

## Research Article

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# Cellular Damage to the Human Caput Epididymis Resulting from Vasal Obstruction

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### Abstract

**Introduction:** This communication describes the histological features of two patients with two different causes of obstructive azoospermia resulting from vasal obstruction and compares these findings with those in an apparently normal fertile man.

**Results:** Two changes are clearly present in the men with obstructive azoospermia when compared to the normal male. There is a marked reduction in the height of the principal cells and an almost total loss of all the other cells that make up the epididymal epithelium. Within the distended tubules are spermatozoa as well as large numbers of giant cells, macrophages and white blood cells. The presence of such cells suggests that these distended tubules are also the site of production of large amounts of superoxide anions.

**Conclusions:** The changes in the epididymis that are associated with vasal obstruction are very similar despite a difference in the cause of such obstruction. It also implies that sperm aspirated from the epididymis for IVF may well be damaged by contact with superoxide anions resulting from the inflammatory-response cells.

### Keywords

Vasectomy; Obstructive azoospermia; Epididymis

## Introduction

Unwanted vasectomy is now a common cause for people attending an infertility clinic. In 2009, around 23,700 vasectomies were carried out in Australia [1]. With the high rate of marriage breakdown, now approaching 50%, many of these vasectomies come to be regretted.

Little is written about the changes that occur proximal to a vasectomy. However the cases described in this small study and elsewhere Flickinger et al. [2] indicate that more attention should be paid to the sperm aspirated from the epididymis among men with an inoperable obstructive lesion of either the epididymis or of the vas deferens.

In this communication, the anatomy of the efferent ductules is examined in three men, i) a normal and almost certainly fertile male, ii) in a man with a long-term vasectomy and iii) a man with obstruction of the lower epididymis and the vas deferens that was the result of an infective epididymo-orchitis.

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## Case Report

### Case 1 - Sudden death victim who died at the scene of a motor vehicle accident

Little is known of this patient except that he was young and had no apparent history of infertility. The epididymal biopsy was collected more than 20 years ago. Testicular size was deemed to be normal at post-mortem.

Histology of the caput epididymis of the young, sudden death victim.

In the caput epididymis of the young sudden death victim, the efferent ductules are clearly devoid of sperm (Figure 1). The principal cells make up the majority of the ductular epithelium but both basal cells and apical cells are also clearly present as well as halo cells. Numerous stereo-cilia are present and the lumen was notable for its total absence of spermatozoa. This epithelium would thus appear to be entirely normal [3].

In the normal epididymis, the basement membrane of the efferent ductules are made up of highly active myoid cells that assist the passage of the spermatozoa down the efferent ductules and into the epididymal duct [3]. Thus in the normal situation, and in the absence of an obstructive lesion, few sperm are ever seen in the normal human caput epididymis.

### Case 2 - A man with a long-term vasectomy in position

The first pathological case was that of a middle-aged man who presented to a Urologist with a swelling alongside his right testis. Some 18 years previously the patient had undergone a vasectomy and this had never been reversed. This postero-lateral, para-testicular swelling was initially thought to be a tumour but an ultrasound examination of the scrotum did not confirm that diagnosis. Testicular size was normal.

An exploration of the right scrotal sac was performed. The swelling proved to be a distended caput epididymis consequent upon

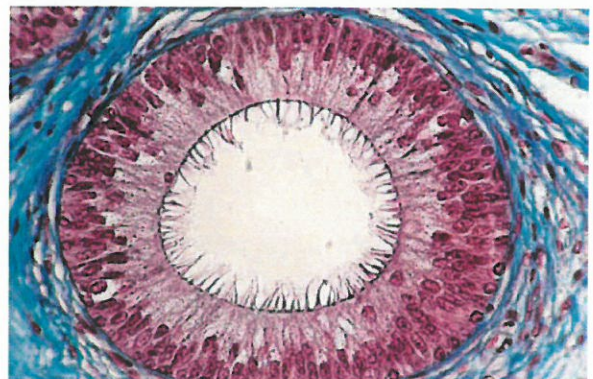


Figure 1: A section of a normal efferent ductule taken from a young sudden death victim. Note the absence of sperm in this ductule. This section is stained using GomoriTrichrome (Magnification x 400).

the presence of the vasectomy. At operation, the upper two thirds of the epididymis were removed and sent for histological examination. Spermatozoa were also collected from the caput epididymis for cryopreservation should further fertility be desired.

Histology of the caput epididymis of the man with the long-term vasectomy (Case 2).

