

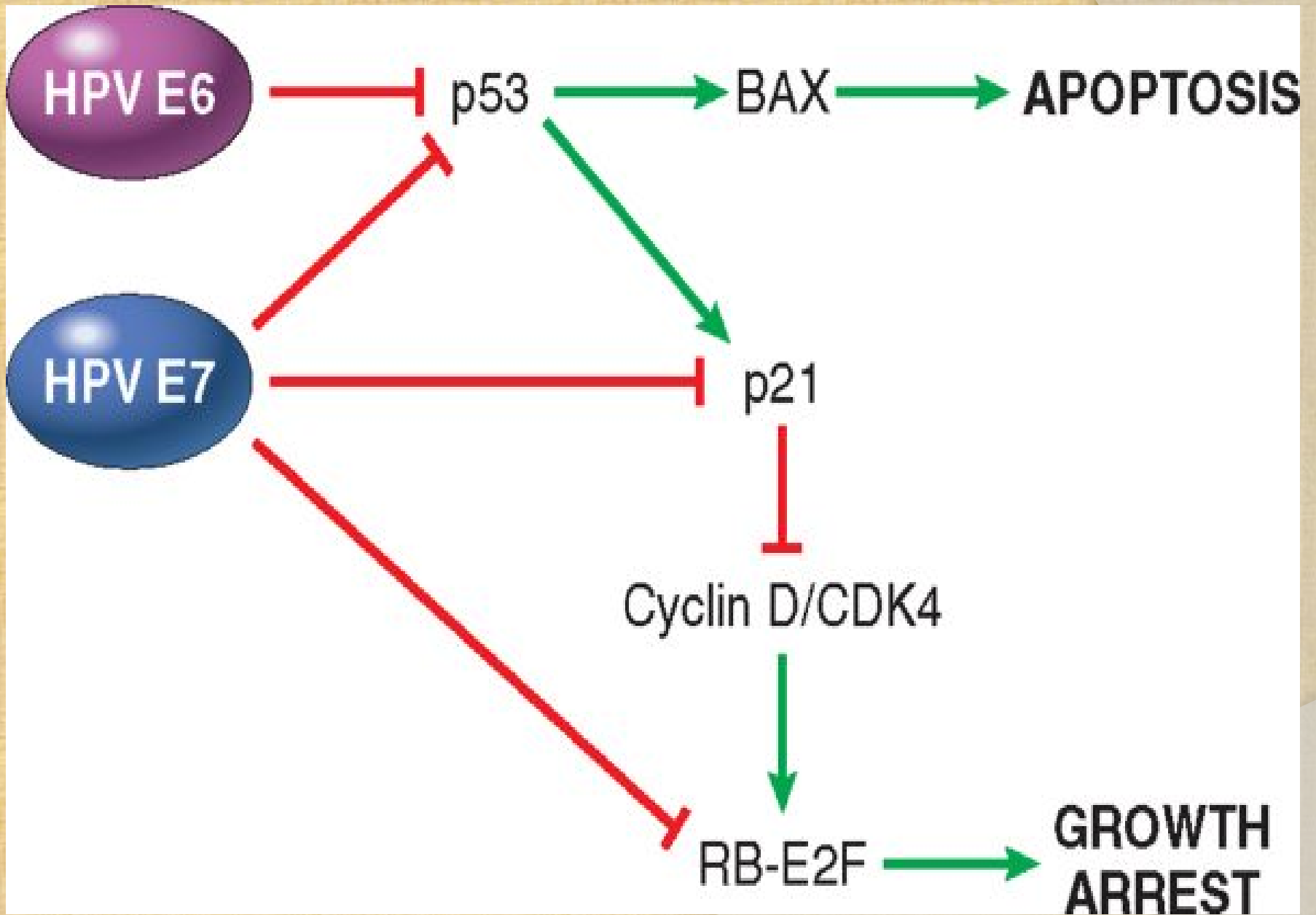
◎ VIRAL & MICROBIAL ONCOGENESIS

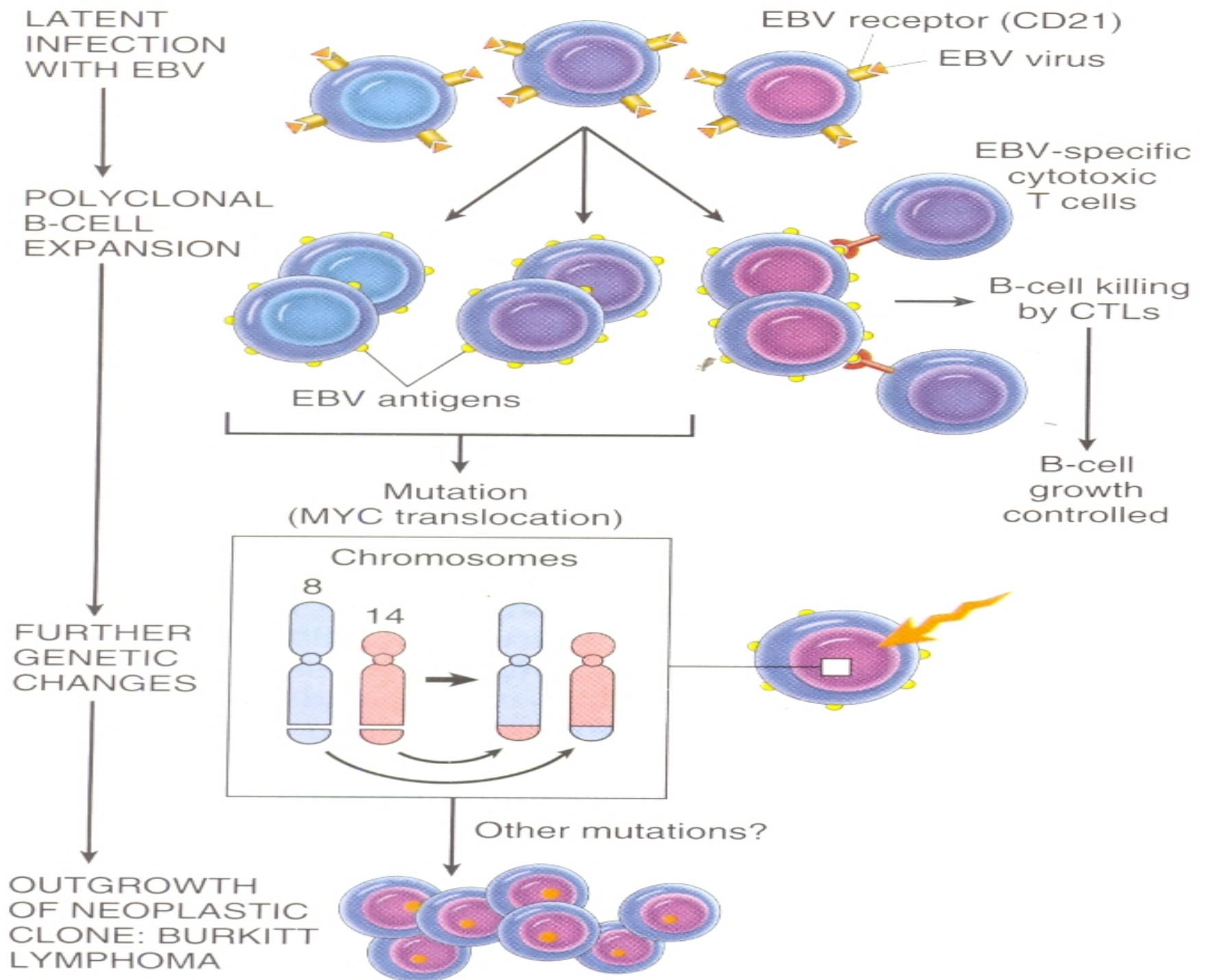
Oncogenic RNA Viruses

- ◎ HTLV1- Only Retrovirus- T cell leukemia
- ◎ In immunodeficient like HIV HTLV1 has tropism for CD4 T cells
- ◎ HTLV-1 encodes viral TAX protein which turns on genes for cytokines & receptors in T cells- it stimulates T-cell proliferation- initially polyclonal- these T-cells are at inc. risk of secondary mutations leading to outgrowth of monoclonal leukemia

ONCOGENIC DNA VIRUSES

- ⊙ HPV, EBV, KSHV-HHV8, HBV, HCV.
- ⊙ 70-80% HCC-multifactorial but dominant effect is immunologically mediated ch. Inf.-hep. Injury- stimulation of hepatocyte proliferation-ROS-DNA damage
- ⊙ H.pylori – immune mediated ch. Inf.-Gastric cell proliferation-ROS-DNA damage





