EDUCATIONAL COMMENTARY – URINE CASTS

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Learning Objectives

On completion of this exercise, the participant should be able to

- understand the formation of urinary casts;
- discern different types of casts; and
- understand the progression of cast formation.

Casts are structures found in urine that can be an indicator of renal function and disease. Their components and composition are diverse. Their most common structure is cylindrical, with parallel sides, rounded/blunt ends, and, as a general rule, length more than two times the diameter of the cylindrical shape. The diameter is an estimate, however, because a microscopic examination of urine sediment is two-dimensional.

Casts are formed in the lumen of the tubules in the kidney anywhere along the length of the tubule. They develop from the secretion or precipitation of uromodulin, also known as Tamm-Horsfall protein. The secreted uromodulin protein concentrates and becomes a more solid matrix when there is less fluid flow through the tubule. As the uromodulin concentrates, the matrix will incorporate any particle along its path. Red blood cells (RBCs), white blood cells (WBCs), crystals, epithelial cells, bacteria, and other particles in the urine flow may be captured. This is why there is so much diversity in casts and how they are described. Casts are divided into classes, but between these classes, there are gradients and mixtures. As a microscopist reporting an observation, one wants to describe the cast as thoroughly as possible for the clinician.

Due to their size, casts are observed and enumerated under low power for reporting. High power is used to observe and analyze the cast in depth, to give a more descriptive report. When casts are primarily composed of uromodulin protein, they are almost transparent. They can be difficult to recognize if there are no inclusions in the matrix. If the microscope is not properly illuminated or adjusted, the light can "wash out" the fine structure, and the cast may look like part of the background if its classic structure is not recognized. Use of phase contrast microscopy greatly enhances the visibility of casts.

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As the uromodulin concentrates, the simplest resulting cast is a hyaline cast. This structure is mostly composed of the protein matrix with no particle capture. Hyaline casts at times may look like mucus threads. However, mucus threads do not have the thickness of a cast's cylindrical shape with parallel sides. The hyaline cast structure is clear, colorless, non-refractile, and almost transparent. Occasionally, after a hyaline cast leaves the tubule, particles from the urine adhere to the protein surface and make the clear hyaline cast appear granular. Hyaline casts are easily missed when the microscope is not properly adjusted. While focusing the microscope within its depth of field, one can observe the three-dimensional look of the cast. This helps in determining whether the particles are on the surface of the cast.

A different structure that can also be considered a cast is commonly known as a cylindroid (**Figure A**). A cylindroid is tapered at one end and may have some paralleling of sides on the other. These are not true hyaline casts because of the tapering, and they are formed higher up in the renal tubule where it is looped and narrow.