As this patient had undergone a partial epididymectomy, it was possible in this case to examine the whole of the caput epididymis. The lower power sections of the caput epididymis, in contra-distinction to that obtained from the sudden death victim, show the efferent ductules to be full of sperm (Figure 2). However, using increased magnification, it was also noted that the lumen of the efferent ductules not only contained spermatozoa but also large multinucleated giant cells, macrophages, white blood cells and germinal cells (Figure 3). The presence of the germinal cells would suggest the possible presence of an unstable germinal epithelium in this patient. However, a testicular biopsy was not undertaken.

The effect of the vasectomy on the epithelium of the efferent ductules was also marked when compared to the histology of the efferent ductule in a normal caput. The most obvious feature was the apparent reduction in height of the principal cells that, in this patient, could now be described as cuboidal rather than columnar (Figure 3). No apical cells could be seen and only a very small number of basal cells were present. The stereo cilia were present but were markedly reduced in number.

### Case 3 - A man with lower epididymal obstruction

The second pathological case was a man with obstructive azoospermia who was in his mid-thirties and who presented to an infertility clinic with azoospermia. The length of time this azoospermia had been present was not known.

Surgical exploration showed the presence of a lower epididymal obstruction. A small incision was made in the caput epididymis and a biopsy of the efferent ductules was performed. As this procedure was purely diagnostic and was carried out prior to the development of Intra-Cytoplasmic Sperm Injection (ICSI), no sperm were collected for potential fertility treatment.

The histology of the caput epididymis in this man with obstructive

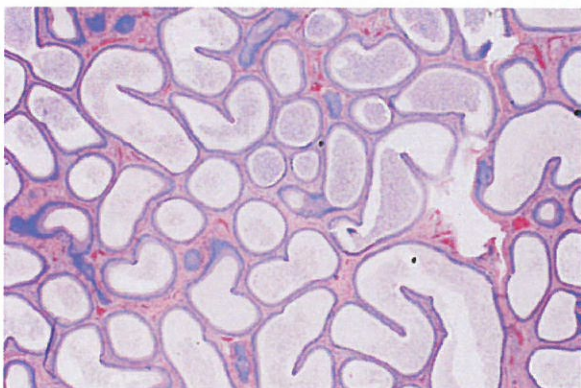


Figure 2: A histological section taken from the caput epididymis of this patient with a vasectomy that had been present for 18 years. Many of the efferent ductules in the caput contain large numbers of spermatozoa. These two sections are both stained with Haematoxylin and Eosin (Magnification x 200).

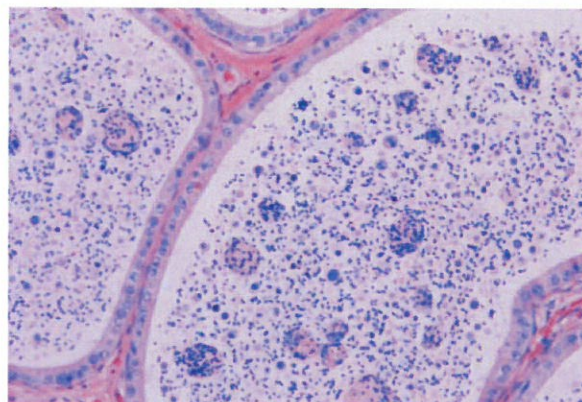


Figure 3: A higher power view of the distended caput epididymis in the patient with a vasectomy that had been carried out 18 years previously. Large numbers of multinucleated giant cells, macrophages and white blood cells are present suggesting but not proving, the presence of excessive amounts of superoxides. (Magnification x 400).

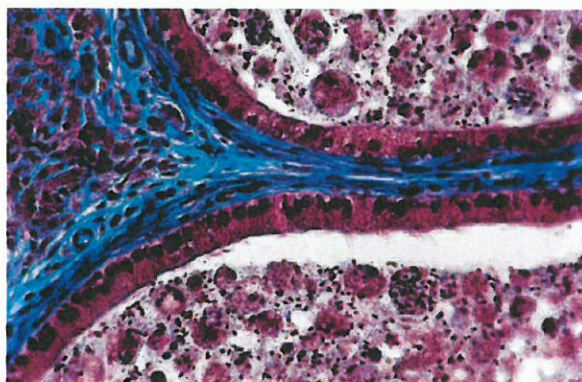


Figure 4: A histological section taken from a man with an upper epididymal obstruction of unknown cause. The histological changes seen here are very similar to those seen in the patient with the long-standing vasectomy. This section has been stained with Gomori Trichrome (Magnification x400).

azoospermia was compared to that taken at post-mortem from the young sudden death victim.

