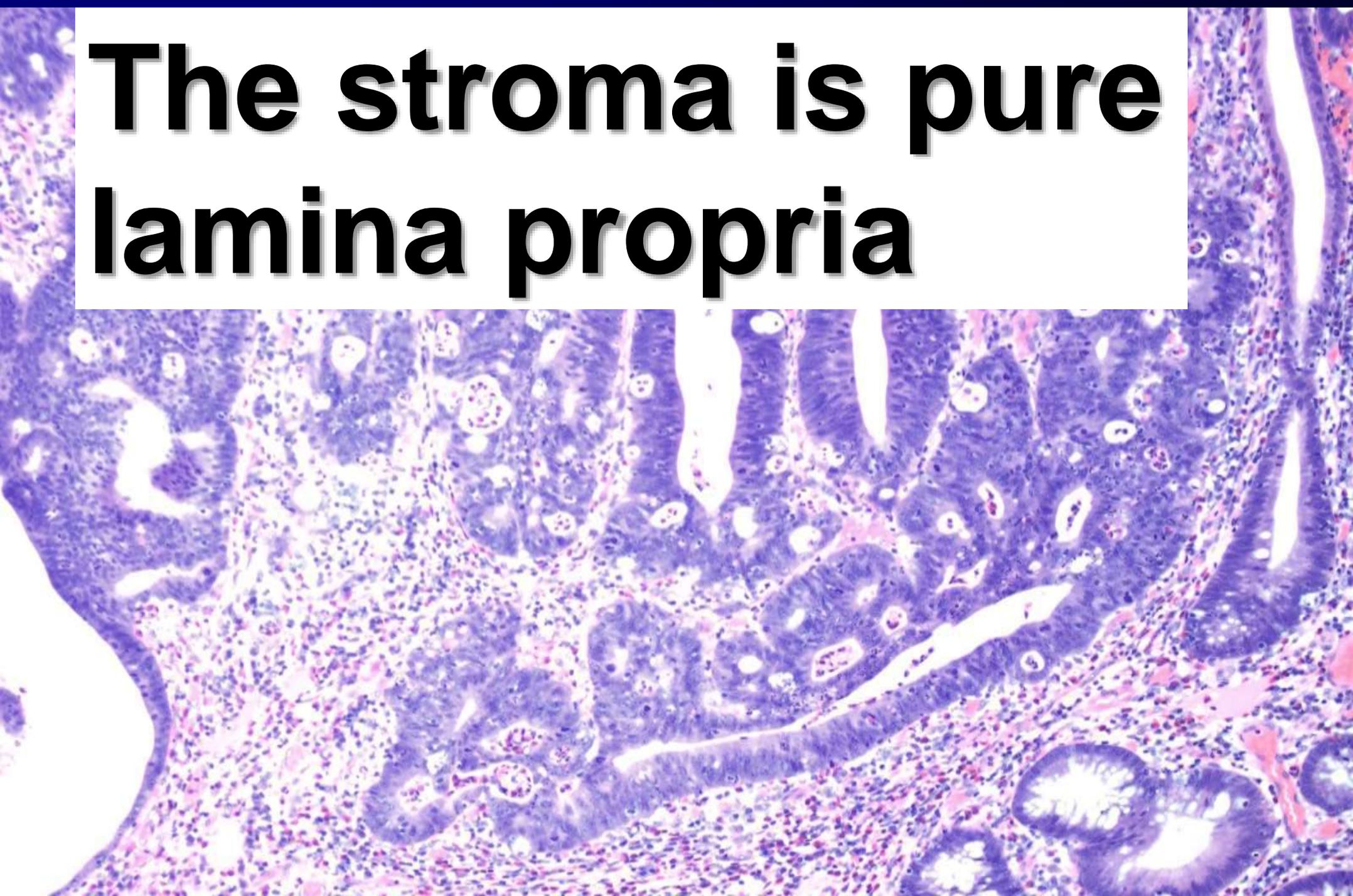
A histological micrograph showing glandular structures, likely from the prostate, stained with hematoxylin and eosin (H&E). The glands are lined by a single layer of columnar epithelial cells. The question asks if the glands have breached their basement membrane, which is a key indicator of malignancy.

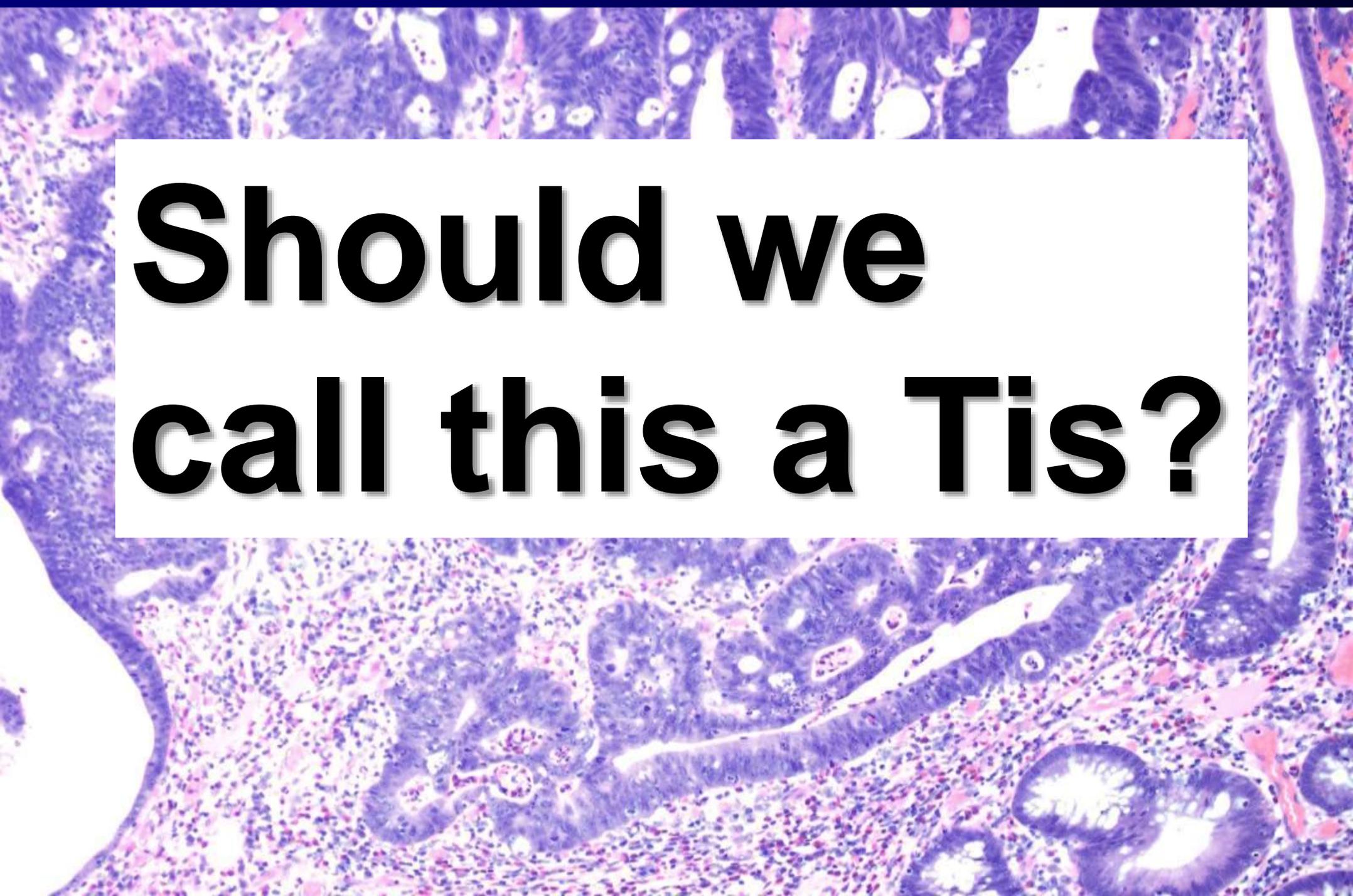
**Has it breached
the glandular
basement
membrane?**



