

Autopsy: The Dying Diagnostic

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Introduction

Autopsy, derived from the Greek 'autos' and 'opsomeri' means 'to see for oneself', originates from mummification using human dissection around 3000 BC. Over five millennia it has facilitated the study of human anatomy, physiology, and pathophysiology culminating in 21st century medicine. Autopsy is divided into medico-scientific (consented, usually by a relative) and medico-legal (required by legal authority such as HM Coroner in the UK). For the last fifty years a worldwide decline in consented autopsy has occurred, such that in many countries it is on the brink of extinction [1]. For example, 30 years ago, consented autopsy rates were around 25% of inpatient deaths in the UK whereas in 2013 the average rate was less than 1%. Despite the rapid decline, autopsy continues to benefit 21st century medicine, including roles in microbiology and diagnostics.

Autopsy Microbiology

Consented autopsy has two main microbiological roles in modern medicine. Firstly; to either confirm an antemortem infectious diagnosis or culture and identify undiagnosed antemortem pathogenic organisms. Infectious disease continues to feature as a major cause of mortality worldwide, especially in the developing world, where autopsy has been shown to identify a plethora of undiagnosed antemortem microbial pathologies [2].

There is, and has been for over a century, florid contention amongst the medical profession over the diagnostic use of post-mortem blood and tissue cultures [3-5]. The basis of the controversy stems from false positive results due to post-mortem indigenous bacterial invasion into the circulation and is founded in two main postulates: transmigration and agonal spread [5]. Transmigration was observed by Gradwohl, as bloodstream bacterial contamination due to the migration of mucosal or tissue flora occurring after the cessation of the systemic circulation leading to a rapidly deficient functional immune system [5,6]. Later, Fredette described agonal spread-bloodstream bacterial contamination during the agonal period due to a declining systemic circulation [5,7].

In order to reduce false positive results, it is recommended that autopsy occurs aseptically, promptly and with preceding cadaveric refrigeration [5]. A key retrospective review of over 2,000 autopsies, published by Carpenter et al. showed that the rate of positive post-mortem blood cultures were positively correlated with time after death [5,8]. However other similar studies have failed to reproduce this and argue against the importance of post-mortem bacterial transmigration [5-9]. Controversy remains.

The second major role of microbiology in autopsy is to enable the consented removal/examination of tissue and cultures of microorganisms to better our understanding of disease and its

pathogenesis. There is a long and thriving history of autopsy providing a pivotal role in the advancement of medical knowledge. Welch et al. discovered a novel bacterium at autopsy in 1891 [10], and since autopsy studies have aided our understanding in invasive fungal disease [11], *Toxoplasma gondii* [12], congenital rubella syndrome [13]. Severe acute respiratory syndrome (SARS) [14], tuberculosis/HIV co-infection [15] and cerebral malaria [16] to name but a few. Most recently consented fetal autopsy has aided in the mounting evidence of a causal link between Zika virus and microcephaly [17]. It is postulated that a lack of autopsy studies into middle east respiratory syndrome (MERS), a modern major public health epidemic with a case fatality of 30%, is one of the reasons behind our reduced knowledge of this coronavirus compared to SARS [14].

Autopsy Diagnostics

A commonly held belief amongst physicians is that classical post-mortem is outdated in the current era of sophisticated antemortem diagnostics [18,19]. There is a widespread belief that the opportunity for autopsy to reveal major discrepancies between antemortem and post-mortem diagnosis has long past [20,21]. One study found that 81% of clinicians believe advances in CT imaging have reduced the value of autopsy [18]. Conflicting research shows little change in misdiagnosis rates over recent decades [22-24] and that modern medicine continues to have significant misdiagnosis rates suggesting the role of autopsy as a useful determinant of underlying pathology remains [21,24-29].

Twenty-two percent of death certificates have been shown to have, "no value at all because of inadequate diagnosis" [30]. Death certificates are frequently completed by junior medical staff and their worryingly high inaccuracy rates contribute to misleading mortality statistics. Autopsy acts as a gold standard for diagnostics which, if widely used, would result in highly accurate morbidity and mortality statistics and thus improved epidemiological data to base resource allocation.

Modern medicine means the population are living longer and accumulating co-morbidities and complex disease. Autopsy enables the interaction of diseases to be studied and hence aid in our understanding of their clinical picture. From comparing antemortem and postmortem diagnoses, clinicians can improve clinicopathological correlation, leading to improved antemortem diagnostics. This would lead to improved detection of disease enabling prompt treatment and also reduced false-positive diagnoses, hence reducing avoidable iatrogenic harm.

A large study of many thousands of autopsies in American intensive care units showed that 8% of patients died with a class 1 diagnostic error-had the diagnosis been made antemortem then the patient would

have has an altered treatment plan and potential increased survival [28]. Intensive care patients are some of the most investigated patients in a hospital which begs the question-what proportion of general medical/surgical patients die misdiagnosed? The most prevalent misdiagnoses in the intensive care setting are pulmonary embolism, myocardial infarction, pneumonia and aspergillosis-all of which are commonly treatable if not preventable [28]. Furthermore, only 48% of patients who die due to myocardial infarction have the diagnosis on their death certificate-if we can increase our antemortem diagnosis then prompt treatment can be initiated and lives saved [30].

Importantly, autopsy should not be restricted to deaths that are complex or unexpected. Death in the terminally ill and elderly provide invaluable information on mortality, diagnostics, comorbidities, and training but also benefits the bereaved families.

Consented autopsy enables advances in medical care and diagnostics-resulting in safer care. For example, autopsy has been used in the development of gene therapies, medical procedures, surgical techniques, pharmacology, diagnostic tests and implantable devices [31-33]. The power of autopsy in the development of new technology is demonstrated historically by Rene Laennec (1781-1826) who invented the stethoscope. Laennec used his new instrument to listen to the sounds of the heart and lungs, but was only able to correlate these sounds to pathology via autopsy [34]. Consented autopsy will continue to inspire clinicians to develop new techniques to improve our quality of care.

Combating the Decline

The terminal decline of consented autopsy has shown few signs of slowing-primarily driven by a lack of clinician request for autopsy due to erroneous beliefs that autopsy is outdated and that consent is rarely granted. Combined with this is a general apathy towards autopsy amongst pathologists and ever increasing financial constraints. Despite this, there are many examples where simple interventions such as physician training and common place autopsy requests have resulted in rapid increases in consented autopsy rates [35,36]. These pilot studies prove that autopsy can be revived if the enthusiasm exists.

Summary

Autopsy has been used for millennia to advance our understanding of medicine and science. While controversies still exist over the use of microbiological diagnostic autopsy culture; there is still a strong and significant role for consented autopsy to enable the removal of tissue for research. Using autopsy appropriately, the link between clinical presentation, investigation results and diagnosis can be improved-individuals can learn from previous mistakes and safety of care could improve. The evidence for consented autopsy is strong yet the decline in autopsy rates has unfortunately been stronger. It is time for the medical community to act, to revive enthusiasm and ensure that consented autopsy is appropriately offered, attended and learnt from-otherwise this invaluable diagnostic source will be extinct imminently throughout much of the world.

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