Hepatitis B and C Viruses

- Epidemiologic Studies suggest close association b/w HBV infection and liver cancer
- 70 to 85% of HCC are due to HBV or HCV
- Oncogenic effects of HBV & HCV are immunologically mediated ch inflammation causing hepatocyte injury, proliferation-ROS-DNA damage



CLINICAL ASPECTS OF NEOPLASIA

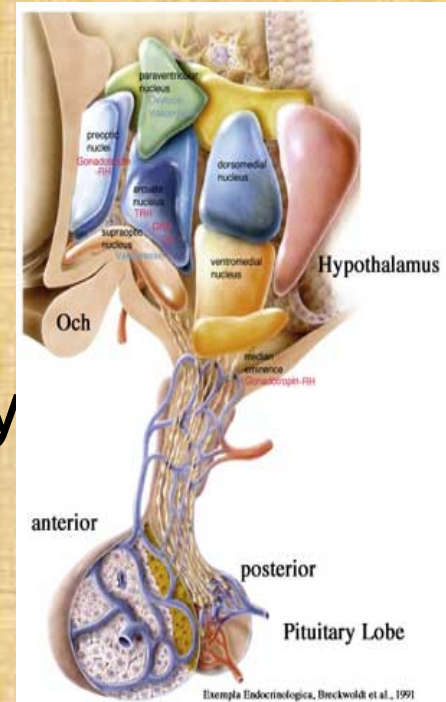
Tumors may cause problems because of:

1. Location & impingement on adjacent st.
2. Functional activity such as hormone synthesis or development of paraneoplastic syndromes
3. Bleeding & infections when tumor ulcerates through adjacent surfaces
4. Symptoms that result from rupture or infarction
5. Cachexia or wasting

Effects Of Tumor On Host

Location is crucial in both benign & malignant tumors

- ⦿ A small pituitary adenoma (1cm)
- ⦿ A small leiomyoma (0.5cm) in wall of Renal A
- ⦿ A small Ca within CBD-Fatal billiary tract obstruction



Hormone Production

- Seen in neoplasms arising in endocrine glands
- Adenomas & Ca arising in β cells of pancreatic islets of langerhans – Fatal **hyperinsulinism**
- Some Adenomas & Ca of adrenal cortex elaborate corticosteroids e.g; **aldosterone**
- A tumor may ulcerate through surface.
 - Tumors that protrude into gut may be caught in peristaltic pull causing intussusception-obs & infarction

CANCER CACHESIA

- ⊙ Progressive loss of **body fat** and **lean body mass**, accompanied by profound weakness, anorexia & anemia, caused by release of **cytokines** by tumor or host
- ⊙ Not caused by nutritional demands of tumor
- ⊙ **TNF** produced by macrophages in response to tumor cells or by tumor cells themselves
- ⊙ TNF suppresses appetite, inhibits lipoprotein lipase □ inhibiting release of FFA

PARANEOPLASTIC SYNDROMES

Systemic symptoms that can not be explained by tumor spread or by hormones appropriate to the tissue, are caused by ectopic production & secretion of bioactive substances such as ACTH, PTHrP, TGF- α



Paraneoplastic Syndrome

- Cushing syndrome -----ACTH
- Hypercalcemia-----PTHrP, TGF- α , TNF,IL-1
- Hypoglycemia-----Insulin or related
- Carcinoid syndroma---Serotonin, Bradykinin
- Polycythemia-----Erythropoitin
- SIADH-----ADH, ANP
- Myasthenia-----Immunological
- Venous thrombosis-----Mucins activate clotting
- Nephrotic Syndrome---Tumor antigens, immune complexes



GRADING AND STAGING OF CANCER

- Grading: Degree of differentiation-grade I-IV
- Staging: Extent of spread of cancer, based on **size** of primary tumor,spread to regional LN & presence or absence of metastasis
- Two methods-TNM & AJC
- T1-T4, N0-N3, M0-M1
- AJC: Stage 0 to IV
- Staging is of greater clinical value than grading

CARCINOGENESIS:

THE MOLECULAR BASIS OF CANCER

- ① Nonlethal genetic damage
- ① 4 classes of normal regulatory genes are principal targets of genetic damage