Alpha-1 Antitrypsin Deficiency Bronchiectasis and NTM

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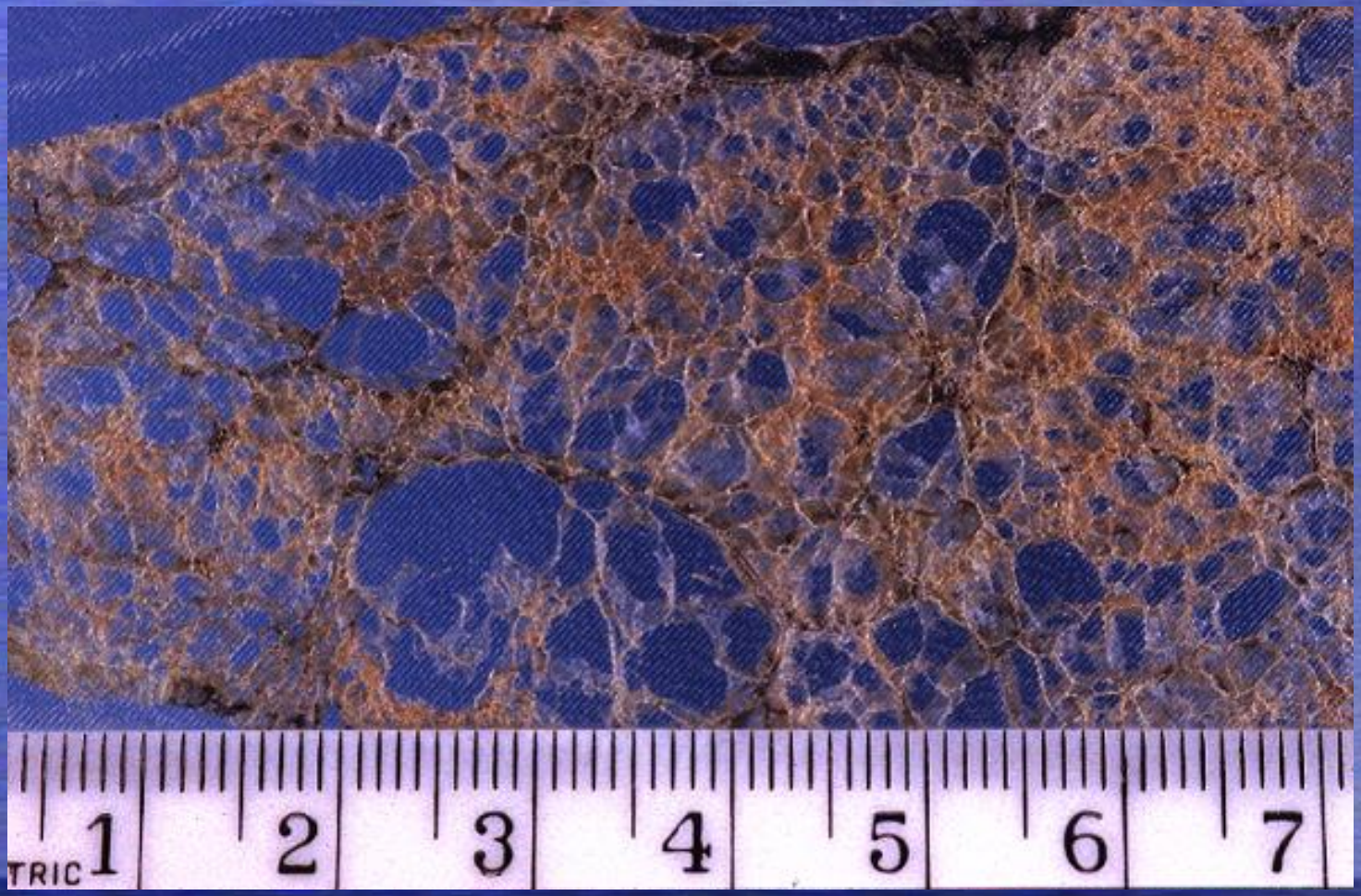
What is Alpha$_1$-Antitrypsin?

- A protein made in liver which circulates throughout body
- AAT suppresses inflammation - a protective **but destructive** process
- Inherited genes dictate type and behavior of our Alpha-1
- The normal gene (protein) is '**M**'
- The most common abnormal genes are '**Z**' and '**S**' (among hundreds)
- Gene makeup – MM, MZ, and ZZ……

$Alpha_1$-Antitrypsin Deficiency?

