Unexplained deaths with a history of fever (UNEX) have been reportable in Arizona since 2004. Health care providers (including hospitals and medical examiners (ME)) are required to report UNEX to their local health department within 24 hours of detection (A.A.C. R9-6-202), after which the local health agency must notify ADHS and initiate an investigation (A.A.C. R9-6-384). The purpose of these UNEX investigations is to identify deaths that might be of public health significance in order to prevent the spread of disease. This could include deaths that are due to infectious diseases transmitted person-to-person, those that require a public health intervention, that represent a new or emerging infection or that are due to an act of terrorism. These investigations involve close collaboration and coordination with outside health agencies including healthcare facilities and the medical examiners (ME) in various counties. The official cause of death is determined by the ME and is a separate process from the UNEX investigation led by public health agencies.

The Arizona Administrative Code defines an “unexplained death with a history of fever” as the “demise of an individual who has had a fever within 48 hours before death and whose illness has not been diagnosed at time of death”. Public health investigations are initiated on all UNEX reports received, but there may not be enough information available at time of report to identify whether a death is of public health significance. The following guidelines are used by public health agencies to identify deaths at high risk of being caused by an agent of public health significance:

1. Hospital/facility-based death, no known cause AND history of fever (>100.4F) OR a temperature of <96.8F within 48 hours of death; OR
2. Patient-reported history of fever within 48 hours of death; OR
3. Clinical suspicion of infectious etiology by a health care provider or medical examiner

An investigation may be stopped when additional information becomes available that suggests the death is unlikely to be due to an agent of public health significance. The summary below details the UNEX investigations conducted by Arizona public health agencies from January to June 2009.

**SUMMARY OF JANUARY TO JUNE 2009 UNEX INVESTIGATIONS**

**UNEX Investigation**

From January to June 2009, 17 unexplained deaths with a history of fever were reported from five counties and tribal lands of Arizona. Thirty-nine unexplained deaths were reported in 2008, with 28 deaths reported from the months of January to June 2008. Unexplained deaths were predominantly reported in Maricopa and Pima Counties as well as on the tribal lands. Yuma and Pinal Counties had the highest rates of UNEX investigations at 0.49 and 0.31 per 100,000 population, respectively (Graph 2).
The most UNEX investigations were reported in May with 7 (41%) deaths (Graph 3). The median number of UNEX reports received was 3.5 per month. All 17 (100%) of the investigations were reported to ADHS within 24 hours. The county reports were received by ADHS within 30 days of investigation closure for 9 (53%) of the deaths. Twelve (71%) UNEX investigations were considered high priority for further investigation as they satisfied one or more of the UNEX guidelines and two were identified to be of public health significance (pediatric influenza-associated deaths). In terms of UNEX guidelines, three (25%) deaths met guideline one, 5 (42%) met guideline two, and all 12 (100%) fulfilled guideline three (see above for UNEX guidelines).
Demographics

Approximately 59% of the reported UNEX deaths occurred in people less than 40 years old (Graph 4). The average age at time of death was 29.7 (total median=28.5; female median=49.5; male median=15). Females represented 53% of the investigations (9 of 17). The age of reported deaths ranged from 1 month old to 60 years old. The highest rate for reported UNEX investigations occurred in the age group ≤9 years old for males with 0.81 per 100,000 population and in the age group 50-59 years old for females with 0.77 per 100,000 population (Graph 4).
Data on race and ethnicity was collected for 94% (16/17) investigations. Caucasians represented the majority with 64% (11/17) of the reported UNEX investigations. The Hispanic/Latino and Native American populations each represented 12% (2/17) of the deaths (Graph 5). According to the 2008 Arizona population denominators, the race and ethnicity breakdown by percentage is as follows: Caucasians (60%), Hispanics/Latinos (28%), Native Americans (5%), African Americans (4%), and Asian or Pacific Islander (3%); however, Native Americans represented 12% of UNEX investigations.

The residence classification (urban or rural) was determined using the 2007 census. An urban residence is defined as an area that has a population density of at least 1,000 people per square mile and surrounding blocks have an overall density of at least 500 people per square mile. Rural is classified as all areas located outside the urban area. Fourteen (82%) deaths were residents in urban areas of the state, whereas three (18%) of the deaths were located in rural areas.

