



College of Pharmacy

Fifth Stage

Clinical Chemistry

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Lecture 1

Tumor Markers

Tumor Markers

Tumor markers: are substances that secreted into body fluids by tumors and antigens expressed on cell surfaces and can reflect the presence or progress of a tumor. A tumor markers include substances like enzymes, proteins and smaller peptides.

A tumor marker should ideally be:

1. One handard per cent **sensitive** (sensitivity is true-positive rate per total affected): levels should be raised if the tumor is present.
2. One handard per cent **specific** (specificity is true-negative rate per total unaffected): levels should not be raised if the tumor is not present.

Tumor markers may be used for the following:

1. To **screen** for disease. A tumor markers that sufficiently sensitive or specific are used to screen for the presence of a tumor.
2. To **diagnose** a tumor. If a patient presents with clinical signs or symptoms, the measurement of a marker in plasma or urine may very occasionally be used to confirm a diagnosis.
3. To determine the **prognosis**. In some cases the concentration of a specific marker is related to the mass or spread of the tumor.
4. To **monitor** the response to treatment. If a tumor marker is present, the rate of its decrease in concentration may be used to assess the response to treatment such as surgery, chemotherapy or radiotherapy.
5. To identify the **recurrence** of a tumor. If the concentration of the marker was previously raised, intermittent measurement during remission may sometimes be used to identify recurrence.

1. Prostate-specific antigen (PSA)

Prostate-specific antigen (PSA) is a marker for prostatic carcinoma, a common **male** tumour, and is a 33-kDa **protein**; it has a plasma half-life of about 3 days. Its level is **raised** in **benign prostatic hyperplasia** (BPH) and **prostatic carcinoma** but also in **prostate infection**, for example prostatitis, and after **rectal examination**. Levels of PSA increase with **age**, which is mainly due to the increase in the volume of the prostate that occurs. Therefore age adjusted reference ranges should be used.

One diagnostic limitation is that the values of PSA overlap in BPH and prostatic carcinoma. After a **radical prostatectomy**, plasma PSA levels become undetectable at 2-3 weeks. **Finasteride**, a 5- α -reductase inhibitor that is sometimes used to treat BPH, decreases plasma PSA by up to 50 per cent.

The PSA is bound in the plasma to either α_1 -antichymotrypsin or α_2 -macroglobulin. The concentration of **bound or complexed PSA is higher in prostate carcinoma**, whereas that of **free PSA is higher in BPH**. The **ratio of free to total PSA** is lower in men with prostatic carcinoma. The **PSA index** is expressed as the percentage of the total plasma PSA that is free; an index **above about 17 per cent is suggestive of BPH** and one of **less than 17 per cent of prostate carcinoma**.

2. Carcinoembryonic antigen (CEA)

Carcinoembryonic antigen may be produced by **some malignant tumors**, especially **colorectal carcinomas**. Plasma CEA estimations may sometimes help to **monitor the effectiveness of treatment**, or **recurrence after treatment**. Plasma concentrations correlate poorly with tumor mass, but a very high concentration usually indicates a bad prognosis. Plasma concentrations may also rise in **non-malignant disease** of the **gastrointestinal tract** and in **smokers**. Thus, **the test is non-specific and thus lacks value in diagnosis**.

3. α -Fetoprotein (AFP)

α -Fetoprotein (AFP) is an **oncofetal protein**, the synthesis of which is suppressed as the fetus matures. Concentrations may be very high in the plasma of patients with certain tumors such as **hepatocellular carcinoma** (primary hepatomas and hepatoblastomas) and **teratoma**.

4. Human chorionic gonadotrophin (hCG)

Human chorionic gonadotrophin (hCG) is normally produced by the placenta, but also by trophoblastic cells of **gonadal and extragonadal germ cell tumors**. Ectopic secretion has been observed in some **bronchial carcinomas**. The measurement of hCG can be used to screen for **choriocarcinoma** in women who have had a hydatidiform mole. Plasma concentrations may be raised in patients with malignancy of the gonads such as **seminomas**, and hCG may be used to monitor the response to treatment and tumor recurrence.

5. Carbohydrate antigens (CAs)

Carbohydrate antigens (CAs) are a group of tumor markers, raised plasma concentrations of which may be used to monitor the response to treatment and the recurrence of certain tumors.

A. **CA-125** concentration may be raised in the plasma of patients with **ovarian carcinoma**. It can also be raised in pregnancy, fibroids, liver and pancreatic disease, endometriosis and pelvic inflammatory disease.

B. **CA-15-3** concentration may be raised in the plasma of some patients with advanced **breast carcinoma**, although it can also be raised in cirrhosis, and with ovarian cysts.

C. **CA-19-9** concentration may be raised in the plasma of patients with **pancreatic or colorectal carcinoma** and those with obstructive liver disease.

None of the CA tumor markers fulfils the criteria of an ideal marker, as none is sufficiently sensitive or specific to be used to screen for early disease.

6. Other tumour markers

- A. **Serum paraprotein** and **urinary Bence Jones protein** for **multiple myeloma**.
- B. **Plasma lactate dehydrogenase (LDH)**: the activity can be raised in certain **haematological tumors** such as **lymphomas**.
- C. **Placental alkaline phosphatase**: true placental alkaline phosphatase and **placental-like isoenzyme** levels are raised in **seminoma** and **dysgerminoma**. Levels are not usually raised in **teratomata**. **In conjunction with AFP and hCG**, it is useful in the **diagnosis** and **monitoring** of **extra gonadal** and **gonadal germ cell tumors**.
- D. **Thyroglobulin**: this high-molecular-weight protein is produced in the follicular cells of the thyroid. Its concentration is raised in **follicular carcinoma of the thyroid**.
- E. **Neuronal-specific enolase**: plasma levels may be raised in **small cell lung carcinoma** and **neuroblastoma**.
- F. **Inhibin**: this is secreted by the granulosa cells of the ovary and by the Sertoli cells of the testis. It can be used as a plasma tumour marker of **ovarian granulosa cell tumors** and **testicular Sertoli cell tumors**.
- G. **Squamous cell carcinoma antigen**: this is a plasma tumor marker of potential use in **squamous cell carcinoma of the cervix**.
- H. **Chromogranin A** is released from neuroendocrine cells such as in **phaeochromocytoma** and **carcinoid tumors**.
- I. **Protein S100B** is a calcium-binding protein. It is expressed in brain astrocytes and glial cells and also in melanocytes and may be useful in monitoring therapy in **malignant melanoma**.
- J. **Human epididymis protein (HE4)** is being used as a tumour marker for **ovarian carcinoma**.