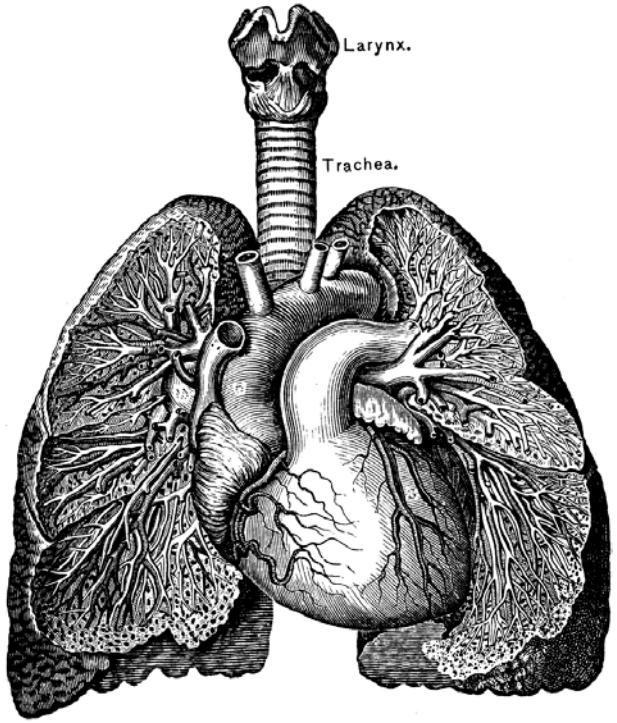
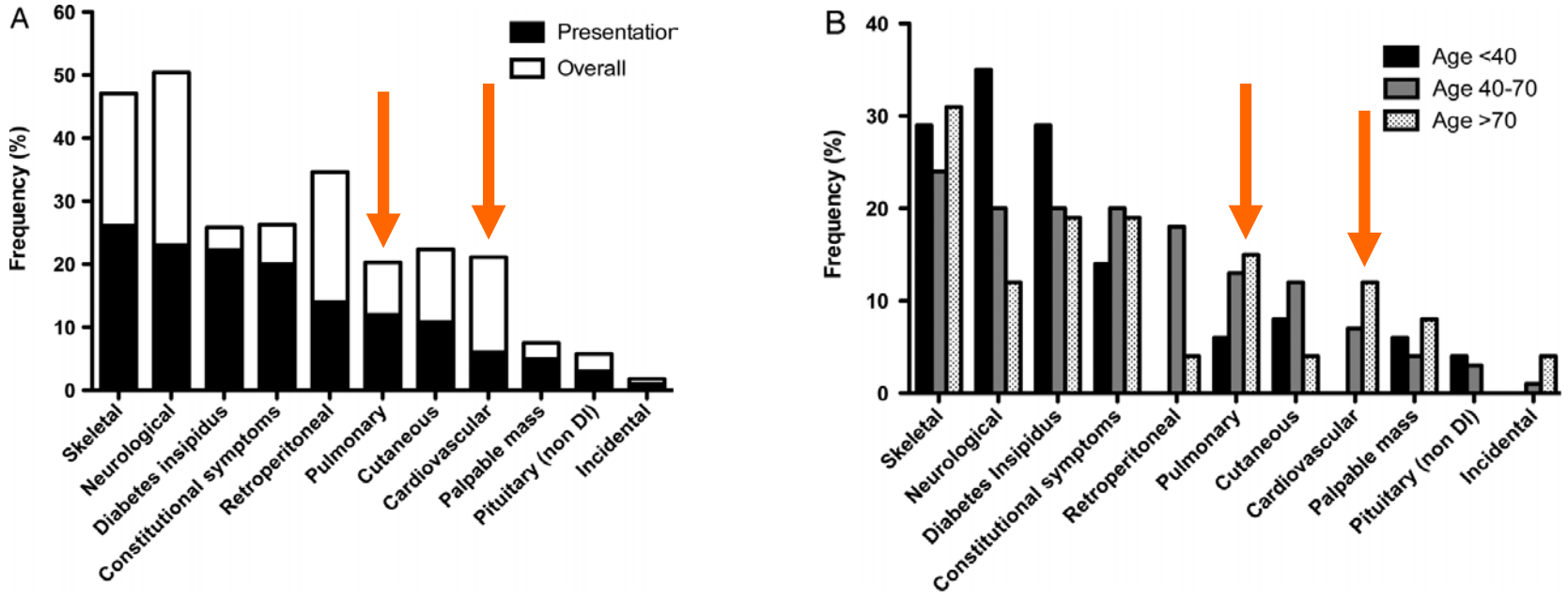
ERDHEIM-CHESTER DISEASE
LUNG & HEART ISSUES