**Complex proliferation
limited to the mucosa**

**The stroma is pure
lamina propria**

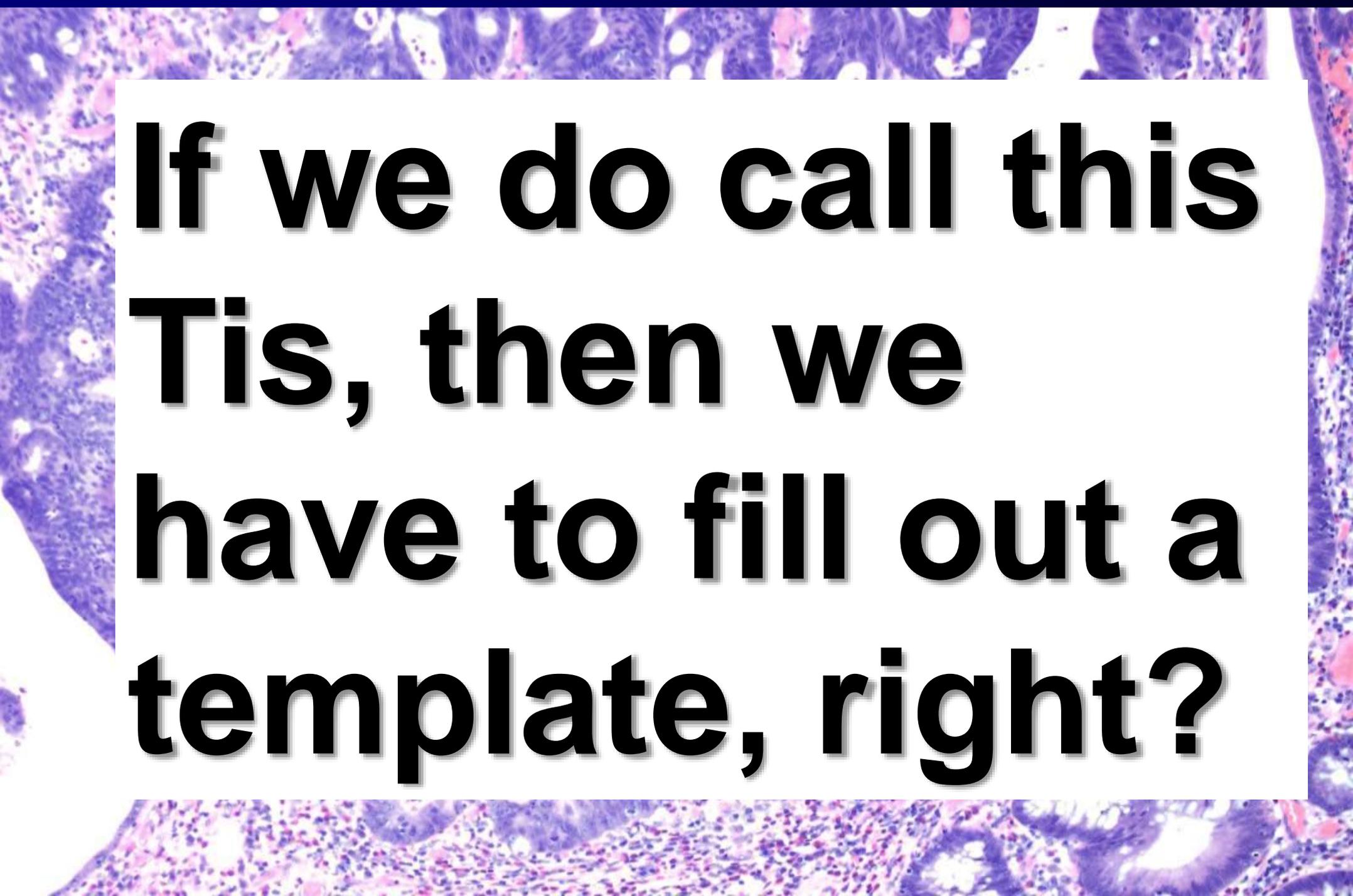


A histological slide showing a cross-section of tissue, likely from the gastrointestinal tract, stained with hematoxylin and eosin (H&E). The tissue exhibits glandular structures with varying degrees of cellular atypia and architectural disorganization. A prominent feature is a large, irregular glandular structure in the lower left quadrant, which is the focus of the text overlay. The surrounding stroma is densely cellular, with many small, dark-staining nuclei. The overall appearance suggests a neoplastic process, possibly adenocarcinoma, but the text overlay questions the classification.

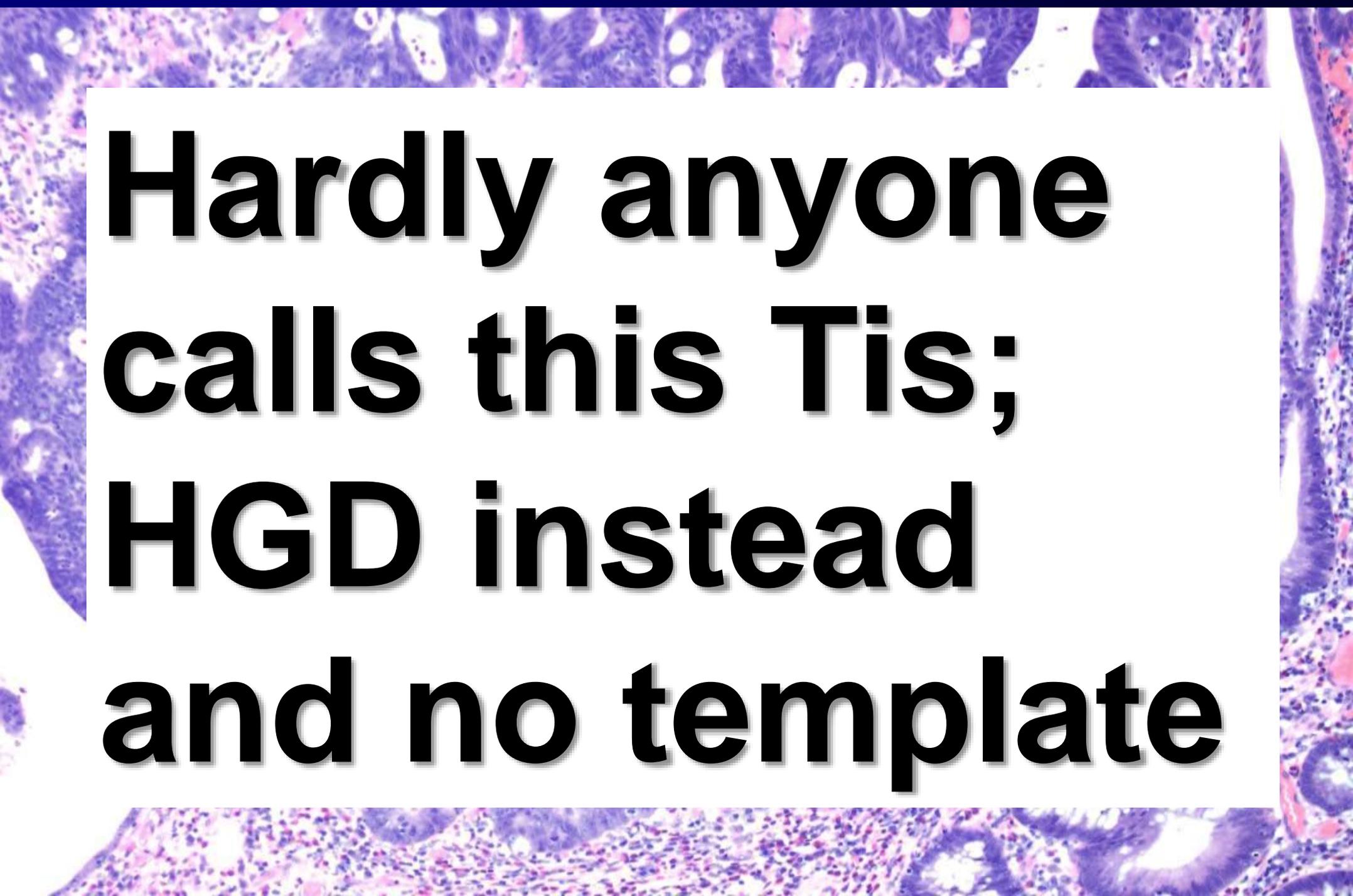
**Should we
call this a Tis?**

A histological slide stained with hematoxylin and eosin (H&E) showing glandular tissue. The glands are lined by a layer of cells, and the basement membrane is visible. There is a clear breach in the basement membrane, with cells from the glandular epithelium invading the surrounding stroma. The text is overlaid on a white rectangular background in the center of the image.