Histology of the caput epididymis in the man with obstructive azoospermia and infertility following epididymo-orchitis (Case 3).

The histological picture of the caput in this patient was strikingly similar to that of the man with the long-term vasectomy (Figure 4). Like the man in Case 2, the efferent ductules are packed full of spermatozoa mixed with many macrophages, giant cells and other white blood cells that are similarly present amongst large numbers of spermatozoa. Also as in Case 2, the size of the principal cells in this patient was similarly reduced and, even in this small specimen, it is fairly clear that there is at least a reduction of both apical and basal cells as well as a marked reduction in the density of the stereo-cilia.

### Discussion

The upper genital tract in the male is anatomically complex. The sperm exit the testis by means of some 10-15 efferent ductules. These ductules are layered and thus lie on top of one another. In the human, they form the caput of the epididymis and have a uniquely complex

epithelium (Cornwall 2009). These efferent ductules all lead into the single epididymal duct.

The male genital tract is a 'one-way' system and thus vasectomy will result in the confinement of all future sperm production behind the site of the vasal obstruction. This obstruction is likely to result in the distension of the duct system proximal to the vasectomy, the trapping of aging and disintegrating spermatozoa within the proximal vas progressing into the epididymal duct. Natural body scavenging mechanisms result in the consequent invasion of the epididymal lumen by macrophages and white blood cells.

There are several features of these cases that have to be considered. Firstly the distension of the upper ducts caused by vasectomy can be sufficiently great as to occasionally be mistaken for a tumour.

From these sections, it is clear that the rete testis fluid has been heavily invaded by white blood cells, macrophages and even multinucleated giant cells [2]. This must mean that the sperm that are trapped behind an obstructive lesion are likely to be in the presence of large amounts of reactive oxygen species and as a consequence could be damaged particularly in relation to their sperm chromatin.

Damaged sperm chromatin may result in both a poor pregnancy rate as well as an increased miscarriage rate [4] due to poor embryo development [5]. Indeed a case could probably be made in this situation for the use of antioxidants prior to any sperm aspiration.

However the situation may be saved if large numbers of sperm can be collected from this rete testis fluid and the diligence of the embryologist is high. If the embryologist is given large numbers of sperm for use in an IVF/ICSI programme, a careful search can reveal the presence of a few morphologically normal sperm with normal movement characteristics. Such sperm, even if few in number, are thus unlikely to be severely affected by oxidative damage. Any perceived normality of the sperm using this selection process is however still only a probability and not a certainty.

This selection process may be the only reason for the good pregnancy rate that is seen among the women using sperm that have been aspirated from above an obstructive lesion of the epididymis [6,7].

The changes in the epithelium of the efferent ductules were clearly profound. Not only was there a change in the size and shape of the principle cells but there was also a change in the type of cells that made up the epithelium. Both the basal cells as well as the apical cells were absent and it appeared that both the clear cells and halo cells had also disappeared from the epithelium of the efferent ductule. As these epithelial changes were present in both the man with the long-term vasectomy as well as in the man with non-iatrogenic obstruction, this would indicate that these changes relate to the obstruction only and not to its cause.

This study has demonstrated the marked changes that may occur among men with long-term obstructive lesions of either the vas deferens or the lower epididymis. These changes appear to have been demonstrated before Silber [8] but for all these years seem to have received scant attention. Whether the epithelium of the efferent ductules ever reverts to normal after relief of such an obstruction is not known. It is difficult to imagine that these changes could ever revert back to normal.

This area needs a great deal more study. It is possible that great

care is needed to select sperm from among those designated an epididymal aspirate within an IVF/ICSI program among men with inoperable obstructive lesions of the upper genital tract. Sperm aspirated from the upper epididymis among men should not necessarily be considered to be normal. It is likely that great care should be taken in selecting sperm for use in an IVF/ICSI programme when the sperm have been aspirated from the epididymis.

## Ethical Statement

Cases 1 and 3 were collected many years ago when Ethics Committee permission for publication was not necessary. Case 2 gave the author permission to publish the histology and again as no identifying information was included, Ethics Committee approval was not required.

## Conflict of Interest Statement

Anne Jequier – None

R. Pemberton – None

SJ Yovich – None

R. Cohen – Performed the histological examination in case 2 for which he was paid a fee.

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