GIULIO CAVALLI, M.D.
INTERNAL MEDICINE AND CLINICAL IMMUNOLOGY
IRCCS SAN RAFFAELE HOSPITAL
VITA-SALUTE SAN RAFFAELE UNIVERSITY
MILAN, ITALY
cavalli.giulio@hsr.it



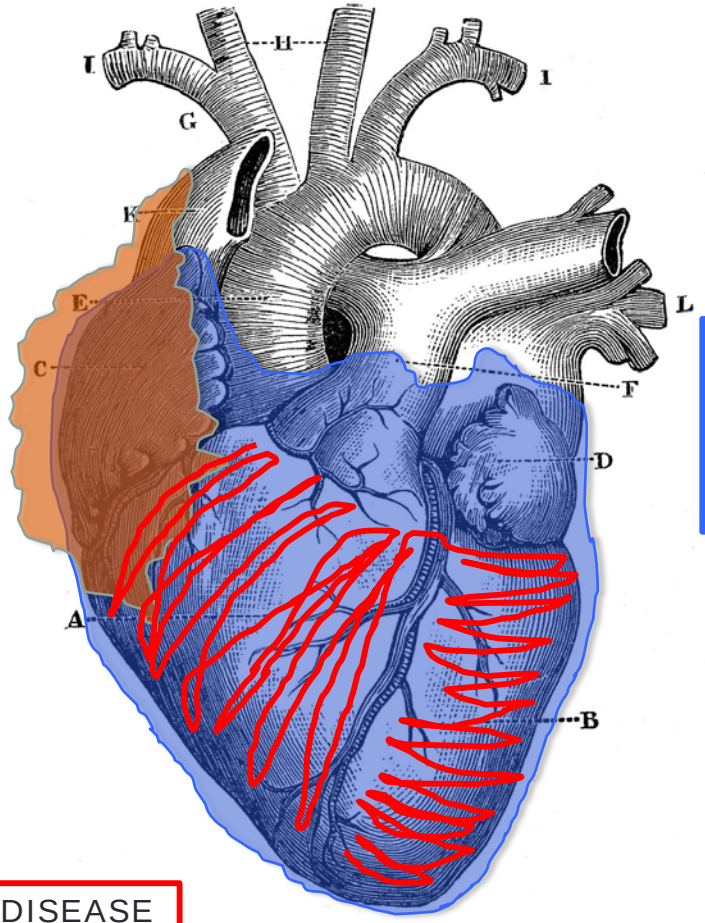
FREQUENCY OF CARDIAC AND PULMONARY ECD



Pulmonary involvement and cardiovascular involvement are both only moderately frequent ECD manifestations at the time of disease onset, but the likelihood of developing these manifestations increases over time. Overall, about **one fourth of ECD patients** develop clinically evident cardiac or pulmonary involvement. Cardiac or pulmonary involvement **often develop concomitantly**.