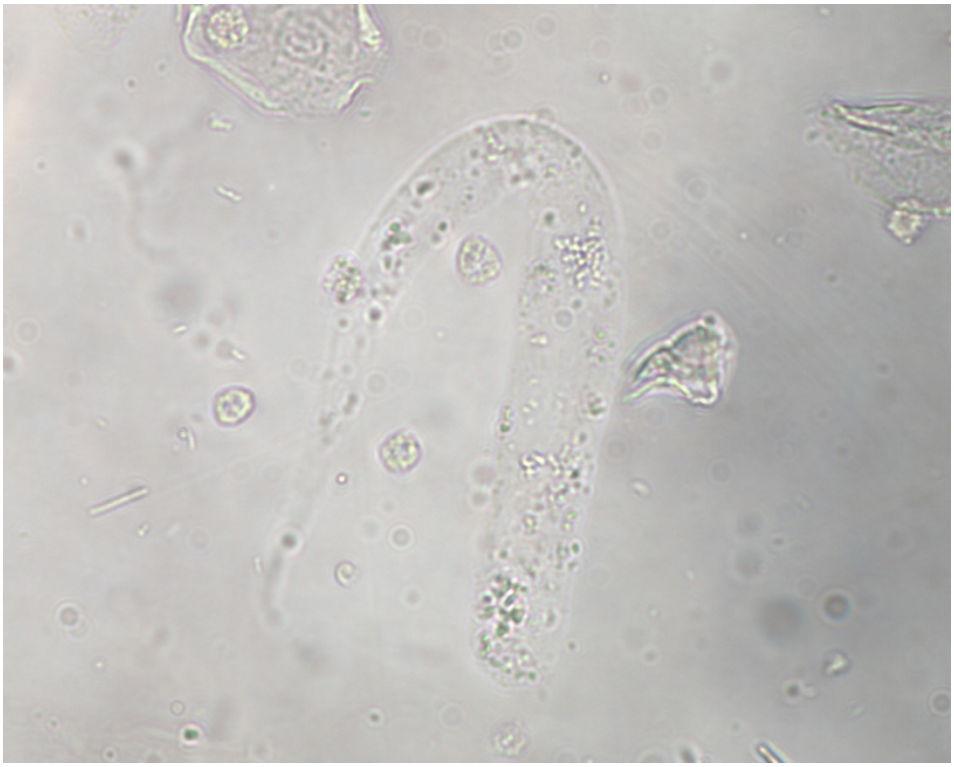

Figure A. This may appear to be a hyaline cast. However, it is a cylindroid where inclusions appear to be on the surface as in the bacteria (which appear clumped, refractile, and out of focus). Notice the tapering of the left end.

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As a hyaline cast forms and condenses in the renal tubule, it can incorporate any particle floating past. If cells are captured and incorporated, casts are identified by the type of cell captured (**Figure B**). These are broadly classified as cellular casts. If RBCs are incorporated, they are called RBC casts; when WBCs are incorporated, they are WBC casts. There are also epithelial cell casts. The incorporated cells must be clearly identifiable and prominent and have an intact cell structure or cell wall.

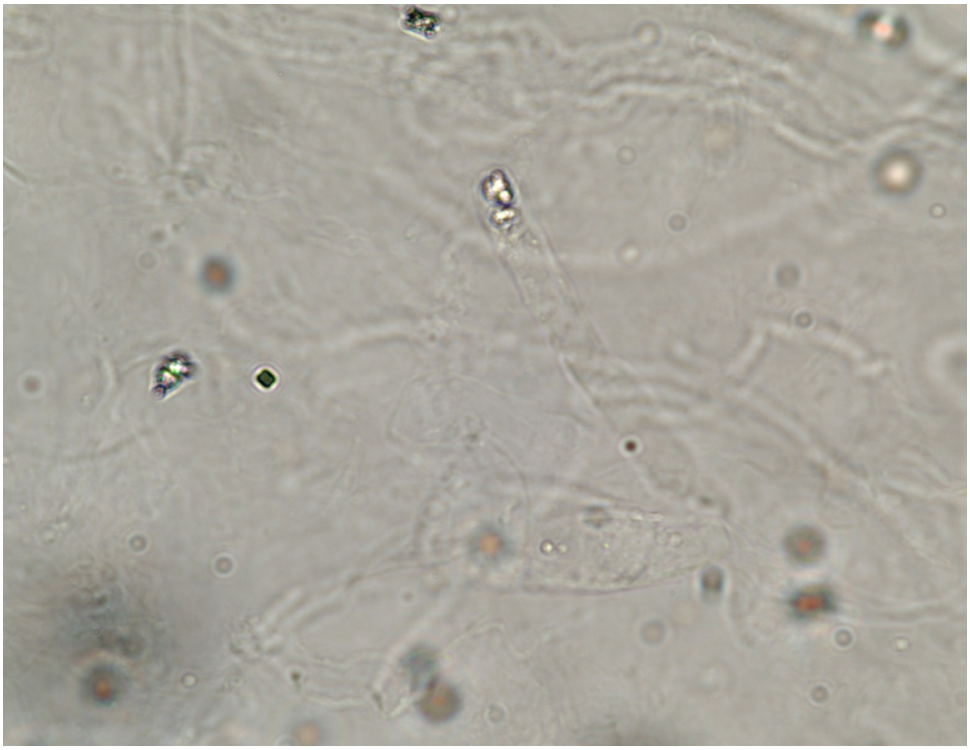

Figure B. Example of a hyaline cast with a possible crystal adhering to it. Notice the parallel sides and rounded ends with a faint outline.

Red blood cell casts are composed primarily of RBCs. When present in the cast, RBCs indicate a disease state or injury to the kidney. There may be few RBCs in the cast, or the cast may be packed with RBCs. When there are a significant number of RBCs in the cast, they tend to displace the uromodulin that holds the cast together. The loss of uromodulin protein weakens structure and the RBC casts break and are usually shorter. As the RBC cast matures in the tubule, the cell membrane may disintegrate. When that happens, the cast becomes a blood or blood pigment cast. There is little or no cellular structure. The cast is orange-yellow color because of the hemoglobin in the RBCs.