**I bet this has
breached the
glandular
basement
membrane.**

A histological image showing glandular structures, likely from the colon, stained with hematoxylin and eosin (H&E). The glands are lined by a simple columnar epithelium. The background is a white rectangular box containing text.

**If we do call this
Tis, then we
have to fill out a
template, right?**

The background of the slide is a histological micrograph showing glandular structures, likely from the colon, stained with hematoxylin and eosin (H&E). The glands are lined by a layer of columnar epithelial cells. The text is overlaid on a white rectangular area in the center of the image.

**Hardly anyone
calls this Tis;
HGD instead
and no template**

In the esophagus

Tis = HGD

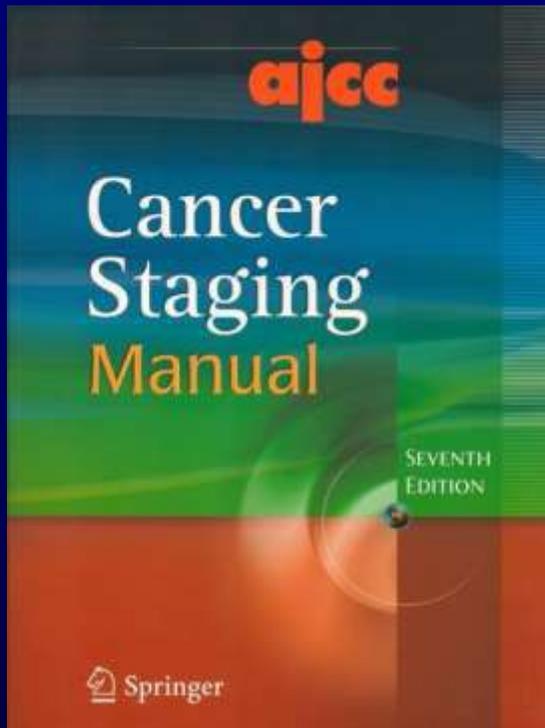
In the stomach

**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

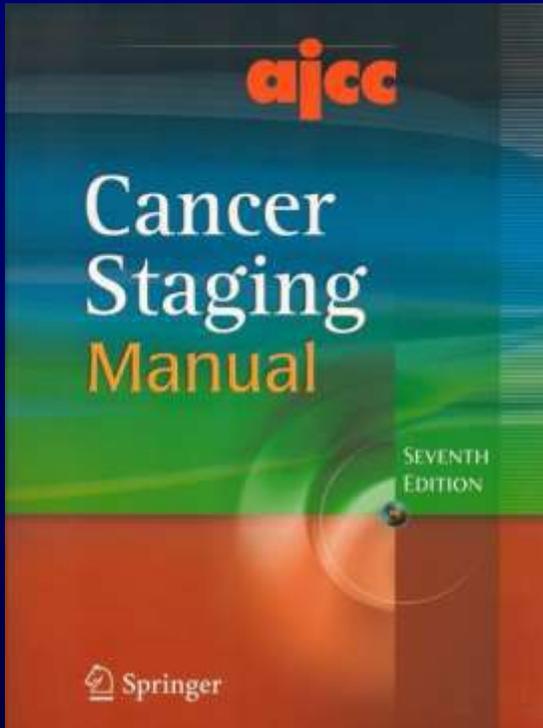
Tis = HGD

In the stomach

**Tis = intraepithelial
without invasion of LP**

In the colon

**Tis = intraepithelial or
invasion of LP**



Maybe, Tis should die!

**Kill
this!**

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 pericorectal 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

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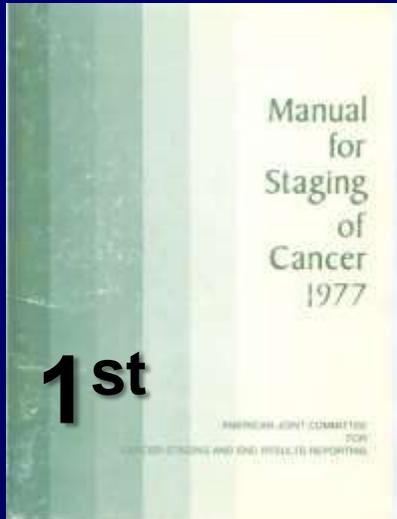
T4a Tumor penetrates to the surface of the visceral peritoneum

T4b Tumor directly invades or is adherent to other organs or structures

**What
about
T4?**



T4 history: fistula time



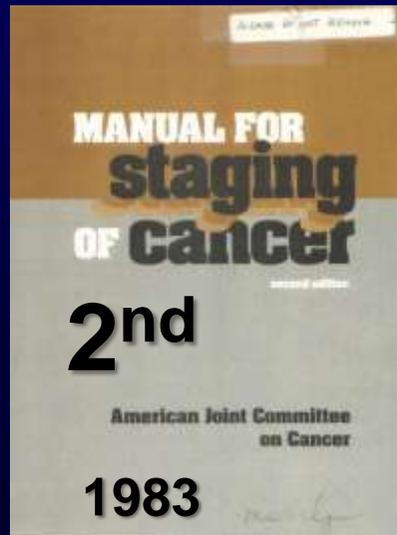
T3 involves all layers with extension to immediately adjacent structures or organs, no fistula