CARDIAC MANIFESTATIONS

RIGHT ATRIUM
Pseudotumoral Appearance
- Right Coronary Artery
- Interatrial Septum
- Atrioventricular Septum
- Mitral Valve



PERICARDIAL DISEASE
Effusion
Thickening
Diastolic Heart Failure
Tamponade

MYOCARDIAL DISEASE
EKG Abnormalities
Ventricular Hypertrophy
Diastolic Heart Failure

CARDIAC MANIFESTATIONS

Pericardial disease is common, and represents 44% of cases of cardiac involvement. It may cause effusion, thickening or fibrosis, or tamponade.

Right atrium involvement occurs in 31% of cases of cardiac involvement. It may cause right atrial pseudo-tumor or symptomatic valvular heart disease (valvular regurgitation), and may rarely cause the occlusion of the right coronary artery, thus causing myocardial infarction to occur.

Myocardial disease occurs in 30% of cases of cardiac involvement. Extensive infiltration of the heart muscle tissues may interfere with cardiac contractility and rhythm.

CLINICAL COMPLAINTS

- Chest Pain
- Shortness of breath
- Fatigue
- Cough
- Palpitations

CARDIAC MANIFESTATIONS

EVOLUTION

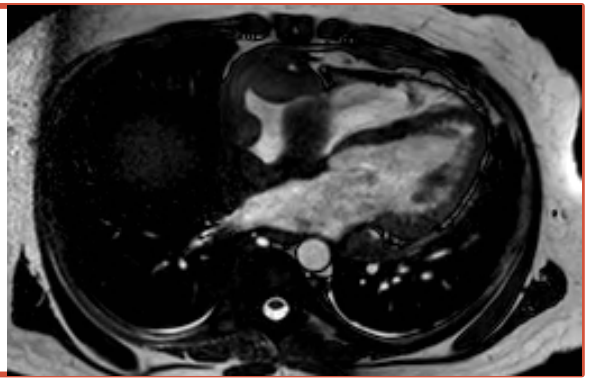
Cardiac involvement not a frequent manifestation of ECD at at the time of disease onset, but its frequency increases over time. Overall, around **one fourth of ECD** patients have symptomatic cardiac involvement.

SURVIVAL

Heart involvement has been classically considered a manifestation of **particular clinical severity**, with a 5-year mortality of 30–40%. However, new therapies are currently available and this estimate is not representative of nowadays reality.

WHEN AND HOW TO SCREEN

Gadolinium-enhanced Cine Cardiac MRI is the gold standard for the evaluation of cardiac involvement in ECD. It is highly sensitive for the evaluation of all heart structures and function.



Trans-thoracic ultrasound can be used as a first-line imaging technique for the detection of gross cardiac or pericardial involvement, and **CT scan** can be used when MRI is not available. Neither technique is optimal.

A **complete radiological evaluation at baseline** is recommended, even in the absence of cardiac complaints, as the heart could be silently involved. Periodic re-evaluations should ensue every **3 months** initially after beginning treatment, every **6 months** once disease stabilization is achieved, and **once yearly** in case of long-standing stability. Changes in clinical status dictate the need for urgent re-evaluation.