**Autopsy and Laboratory Findings**

As part of the UNEX investigation, public health agencies work in collaboration with medical examiner’s to investigate demographic information, description of course of illness that resulted in death, preliminary autopsy results, need for additional public health testing to identify infectious agents of public health significance, and the suspected cause(s) of death. An autopsy was conducted for 15 (88%) of the 17 reported deaths. The ME Preliminary Autopsy Findings Form was received for 7 (47%) of the 15 reported investigations with an autopsy of which four (57%) mentioned a suspected infectious etiology. Five (71%) of the investigations presented with one or more abnormal systems, including but not limited to respiratory system, cardiovascular system, endocrine system/thyroid, gastrointestinal system, and renal system. Hospital deaths accounted for 59% (10/17) of the death locations (Table 1) and the primary reporting source were the county medical examiner offices (MEO) throughout the state (Table 2).

<table>
<thead>
<tr>
<th>Location of Death</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare Facility</td>
<td>10 (59)</td>
</tr>
<tr>
<td>Residence</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Table 1: Location of Death of UNEX Investigations**

<table>
<thead>
<tr>
<th>Reporting Source:</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Examiner Office</td>
<td>13 (76)</td>
</tr>
<tr>
<td>Healthcare Facility</td>
<td>2 (12)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (12)</td>
</tr>
</tbody>
</table>

**Table 2: Reporting Source for UNEX Investigations**
Specimen testing at the Arizona State Health Laboratory (ASHL) and/or the Centers for Disease Control and Prevention (CDC) was conducted for 13 (77%) of the investigations to determine whether the cause was due to an agent of public health significance (Table 3). Laboratory testing as part of the public health investigation was not conducted for 4 (24%) of these investigations either because no laboratory testing was deemed necessary, no specimens were available for laboratory testing, or hospital laboratory testing was sufficient to rule out any potential agents of public health significance. Pre-mortem specimens were collected for 1 (6%) investigation, while post-mortem specimens were collected for 12 (71%) of the deaths (Table 3).

**Medical Course of Illness**

An investigation of the medical course of illness, including co-morbidities and social history, for the 17 reported deaths was conducted. The majority of the reported UNEX investigations presented with signs of respiratory infection (42%) (Graph 6). Eight deaths presented with signs and/or symptoms of fever, vomiting/diarrhea, and unexplained symptoms. The overall syndrome of 8 (47%) of the 17 reported UNEX investigations had a respiratory infection, while 7 (41%) of the deaths were noted to have ‘Other’ overall syndromes (Graph 7). Five (71%) of these 7 deaths that presented with an overall syndrome of ‘Other’ did not satisfy any of the UNEX guidelines. An infectious nature classified by public health was confirmed for seven (42%) investigations (Graph 8).

![Graph 6: UNEX Investigations by Presenting Signs and Symptoms, Arizona YTD 2009](image)
Graph 7: UNEX Investigations by Overall Syndrome, Arizona YTD 2009

If the death can be classified as more than one of the listed overall syndromes, the syndrome that most closely represents the course of illness, autopsy findings and laboratory results was chosen. If that was not possible, then the “other” option was chosen. If the overall syndrome could not be determined, the “other” option was chosen.

Graph 8: UNEX Investigations by Infectious Nature Classified by Public Health, Arizona YTD 2009

Confirmed: Positive labs and consistent with clinical picture. Possible: Positive clinical picture with no labs or negative labs and/or positive labs with inconsistent clinical picture. Not Infectious: Did not satisfy any of the UNEX guidelines AND labs do not indicate infectious disease and/or Non-infectious cause determined after initial report by MEO or hospital clinicians

The epidemiologic risk factors identified during the UNEX investigations include known infectious disease exposure 21 days prior to illness onset (6%), occupational and recreational risk (18%), exposure to ill persons (12%), and consumption of questionable food (6%). Examples of occupational and recreational exposures include contact with animals and/or insects, work with chemicals and/or toxins, and work in a healthcare facility.

Conclusion

During the investigation of UNEX reports, the local and state health departments work with the MEO and health care providers to identify potential agents of public health significance. The public health investigation includes creating a differential diagnosis through consultation with the MEO, supporting selected laboratory testing to identify agents of public health significance, and, if applicable, implementing control measures. UNEX investigations may be closed at different points of an investigation. Additional laboratory or clinical findings may be identified which show that the death does not satisfy the UNEX guidelines and is unlikely to be caused by an agent of public health significance. At the close of each investigation, 12 (71%) of the 17 reports satisfied one or more of the UNEX guidelines. In the months of January to June 2009, two deaths were identified that were due to an agent of public health significance (pediatric influenza-associated deaths) or for which there was concern of the spread of disease. In the two previous years, deaths of public health significance were identified through UNEX investigations, including Hantavirus, Rocky Mountain spotted fever, meningococcal disease, and plague. These findings allowed public health follow-up and control to occur to prevent additional deaths. The etiology of five (29%) deaths in 2009 remained unexplained after a public health investigation; however, laboratory testing ruled out any agents of public health significance that fit the clinical presentation.