T4 Fistula with any depth of invasion

T5 further extension

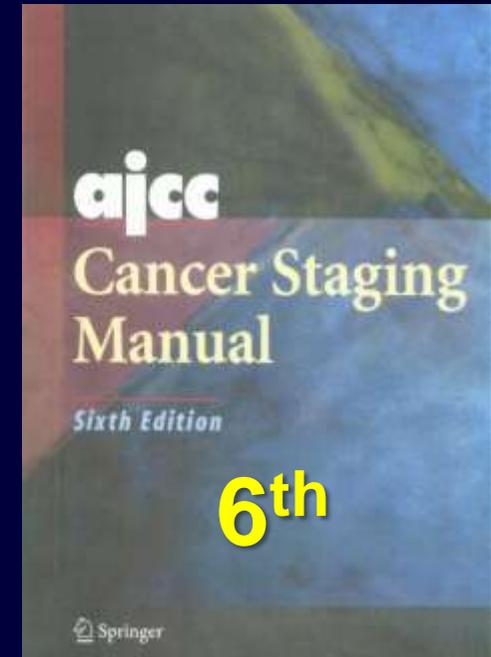
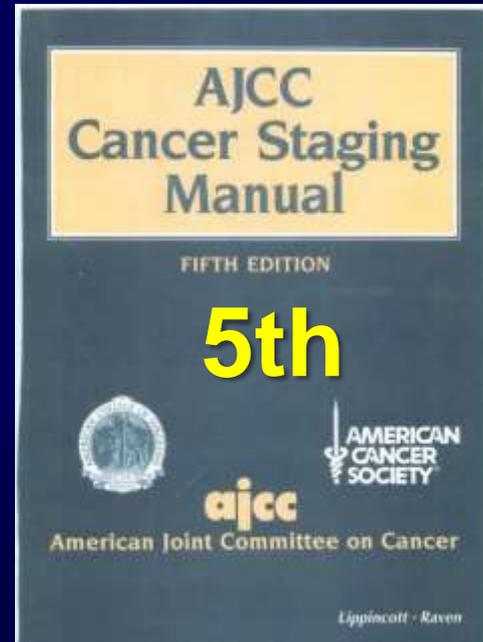
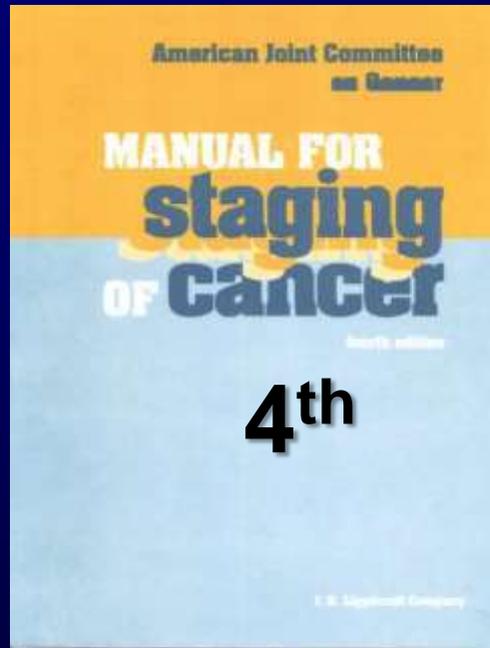
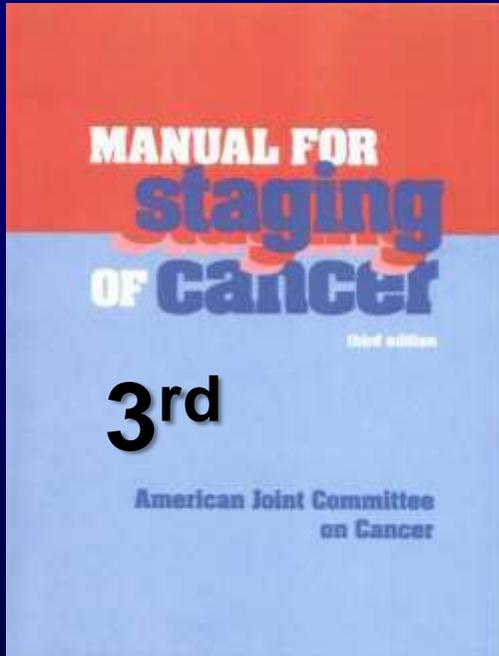
T3 invades all layers including serosa with or without extension to adjacent or contiguous tissues +/- fistula

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

PRIMARY TUMOR (T)

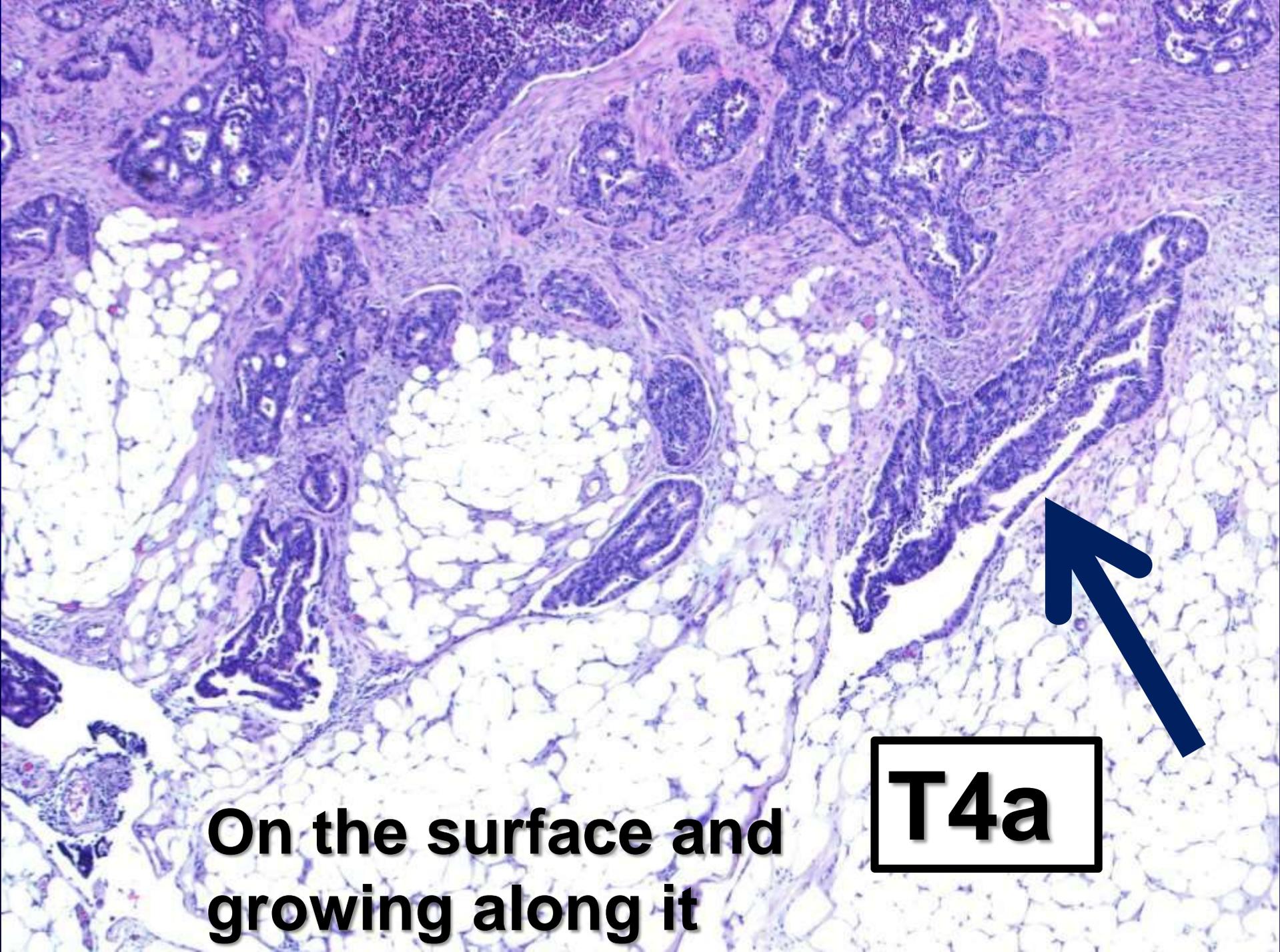
| | |
|-----|--|
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| Tis | Carcinoma <i>in situ</i> : intraepithelial or invasion of lamina propria* |
| T1 | Tumor invades submucosa |
| T2 | Tumor invades muscularis propria |
| T3 | Tumor invades through the muscularis propria 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 [^] ,** |