WHEN AND HOW TO TREAT

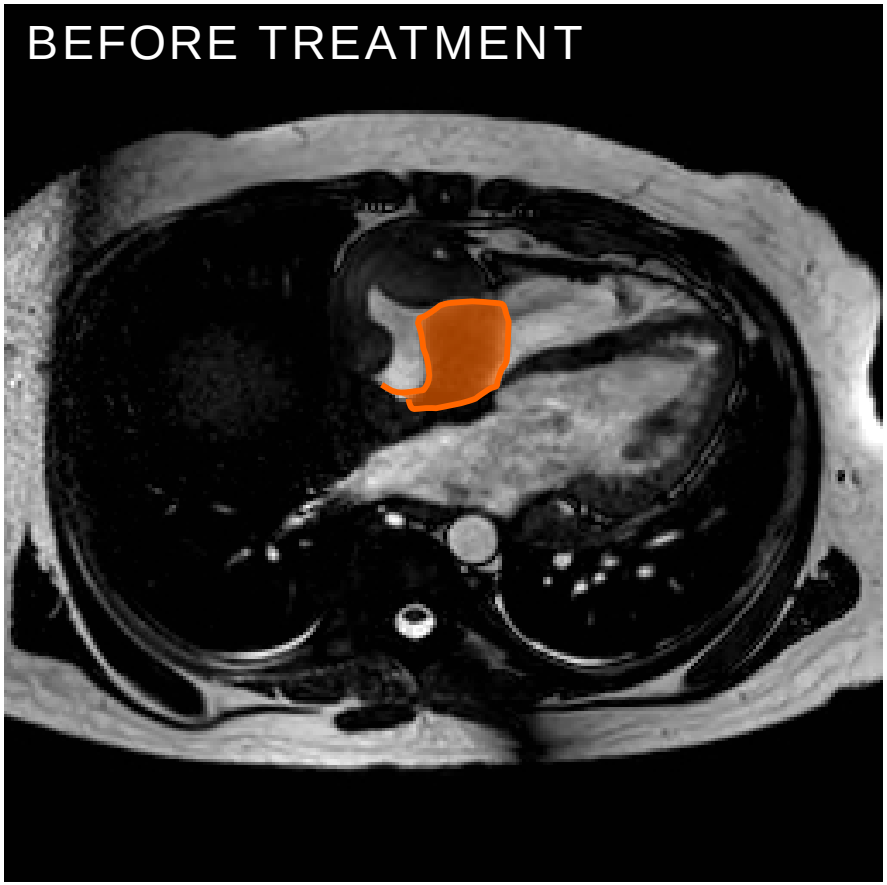
All patients with heart involvement should be treated as aggressively as tolerated due to the risk of progression and severe complications.

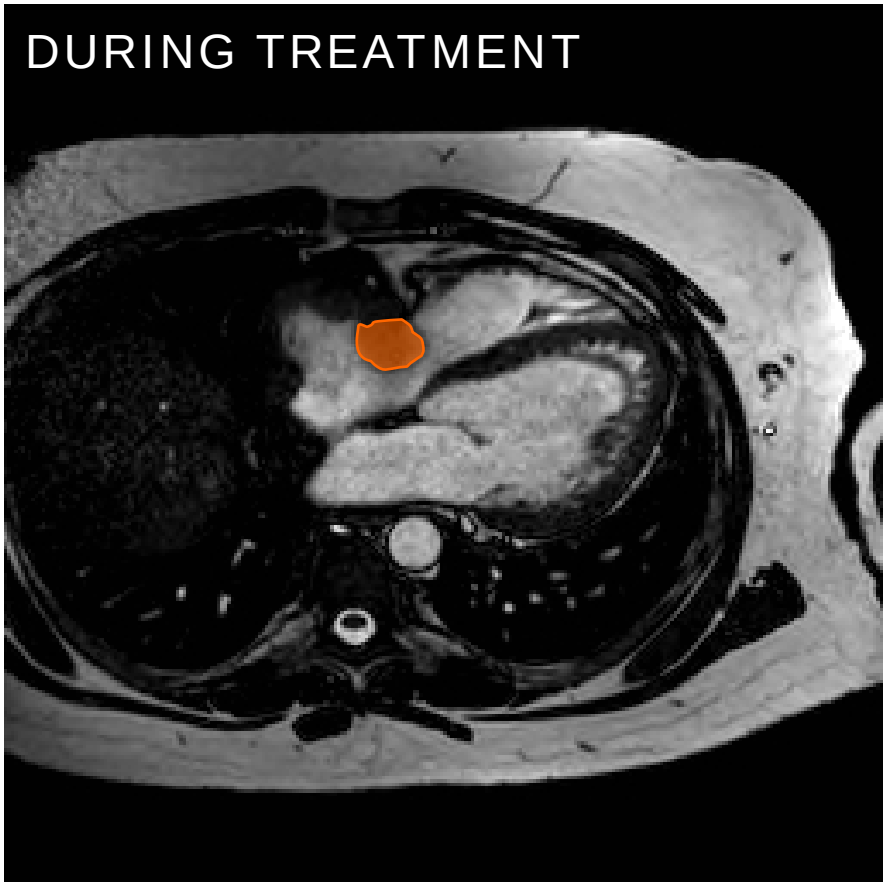
IFN-α (3-9 million units 3 times a week): recommended as the first-line therapy, administered at the highest tolerable dose depending on disease severity.
PEG-IFN-α (>180 μg/wk): more handy alternative administered once weekly. Clinical response is highly variable, some patients will not respond, side effects are burdensome.

