INTRODUCTION

Nonseminomatous germ cell tumors (NSGCT) are the most frequent malignancies in males aged 25 to 35 years.

NSGCT of the testis may contain six histological components: seminoma, embryonal carcinoma, mature and immature teratoma, yolk sac tumor and choriocarcinoma.

Different classification systems exist, based on different theories about the histogenesis of these tumors, although it is now well agreed upon that these tumors originate from transformed germ cells showing the carcinoma in situ pattern (CIS).

The six histological components (mentioned above) have a different biological behaviour, response to chemotherapy and prognosis.

In the past decade the prognosis of NSGCT patients has much improved, which is mainly due to the development of effective combination chemotherapy. After chemotherapy metastases frequently consist of mature teratoma only, which is considered to be a benign remnant.

Another improvement in the clinical management of NSGCT patients has been the discovery of tumor markers, such as alphafetoprotein (AFP) and human chorionic gonadotropin (HCG), which have shown to be very useful in the detection of tumor recurrence after chemotherapy.

With the use of immunohistochemical techniques it is possible to visualize the presence of tumor markers in tumor tissue sections. Correlating immunohistochemical staining of tumor markers in tumor tissue with serum tumor marker levels has given much insight in the behaviour of serum tumor marker concentrations before, during and after chemotherapy.

This thesis, written from a pathologist's point of view, deals with these two topics in the pathology of NSGCT: tumor maturation due to chemotherapy and immunohistochemical analysis of tumor marker production by the different histological components.

The aim of this thesis was:

a. to study the development of mature teratoma which is left following chemotherapy, comparing the histology of testicular NSGCT and retroperitoneal (RLN) metastases in untreated patients and in patients treated with dactinomycin and PVB.
b. to record differences in the macroscopical and microscopical appearance of retroperitoneal mature teratoma, surgically removed 4 to 6 weeks as opposed to 4 to 6 months after PVB chemotherapy.

c. to correlate the presence of AFP, HCG, SP-1 and CEA in tissue sections of testicular NSGCT and RLN metastases after chemotherapy with the serum levels of these tumor markers.
d. to determine the value of AFP, HCG, SP-1 and CEA as tumor marker for advanced stage testicular NSGCT.
e. to analyse AFP, HCG and CEA production in mature teratomatous elements in RLN metastases after PVB chemotherapy.

In chapter 1 the pathology of germ cell tumors of the testis is reviewed. In addition data on epidemiology, etiology, histology, histological classification, theories of histogenesis and clinical behaviour of these tumors are discussed.

In chapters 2 and 3 the histogenesis of fully differentiated mature teratoma as only component in retroperitoneal lymph node metastases following PVB chemotherapy and the apparent benign growth of this component that may occur in the course of time was studied using patients treated in the University Hospital in Groningen.

In chapters 4, 5 and 6 the production of the tumor markers AFP, HCG, SP-1 and CEA in NSGCT patients was analyzed, relating serum tumor marker levels to the immunoperoxidase localization of these substances in the different histological components of NSGCT, both in testicular tumors and residual retroperitoneal tumors following PVB chemotherapy.