General Introduction
INTRODUCTION

Autopsy pathology is artificially divided in clinical and forensic autopsies. In this modern era with changing political, ethical and financial views, questions concerning both clinical and forensic autopsies are raised. While on one hand advances in medicine give rise to these questions, on the other hand these advances generate possibilities to create additional tools, which are needed to improve autopsy diagnostics. In the field of forensic pathology different research areas are still in development stage, like wound age determination, of which knowledge is limited. Wound age determination of skin injuries is however not only crucial for autopsy diagnostics but also in wounds of living subjects, related to forensic medicine. In this thesis we aimed to answer raised questions about autopsy pathology, both clinical and forensic, and at the same time tried to improve the diagnosis of skin injuries.

I: Autopsy pathology
The autopsy is the most important tool for retrospective quality assessment of clinical diagnoses and a key educational tool. Through the years the rates of clinical autopsies however have been declining worldwide, for which different reasons can be pointed out. One of the main reasons is the belief among clinicians that the autopsy had become redundant due to advances in laboratory testing and modern imaging techniques. However, previous studies comparing clinical diagnoses and autopsy findings showed a major discrepancy rate of approximately 25%. We wanted to evaluate the value of clinical autopsies in this modern era in the Netherlands and have studied this by determining the major and minor discrepancy rates between autopsy findings and clinical data, and analyzed the influence of several factors on the frequency of these major and minor discrepancies (Chapter 2), including the role of microscopical examination to identify the cause of death.

In the Netherlands there are no rules or limitations regarding the sampling or retention of material at post-mortem examination. However in the U.K., there are strict rules regarding tissue retention for microscopic examination as there is a conflict for the pathologist between the legal authority and codes of practice for medico-legal investigation of death, which could negatively influence the diagnostic process. Pathologists in the U.K. are namely authorized to retain only that material which ‘bears upon the cause of death’ or ‘the identification of the deceased’ when performing a post-mortem examination under the authority of HM Coroner. In contrast, general guidelines from The Royal College of Pathologists (RCPath) advise the pathologist to undertake a histological examination of all major organs in all cases. Studies concerning the use of routine histological examination in forensic post-mortem examinations are contradictory. We therefore evaluated the role of histology when determining the cause of death in forensic autopsies performed at a forensic pathology unit in England (Chapter 3).
Next to the use of histology, which in previous studies has shown to have major impact on previously made diagnoses in hospital autopsies, additional techniques could also improve autopsy diagnostics, like f.i. immunohistochemistry in the diagnosis of lymphocytic myocarditis. Lymphocytic myocarditis namely is a cardiac disease that is difficult to diagnose on histological slides only while it is a cause of sudden death, also in young patients. Its cause is most often viral and/or autoimmune-mediated. For endomyocardial biopsies obtained from living patients the so-called Dallas criteria have been developed to diagnose myocarditis. According to these Dallas criteria, a myocarditis is diagnosed in case histologically inflammatory infiltrates are found within the myocardium associated with myocyte necrosis of non-ischemic origin. However, it also has become clear that these criteria are not that adequate for diagnosing lymphocytic myocarditis in endomyocardial biopsies due to sampling error. Different quantitative and non-quantitative criteria for the diagnosis lymphocytic myocarditis in endomyocardial biopsies since then have been developed. Clear criteria for the diagnosis of lymphocytic myocarditis in autopsy hearts however do not exist. Incidences of lymphocytic myocarditis in the adult autopsy population are not well known, while unequivocal guidelines for its diagnosis in autopsy hearts are needed. We have therefore analyzed a new method for diagnosing (borderline) lymphocytic myocarditis in a cohort of adult autopsies, for which we combined the use of immunohistochemical stainings with the Dallas criteria (Chapter 4).

II: Skin wound age determination
The determination of skin wound age in a forensic case including the determination whether a wound is vital or post-mortem induced, is crucial, f.i. to relate a reported moment of impact to a skin injury. It however remains challenging to the (forensic) pathologist to give a correct estimation of skin wound age since the golden standard has yet to be found. For this, the combination of amnestic information with macroscopic and microscopic analysis of the wound is pivotal. Although several histological characteristics have been suggested to prove wound vitality in autopsies, such as hemorrhage, these have shown not to be discriminative. Immunohistochemical markers have shown to be useful in wound age analysis, including markers identifying inflammatory cells or extracellular matrix component. Relatively less is known of the role of coagulation in wound age determination. We hypothesized that activation of the coagulation cascade proteins Fibronectin, P-selectin (CD62p) and Factor VIII in wound hemorrhage, could form additional discriminating factors in wound age determination and we wondered whether they could discriminate between vital and post mortem wounds (Chapter 5). Subsequently we developed a probability scoring system for wound injury dating in autopsy wounds.
Next to forensic pathologists, in the Netherlands also forensic physicians have to evaluate skin injuries. They are then asked to give an estimation of wound age in living victims of violence or molestation. However, the reproducibility of macroscopic findings is low and not strong enough to hold in court. As opposed to forensic autopsies, in living subjects it is not ethical to excise skin wounds. However small skin biopsies, representing the superficial border area of a wound, can be taken. We wondered whether skin biopsies would also be suitable for (immuno)histochemical analysis to determine wound age. For this we studied histological markers that have been described in wound healing and several extracellular matrix proteins that have already been applied in autopsy wounds. We subsequently analysed different inflammatory markers that were mostly studied in previous autopsy studies in skin biopsies of living subjects, including the development of a probability scoring system.
REFERENCES


59. Howes S, Harrey SC. Healing of wounds as determined by their tensile strength. JAMA 1929;92:42.