**In the 7th edition
T4 is split into 2 parts**

The T4a mess

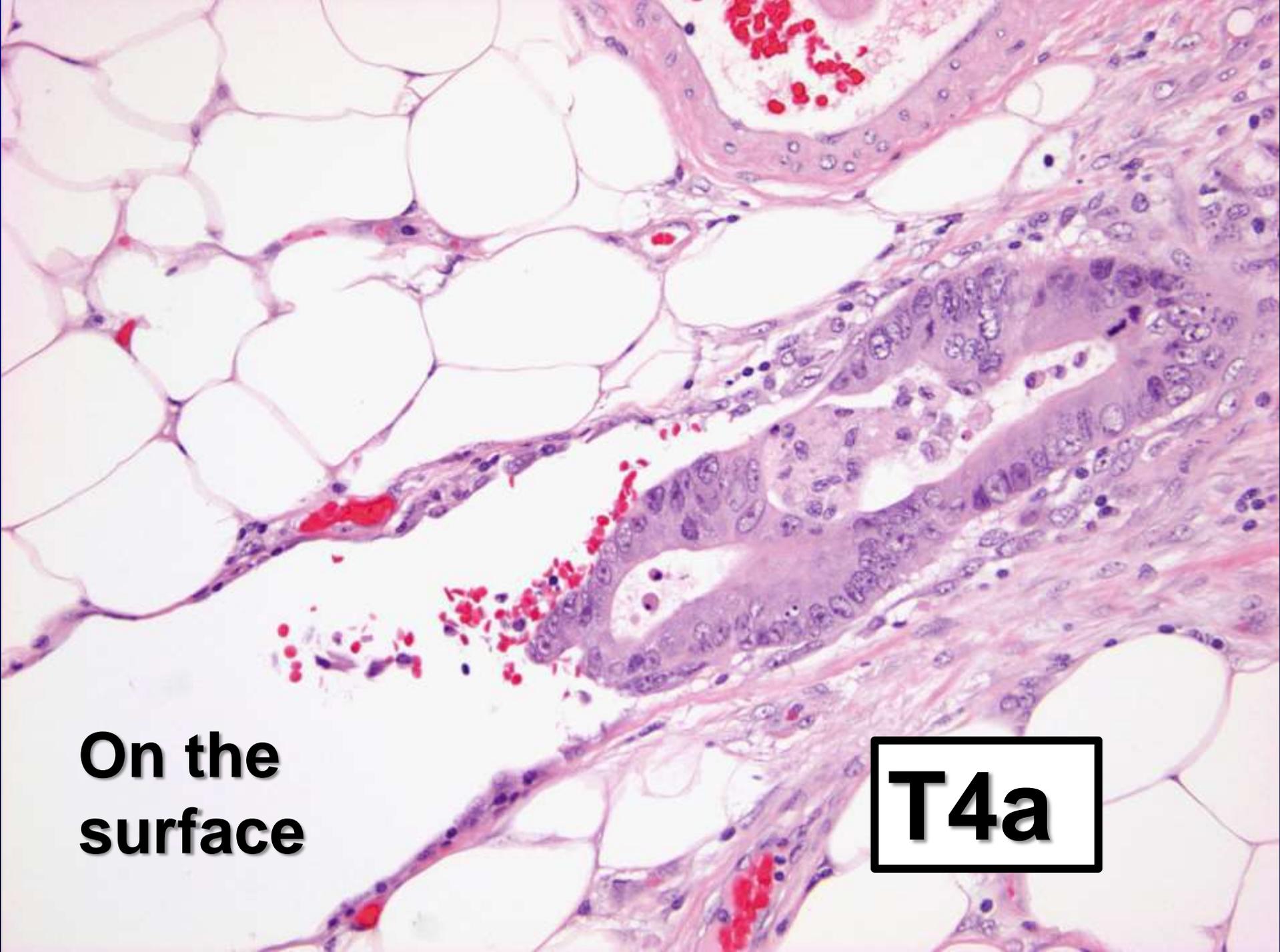
T4a

**Tumor penetrates
to the surface of the
visceral peritoneum**



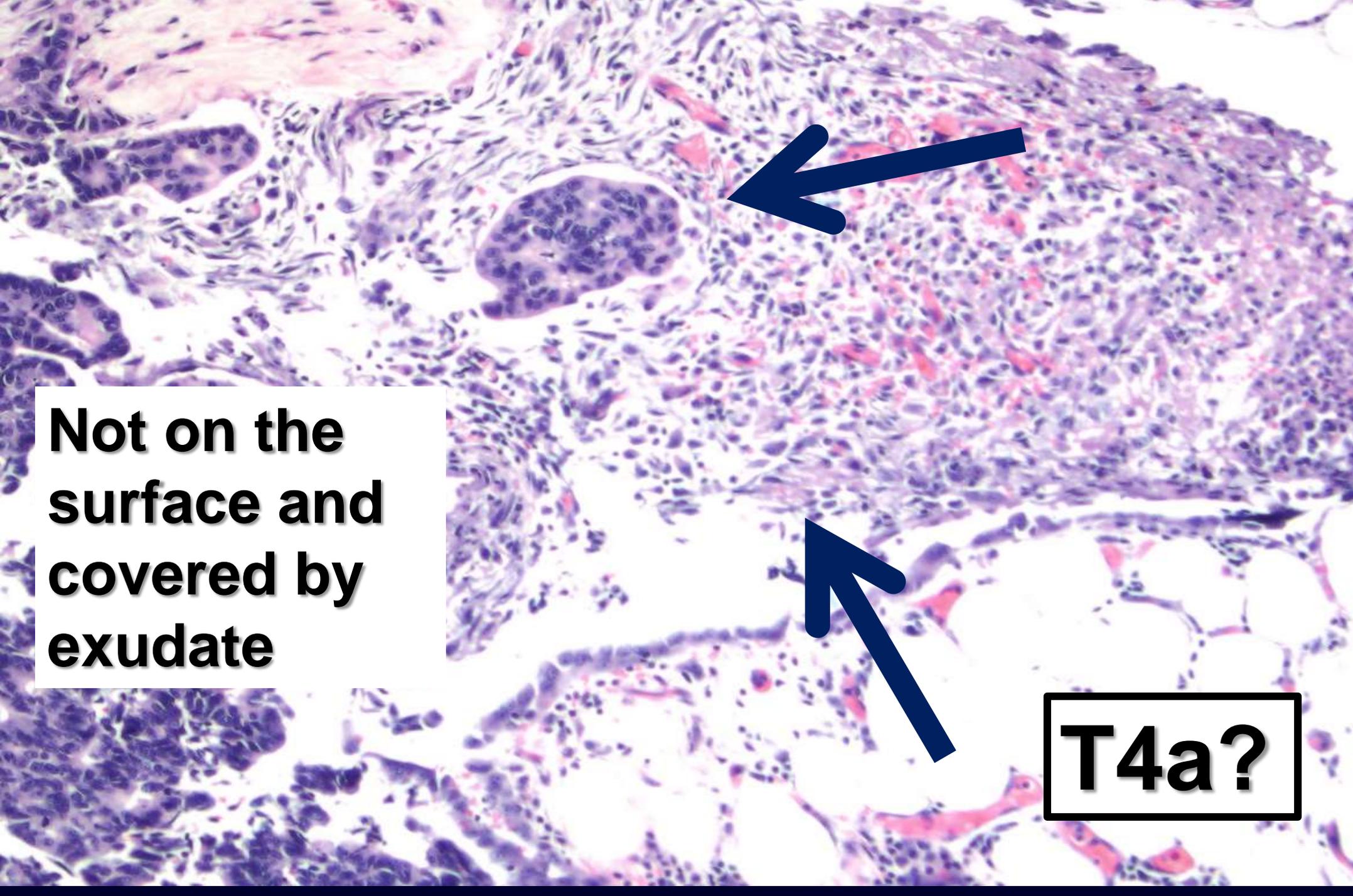
**On the surface and
growing along it**

T4a



**On the
surface**

T4a

