Tumour markers are not for screening!

1) Recognise the limitations of serum tumour markers in the asymptomatic patient

2) Identify the role of serum tumour markers in monitoring treatment response in metastatic disease
Population based Screening or opportunistic case finding.
Population-based screening

- is where a test is offered systematically to all individuals in the defined target group within a framework of agreed policy, protocols, quality management, monitoring and evaluation.
WHO Principles of Early Disease Detection

- **The condition:**
  The condition should be an important health problem.
  There should be a recognisable latent or early symptomatic stage.
  The natural history of the condition, including development from latent to declared disease should be adequately understood.

- **Test**
  There should be a suitable test or examination.
  The test should be acceptable to the population.

- **Treatment**
  There should be an accepted treatment for patients with recognised disease.

- **Screening Program**
  There should be an agreed policy on whom to treat as patients.
  Facilities for diagnosis and treatment should be available.
  The cost of case-findings (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
  Case-findings should be a continuing process and not a ‘once and for all’ project.
Testing for a condition.

- How likely is the test to detect the presence of a characteristic in someone with the characteristic (sensitivity)?
- How likely is the test to detect the absence of a characteristic in someone without the characteristic (specificity)?
- How likely is someone with a positive test result to actually have the characteristic (positive predictive value)?
- How likely is someone with a negative test result to actually not have the characteristic (negative predictive value)?
Positive and negative predictive values

Depend on the prevalence of the characteristic in a given population.

the rarer the characteristic, the lower the positive predictive value.

e.g. a positive stress test in a 24 yr old athlete with atypical chest pain has a very low positive predictive value, because coronary heart disease is rare in that population.
Remember

Pretest probability is low for rare characteristics
Opportunistic case-finding

- occurs when a test is offered to an individual without symptoms of the disease when they present to a health care practitioner for reasons unrelated to that disease.
Testing in the high risk individual

- The rare but real patients who are truly at high risk.
  - e.g. a member of a known BRCA1 or 2 family
The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO)

- prospective, randomised controlled trial investigating ovarian cancer screening in over 70,000 women aged 55 to 74 years recruited from 1993–2001 in USA. The participants were randomised to control (no screening) or to CA125 and TVUS. The primary endpoint of the study is the effect on ovarian cancer mortality. Preliminary data have been reported based on initial screening results in the group that received screening (n=28,816 women who received at least one test). The positive predictive value for invasive cancer for an abnormal CA125 was 3.7%, for abnormal TVUS was 1%, and if both CA125 and TVUS were abnormal was 23.5%.
CONCLUSIONS:

Among women in the general US population, simultaneous screening with CA-125 and transvaginal ultrasound compared with usual care did not reduce ovarian cancer mortality. Diagnostic evaluation following a false-positive screening test result was associated with complications.
CA125 in patients without ovarian cancer.

- Due to lack of sensitivity for stage I disease and lack of specificity, CA125 is of little value in the detection of early ovarian cancer. At present, therefore, CA125, either alone or in combination with other modalities, cannot be recommended for screening for ovarian cancer in asymptomatic women outside the context of a randomized controlled trial.
BUT

- In a woman with a pelvic mass...

- Preoperative levels, may aid the differentiation of benign and malignant pelvic masses
Serial levels during chemotherapy for ovarian cancer are useful for assessing response to treatment.
BUT

- Although serial monitoring following initial chemotherapy can lead to the early detection of recurrent disease, the clinical value of this lead-time is unclear.

- Implications???
Serum CA 125, quantified by an immunoradiometric assay employing the monoclonal antibody 0C125 was found to be elevated in 48/58 (83%) of patients with established ovarian cancer.

There was a positive correlation between the level of serum CA125 and body burden of tumour.
AND

- Variation in CA125 level reflected disease progression or regression in 21/23 instances.

- Three of 9 patients tested showed an acute elevation of CA125 in the first week following chemotherapy and this effect predicted a good response to treatment.

- 11/27 patients with non-ovarian adenocarcinoma showed elevated CA125 levels.
Tumour markers and Breast cancer

- Not used as screening test
- Used to monitor response in those patients who secrete the protein
- CA15-3 was above the normal limits of 25 U/ml in 31% of the patients with breast cancer, in 22% of patients with other malignancies, and in 9% of patients with benign diseases.
CA15.3 at presentation with ascites and abn bone scan
CA15.3 metastatic Breast Cancer

CA 15-3 - Architect (kU/L)
Value of 55.000 is abnormally high.
PSA Architect

PSA Total - Architect

PSA Total - Architect (ug/L)

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KNIGHT, DEREK JOHN
CEA in patients with a history of bowel cancer

- IS recommended in the Follow up of patients after surgery and adjuvant chemotherapy.
- BECAUSE it has been demonstrated that a patient with low volume liver metastases can be cured by surgery ( +/- other modalities)
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