White blood cells incorporated in casts are often seen in an infection. The cast may have a few WBCs or it may become packed with WBCs (**Figure C**). Most important for the microscopist when casts are

packed and compressed is the ability to recognize the cells present. One should be able to distinguish the multi-lobular nucleus of the WBCs. Clumps of WBCs in the urine can complicate the recognition of WBC casts. Some WBC clumps mimic the look of a cast. However, WBC clumps do not have the characteristic parallel sides and rounded ends of a cast. The significance of WBC clumps and WBC casts is that they may help with differential diagnosis. Casts indicate disease of the kidney, whereas clumps indicate that the infection may involve the bladder.

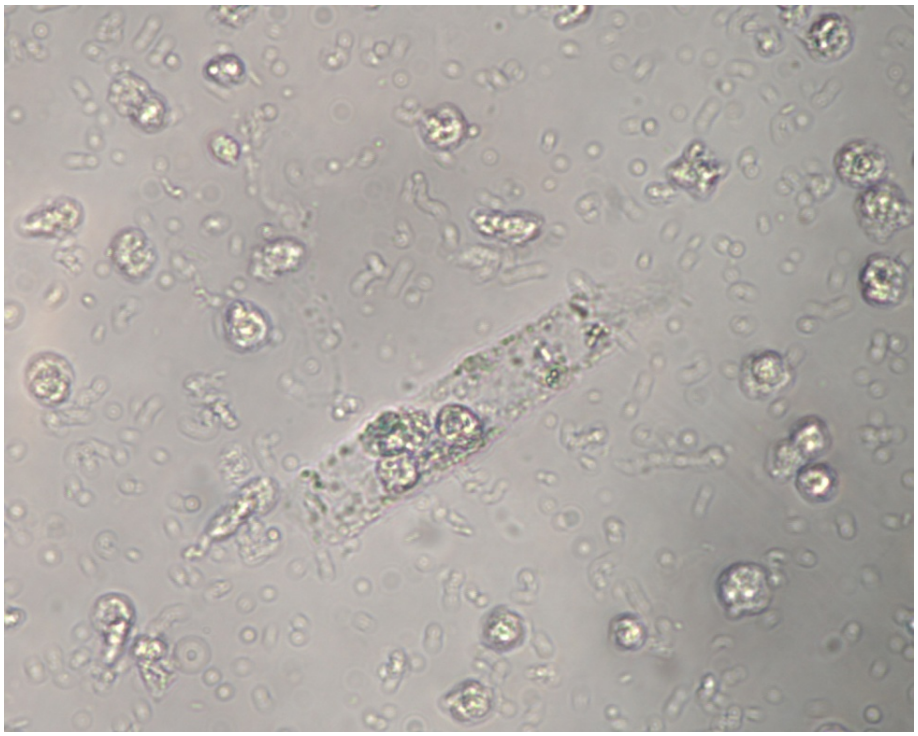

Figure C. Example of a WBC cast. The distinction is the family of cells in the urine that are WBCs.

Another significant but rarely seen cast is the epithelial cell cast (**Figure D**). When present, these are usually composed of renal epithelial cells. Considering that casts are formed in the renal tubules, when renal epithelial cell casts are observed, they indicate severe destruction of the renal tubule and kidney function. Because they are of the renal tubule cell line, there is a tendency for these epithelial cells to be columnar, in alignment within the cast. Because epithelial cells are themselves columnar and may resemble casts, they must be in a cast matrix to be identified as such.