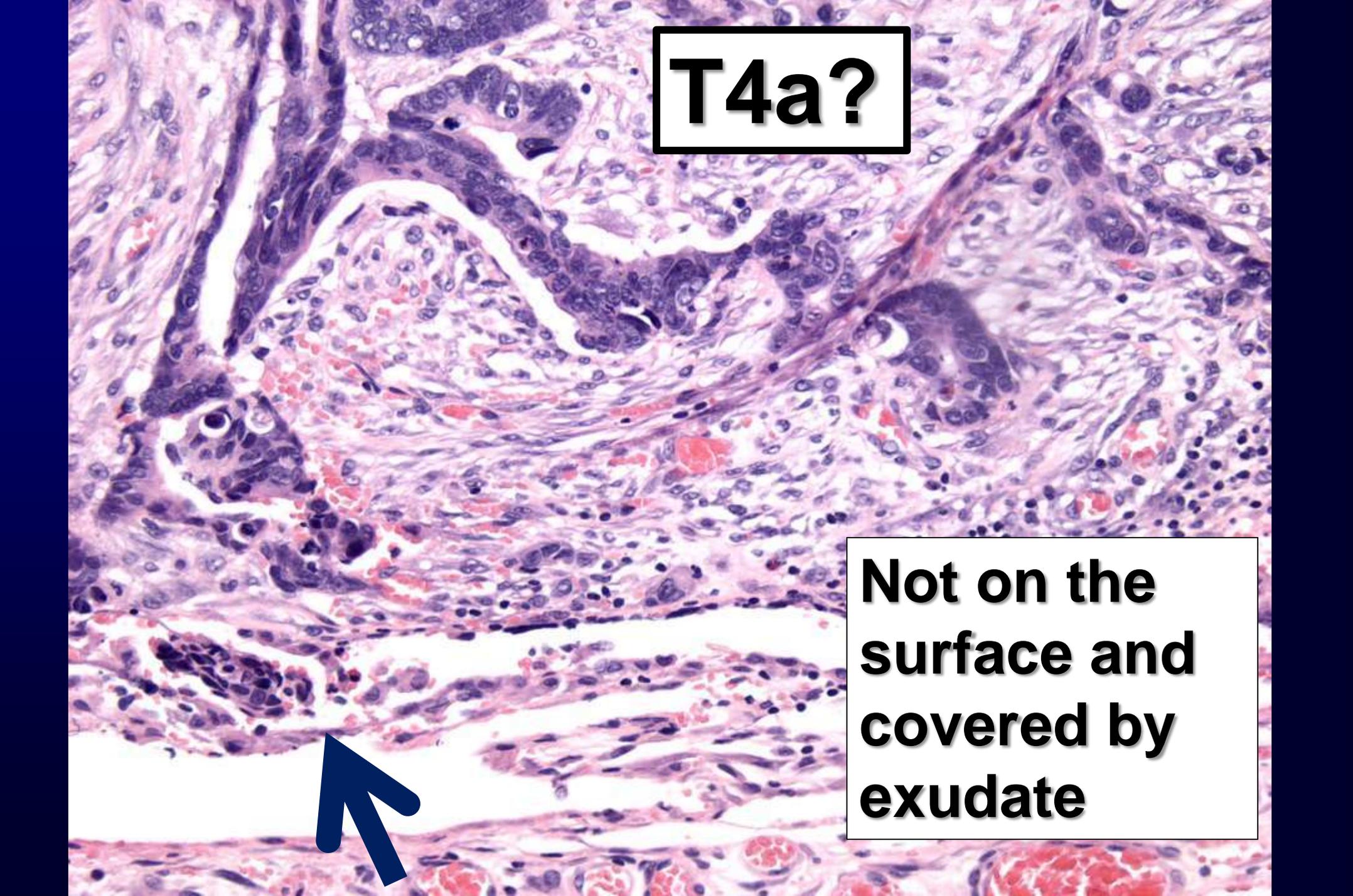


Not on the surface and covered by exudate

T4a?

T4a?

Not on the surface and covered by exudate



Various definitions of a T4a tumor:

Tumor actually on the peritoneal surface

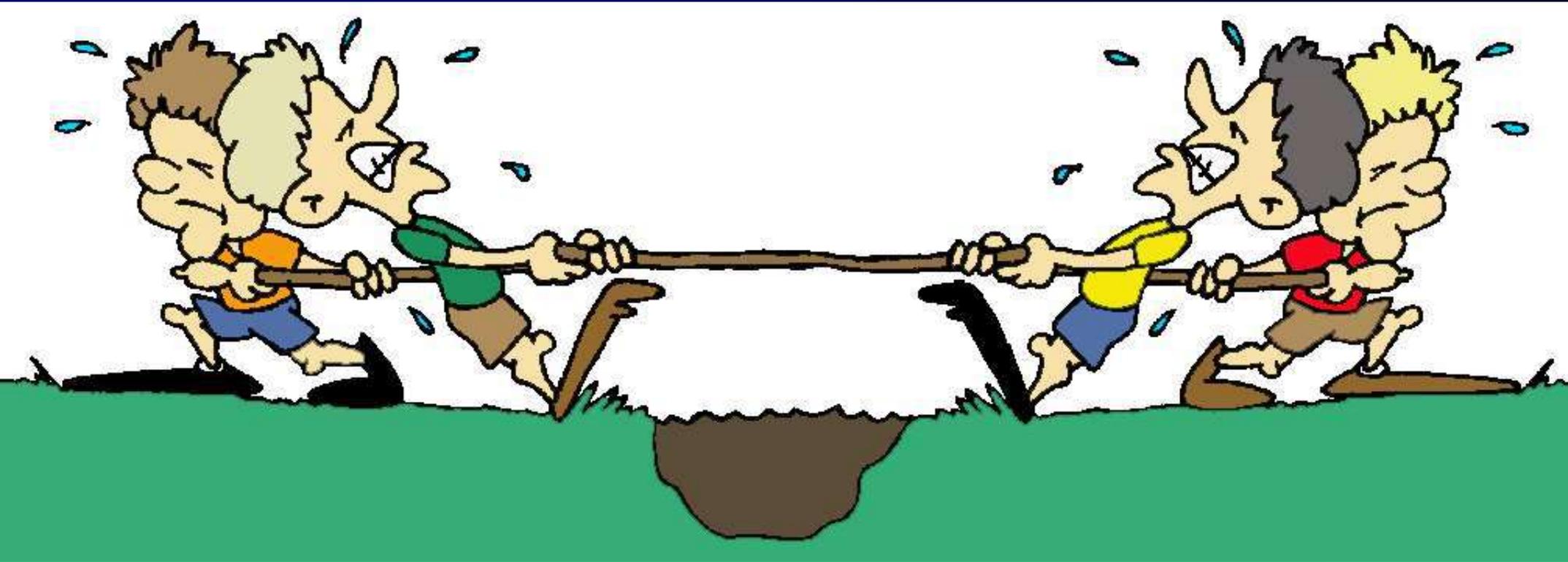
Tumor close to the surface with overlying mesothelial hyperplasia

