

Expert Look at Coping Corner
Importance of Causes of Death (COD) Research

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While our hope is that all individuals with CdLS live long and happy lives, unfortunately many children and adults with CdLS die prematurely. Causes of death (COD) research identifies important etiologies contributing to the morbidity and mortality of specific diagnoses. This ultimately allows for an improved understanding of the potential clinical complications and management for children and adults in certain populations. In 2011 Schrier et al. (*Am J Med Genet*) reviewed 295 individuals with a clinical diagnosis of CdLS and known COD. Respiratory causes including aspiration/reflux and pneumonias being the most common primary causes of death (31%), followed by gastrointestinal disease, including obstruction/volvulus (19%). Congenital anomalies accounted for 15% of deaths and included congenital diaphragmatic hernia and congenital heart defects. Acquired cardiac disease accounted for 3% of deaths, neurological causes and accidents each accounted for 8%, sepsis for 4%, cancer for 2%, renal disease for 1.7%, and other causes, 9% of deaths.

The use of COD research goes well beyond statistics and can be used to improve medical management guidelines and to avoid morbidity and mortality. Through a detailed understanding of medical issues that lead to illness and death in the CdLS population, we hope to be able to act more proactively to identify these medical issues before they result in significant complications or even presymptomatically. Such findings allow caregivers and physicians to recognize early symptoms, provide appropriate management recommendations and surveillance, and to intervene expediently when needed. An example of this in CdLS is our understanding of the contribution of intestinal malrotation to significant medical complications and even death in individuals with CdLS which has changed our management guidelines to make evaluation for malrotation a recommendation in all children with CdLS as early as possible. If identified, corrective surgery can be undertaken that significantly reduces the risk of medical complications.

As with many rare genetic diagnoses, the ability to identify large numbers of affected individuals is limited. Small numbers have poor statistical power and prior reports focus mainly on observed trends. Much of this prior research was collected from families who submitted clinical records, autopsy reports, and death certificates to research. The data provided by families was invaluable as it made this research possible that would not otherwise be feasible.



In addition to submitting clinical records and autopsy results some families have made the decision to donate post-mortem samples to research. Tissues from organs such as the brain, heart, liver, kidney, intestines, lung, ovaries and skeletal muscle can all be donated to research and used for DNA/RNA extraction. Samples from specific tissues can be important in answering targeted research questions. For example, most recently our team at CHOP has been collaborating with a group in the UK to investigate gene expression in neuronal nuclei isolated from post-mortem cerebral cortex of individuals with CdLS. This type of study is important for addressing mechanisms of neuronal dysfunction in CdLS and is one example of how valuable such donations can be to forward research initiatives and uncover a deeper understanding of certain clinical issues.

The Center for CdLS and Related Diagnoses within the Roberts Individualized Medical Genetics Center (RIMGC) at the Children's Hospital of Philadelphia (CHOP) is continuing to collect information on causes of death in CdLS to expand upon the prior information reported by Schrier et al., as well as banking samples donated from individuals with CdLS who have undergone an autopsy. If you would like to share information with the CHOP research team please contact them at rimgresearch@email.chop.edu or 267-426-7418.