Infliximab (anti-TNF-α): prevents exudate formation.
Anakinra (anti-IL-1): fosters cardiac contractility and is very well tolerated. It is even speculated that the efficacy of IFN-α relies on analogous mechanisms.

Vemurafenib (480 mg twice a day): may allow to achieve stabilization or regression of severe cardiac involvement. Severe cutaneous adverse effects are common and include rash, keratosis pilaris, xerosis, or photosensitivity.

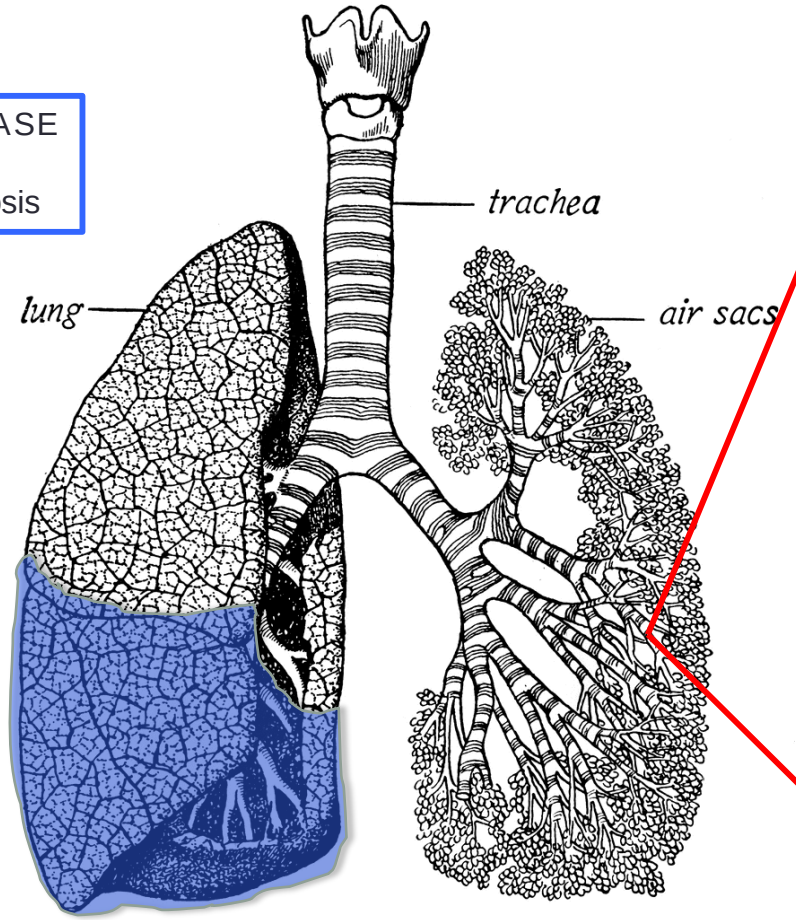
TREATMENT WITH VEMURAFENIB



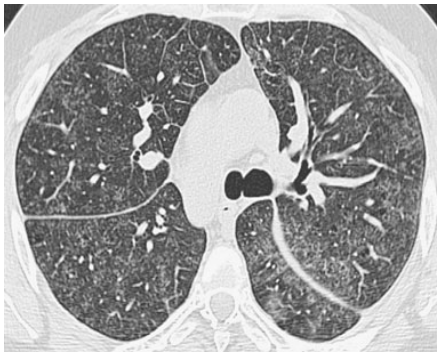


PULMONARY MANIFESTATIONS

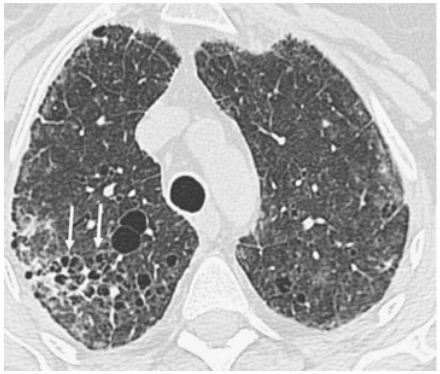
PLEURAL DISEASE
Effusion
Thickening or Fibrosis



PARENCHIMAL DISEASE



Thickening of fissures and interlobular septa; diffuse, small, ill-defined nodular opacities



Ground-glass opacities, fibrosis, honeycombing, small cysts.

PULMONARY MANIFESTATIONS

CLINICAL COMPLAINTS

Respiratory complaints may be due primarily to pulmonary involvement, or to cardiogenic pulmonary edema resulting from primary cardiac involvement.

- Cough (persistent and dry)
- Shortness of Breath (chronic dyspnea)
- Fatigue

Pulmonary hypertension is not common.

PULMONARY MANIFESTATIONS

EVOLUTION

Pulmonary involvement not a frequent manifestation of ECD at at the time of disease onset, but its frequency increases over time. Overall, around **one fourth of ECD** patients have pulmonary involvement.
The evolution of pulmonary involvement in ECD, as evaluated by radiologic changes, is normally characterized by **stability or mild progression** of lesions.

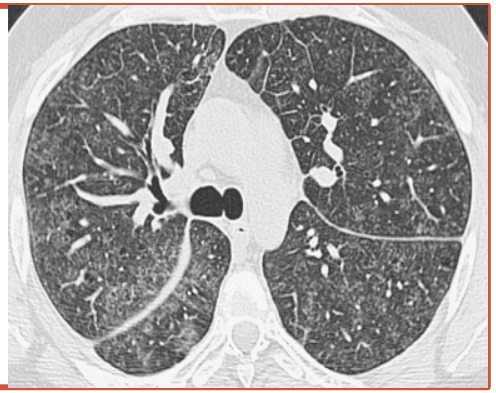
SURVIVAL