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!!!**



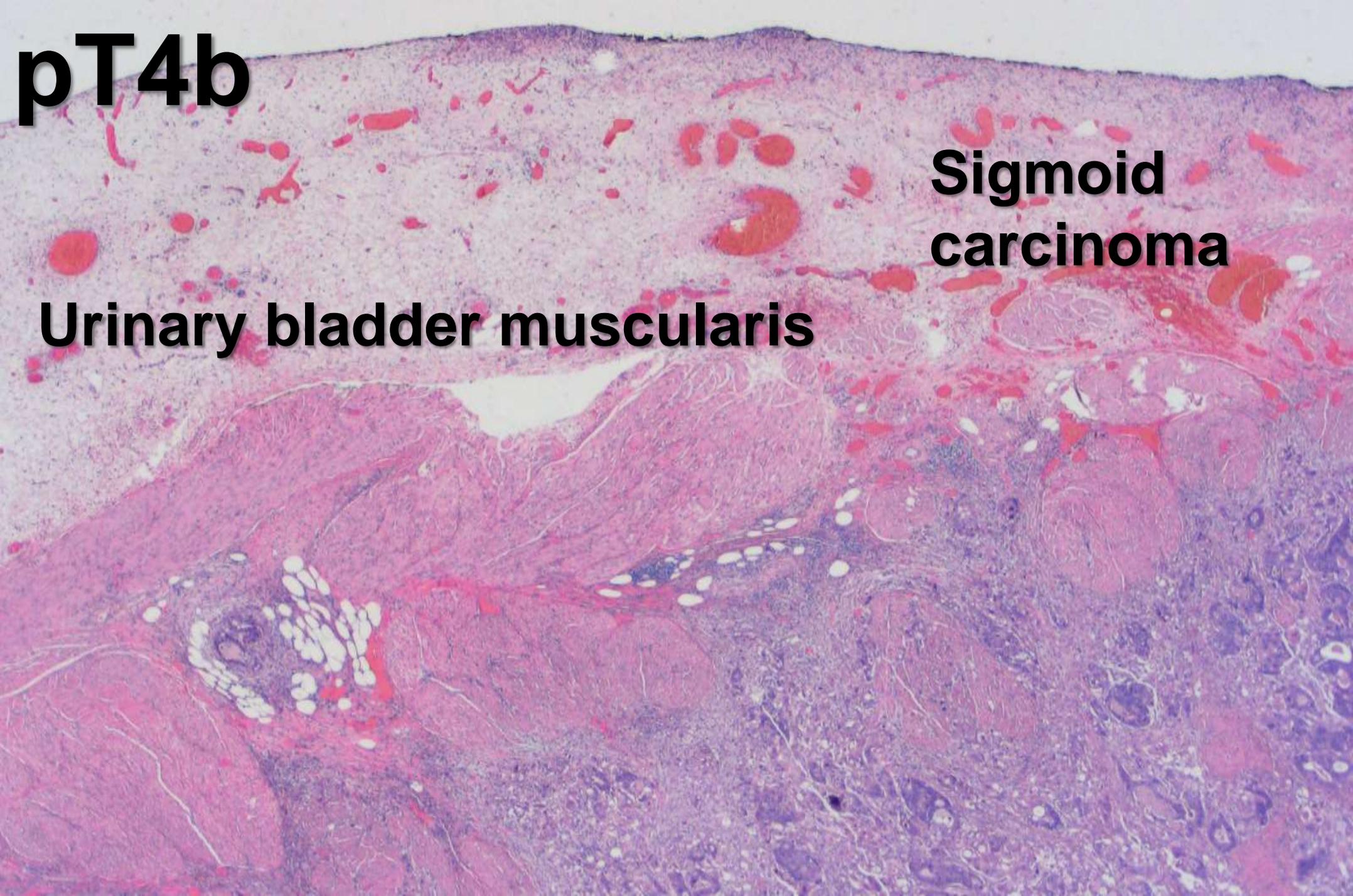
The T4b mess

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

pT4b

**Sigmoid
carcinoma**

Urinary bladder muscularis



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

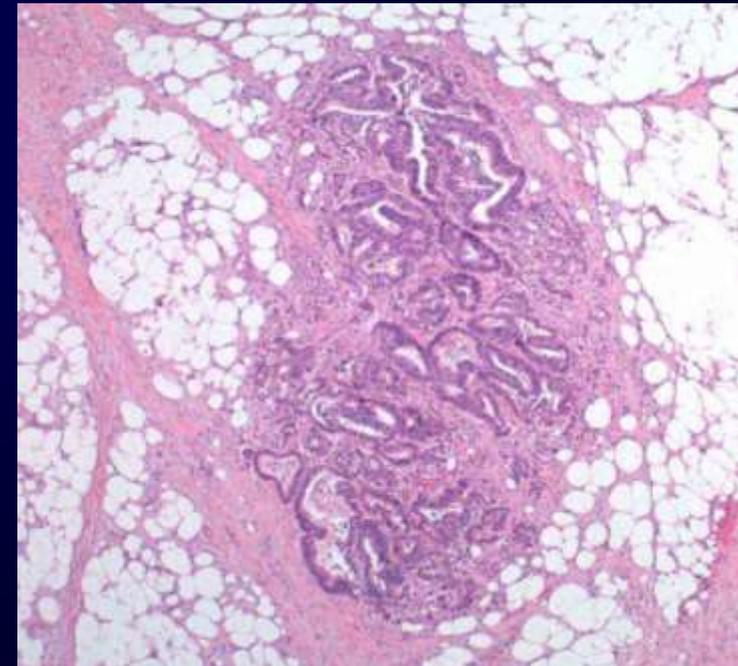
**Enough of the
T stuff!**

**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**

1st
ed

Manual
for
Staging
of
Cancer
1977

AMERICAN JOINT COMMITTEE
FOR
CANCER STAGING AND END-RESULTS REPORTING

Nodal Involvement (N) 1st Edition

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

ajcc
Cancer Staging
Manual

Sixth Edition

6th
ed

Springer

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

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

ajcc

Cancer Staging Manual

Sixth Edition

Springer

In the 6th edition, a new twist:

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⁽¹⁻³⁾
- 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⁽²⁻³⁾

Regional Lymph Nodes (N)

- NX Regional lymph nodes cannot be assessed⁽⁴⁾
- 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 _____

Regional Lymph Nodes (N)

- NX Regional lymph nodes cannot be assessed⁽⁴⁾
- 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 = _____

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!

Regional Lymph Nodes (N)

- NX Regional lymph nodes cannot be assessed⁽⁴⁾
- 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 = _____

However, it was not important for long, because this was dropped from the 7th edition, only 8 years later.

**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?

AJCC Cancer Staging Manual

FIFTH EDITION



ajcc

American Joint Committee on Cancer

Lippincott - Raven

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?

ajcc

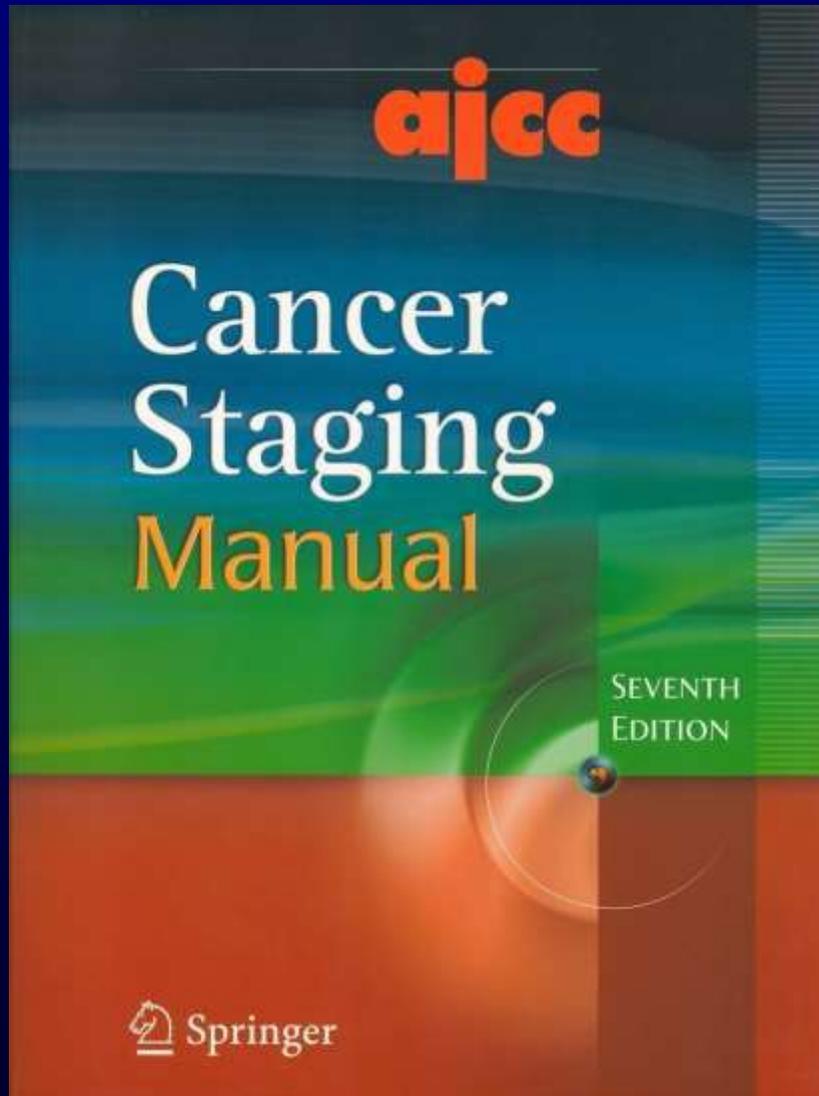
Cancer Staging
Manual

Sixth Edition

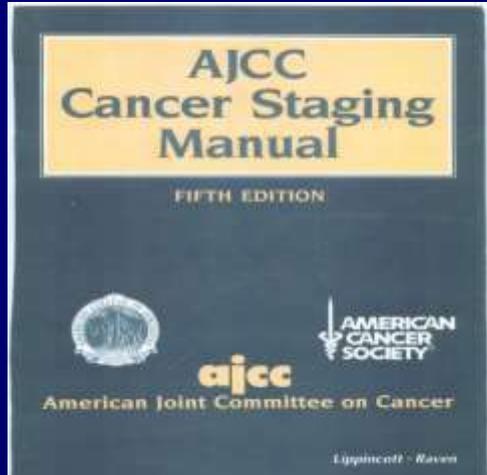
 Springer

The 6th edition
“it is important
to obtain at
least 7-14
lymph nodes...”