- The genetic condition leading to decreased levels in blood/tissues
  - MM ~ 125 MZ ~ 80 ZZ ~ 25
- Without protective levels, inflammation
  - In lungs leads to emphysema

Severe Emphysema



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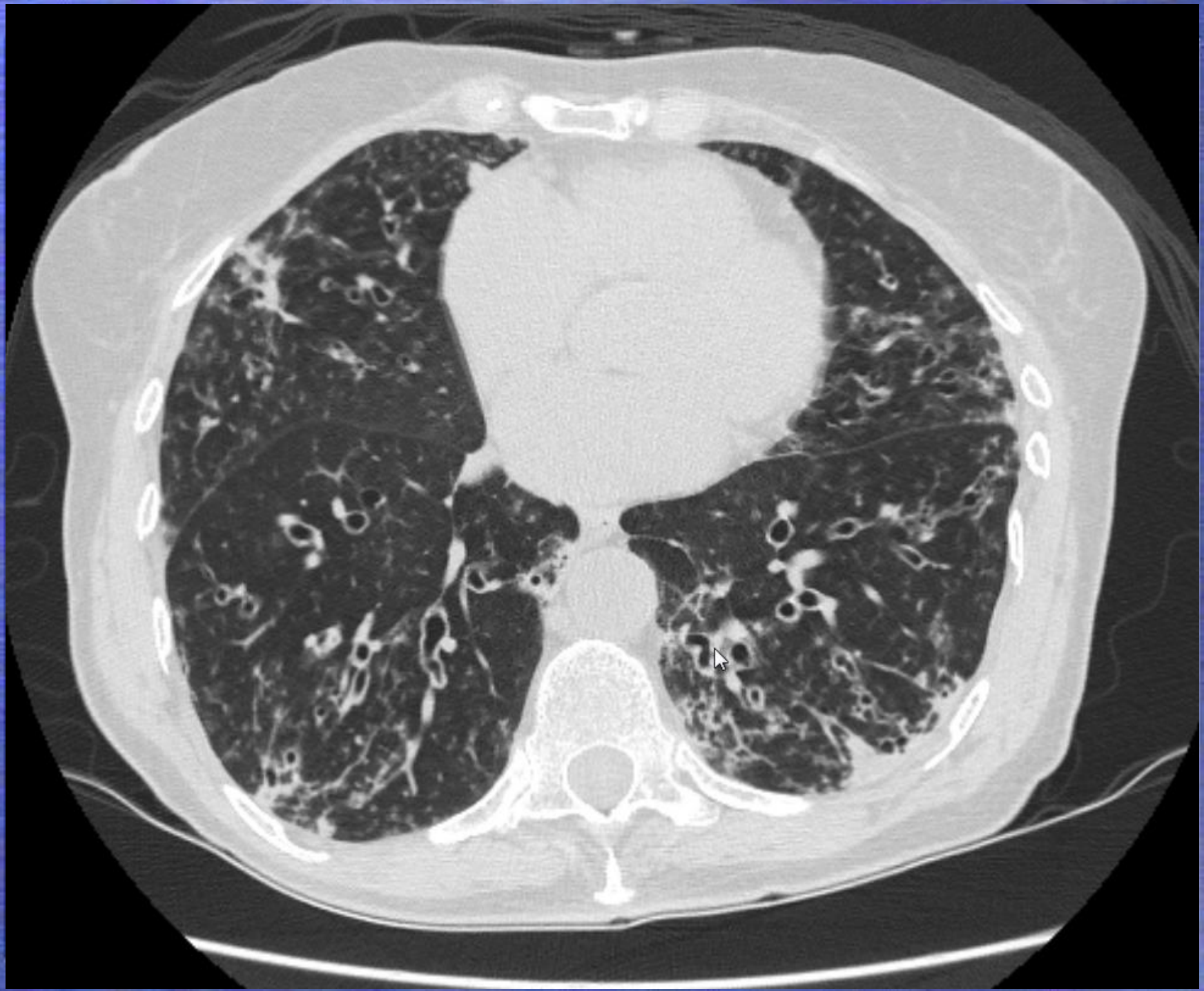

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- Alphas may have emphysema and/or bronchiectasis

AATD, Bronchiectasis, and NTM

- Most ZZ Alphas have CT evidence of some bronchiectasis
- Roughly 1/3 of ZZ Alphas have clinically significant bronchiectasis
- As many as 30% with bronchiectasis will develop NTM
- Up to 27% of NTM have abnormal alpha-1 genetics
  - Including MZ individuals – mild deficiency
- Less than 1% of bronchiectasis is ZZ

Augmentation Therapy

- Pooled plasma derivative
- Weekly IV infusion - $$$
- Slows progression of ZZ emphysema
- Improves ZZ survival

?

- Why are Alphas at risk for NTM?
  - Structural integrity or biochemistry
- Does augmentation Tx benefit?
  - Non-emphysema bronchiectasis
  - NTM infection