A comparison of the survival between patients with and those without pulmonary involvement yielded no significant differences between the 2 groups.
This observation corroborates the relatively **limited impact of pulmonary involvement on the overall prognosis** of the disease.

WHEN AND HOW TO SCREEN

High Resolution CT Scan is the gold standard for the evaluation of pulmonary involvement in ECD. It is highly sensitive for the evaluation of all pulmonary structures.

Plain radiographs are not useful.



Pulmonary Function Tests
Normal Pattern
Restrictive Pattern
Reduced DLCO

Radiological evaluation is mandatory at baseline, even in the absence of respiratory complaints, as the wider availability of HRCT has increased the likelihood of detecting silent pulmonary involvement. Periodic re-evaluations should ensue **once yearly,** or earlier if clinically indicated.

WHEN AND HOW TO TREAT

In general, patients with pulmonary ECD should receive treatment. The response to treatment in most cases of pulmonary involvement in ECD is only satisfactory. Treatment choice should also be guided by the overall disease burden and by the concomitant involvement of other organs.

IFN-α (3-9 million units 3 times a week): recommended as the first-line therapy, administered at the highest tolerable dose depending on disease severity.
PEG-IFN-α (>180 µg/wk): more handy alternative administered once weekly.

Clinical response is highly variable, some patients will not respond, side effects are burdensome.

Vemurafenib (480 mg twice a day): indicated in more severe cases. Severe cutaneous adverse effects are common and include rash, keratosis pilaris, xerosis, or photosensitivity.