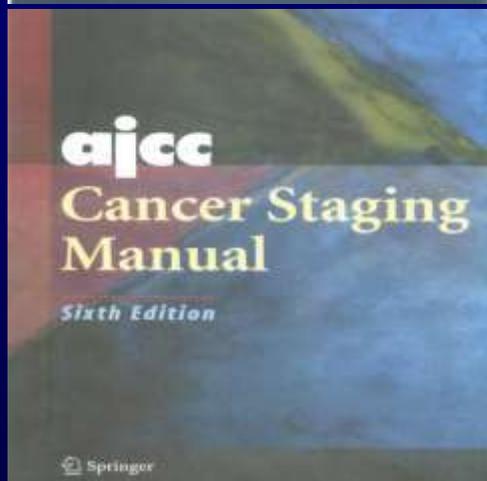
How many nodes are enough?



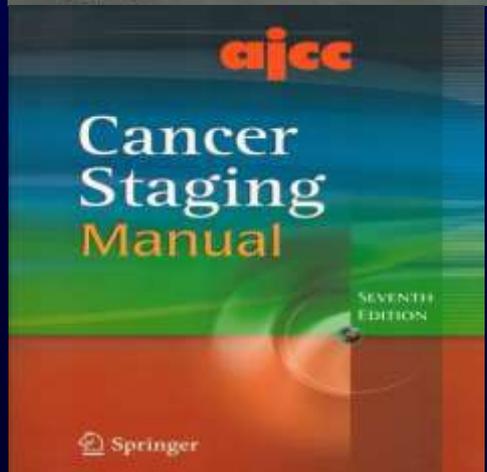
The 7th edition:
“it is important to
obtain at least
10-14 lymph
nodes”



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 examineis 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.

Wong SL, et al. JAMA. 2007;298:2149-54

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....”

**CAP: Where in the
hell did those
guys come from?
They are
everywhere!**

houses....

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!**

In the
10-
“wh
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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....”



**200 nodes
recovered**

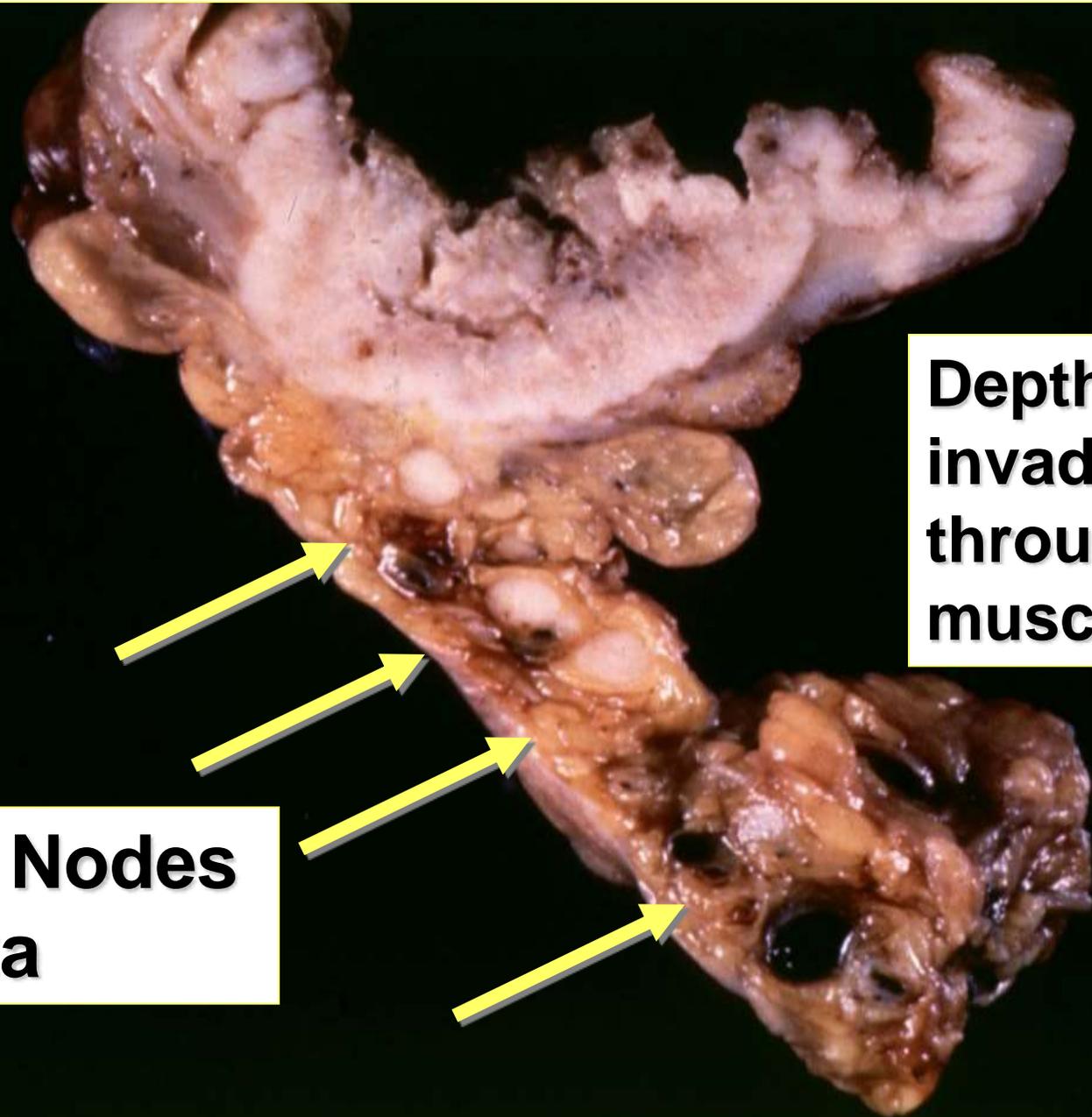
T3

N2a

**M not
used**

**4+ Nodes
N2a**

**Depth: T3
invades
through
muscularis**



**Wrong
stage?**

**As of
Jan
2010
SEER**

| Stage | T | N | M | 5-Yr Surv |
|-------------|--------------|---------------|------------|---------------|
| I | T1-2 | N0 | M0 | 74-79% |
| IIA | T3 | N0 | M0 | 67% |
| IIB | T4a | N0 | M0 | 61% |
| IIC | T4b | N0 | M0 | 46% |
| IIIA | T1-2 | N1/N1c | M0 | 67-74% |
| | T1 | N2a | M0 | 65% |
| IIIB | T3-4a | N1/N1c | M0 | 52-58% |
| | T3 | N2a | M0 | 43% |
| | T1-2 | N2b | M0 | 52% |
| IIIC | T4a | N2a | M0 | 33% |
| | T4a | N2b | M0 | 18% |
| | T4b | N1 | M0 | 30% |
| IVA | Any T | Any N | M1a | ~6% |
| IVB | Any T | Any N | M1b | ~5% |

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

**no pathologic M0; use 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 peritoneum**