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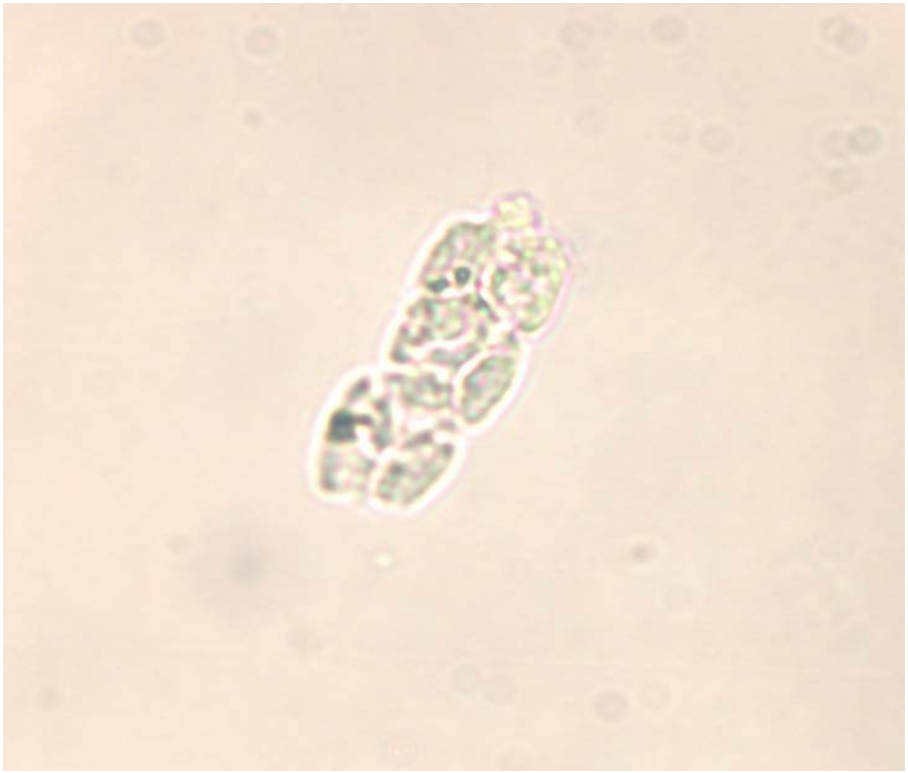

Figure D. Example of a short epithelial cell cast. Notice the prominent nucleus, parallel sides, and the other cells in the cast. The "ghost" RBCs are a clue that the cast cells are larger than WBCs.

Not seen very often are casts with inclusions such as bacteria, crystals, and any other element in the urine. Bacteria in casts are difficult to discern due to the use of low power on the microscopic examination. Frequently, bacteria adhere to the surface of a hyaline cast and are not truly incorporated within the cast matrix (Figure A). Crystals are a little easier to see. However, many times crystals, like bacteria, adhere to the surface of the cast. When classifying a cast, only the elements that are incorporated in the uromodulin matrix should be considered.

If fat globules are present, they may be incorporated into the cast matrix. The globules are round and are retractile, mimicking an RBC. Because they are incorporated within the cast, identifying the fat globule may require the use of stains and polarization. Cholesterol fat globules will have the characteristic "Maltese cross" pattern under polarized light.

As the inclusions stay in the cast matrix and the cast is not eliminated from the tubule, the inclusions will eventually disintegrate. Crystals dissolve, as well as the fat globules, and may give the cast some color.

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Cellular inclusions degenerate; the cell membrane dissolves first, leaving the cytoplasmic material in the cast matrix. This leads to the classification of granular cast. As in the WBC cast, without the cell wall present, all that remains is the cellular material that appears like granules. Granules can be large or small in the cast matrix. As the cast develops, the granules start to dissolve and become smaller and appear diffuse. At this point, the cast is considered a fine granular cast. There is a wide gradient of granular cast appearance and description. Depending on the laboratory's identification and description practice, granular casts may be called coarse granular, granular, or fine granular casts. See **Figure E**.

Figure E. Example of a fine granular cast degenerating to almost the appearance of a waxy cast. Note the granularity of the right side of the cast and the gradual dissolution on the left of the cast, showing cracks along its body. Notice the refractile edges; the hyaline cast does not have the sharp appearance.

As a fine granular cast continues to degrade, the granules completely dissolve and they appear almost translucent, homogenous in color, with sharper, almost refractile, outlines. The cast may also have cracks along its body with sharp blunt ends. Casts at this stage are called waxy casts, because they resemble a candle. They may have some pigmentation, as when an RBC cast degenerates. At times, a hyaline cast may look like a waxy cast, but the distinctions are the sharper outline, cracks along the body, and the blunt ends in the waxy cast. The waxy look and small inclusions are also distinctive. Clinically, waxy casts indicate little to no renal activity, which is associated with severe renal disease or failure.

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Conclusion

Understanding the formation and identification of casts is an important part of Urine Microscopic analysis. Casts can provide important information to the clinician regarding renal function and disease states.

References

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