CONCLUSIONS

Clinically evident cardiac or pulmonary involvement develop in approximately **one fourth of ECD patients**. In these patients, cardiac and pulmonary involvement are **often concomitantly present**.

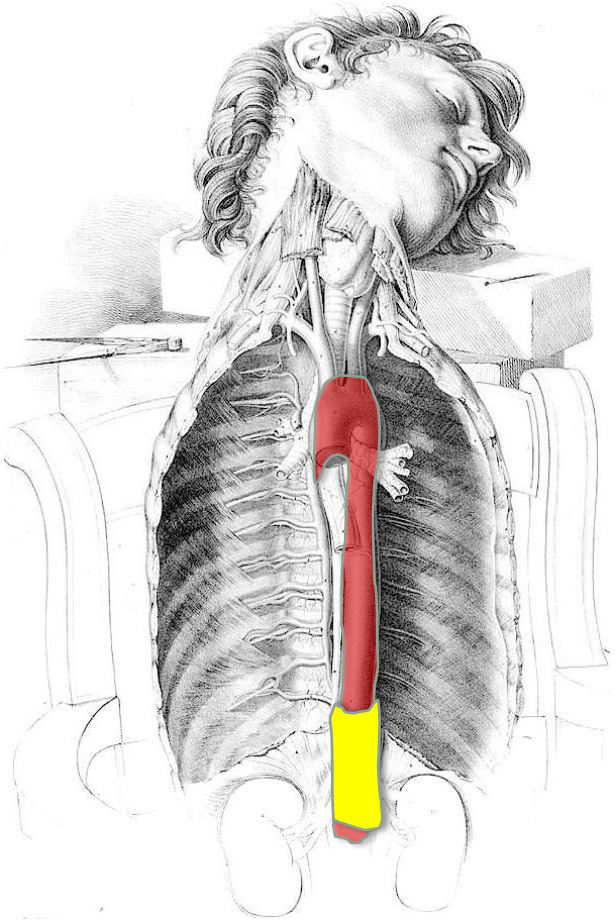
In many more patients, cardiac or pulmonary involvement may be present but **silent**, or will develop eventually during the course of the disease.

All ECD patients should be **systematically and periodically screened** for occult cardiovascular or pulmonary involvement with highly sensitive imaging tools.

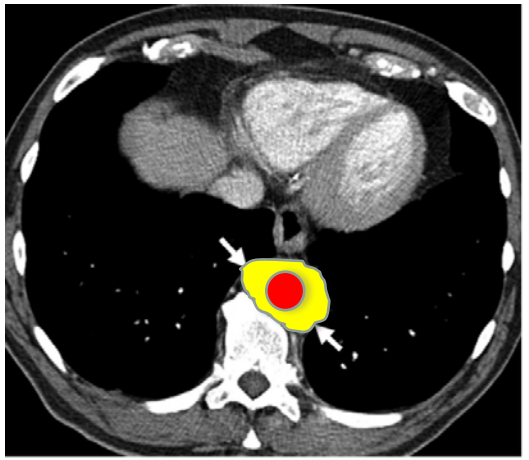
Cardiac and pulmonary involvement are **severe manifestations of ECD**. Although their severity is highly variable on an individual basis, the development of cardiac or pulmonary involvement in ECD tends to indicate a **high disease burden.**

Treatment is indicated in all cases and should be aggressive.

VASCULAR MANIFESTATIONS



AORTIC INVOLVEMENT
Circumferential regular thickening
Abdominal 25%
Thoracic 25%
Both 50%
No stenosis
‘Coated Aorta’



VASCULAR MANIFESTATIONS

VENOUS INVOLVEMENT

Venous involvement in ECD is very uncommon. Case reports describe deep vein **thrombosis** and pulmonary embolism, sagittal sinus thrombosis, obstruction of the superior vena cava, and coronary sinus involvement.