Polycythemia Vera Expert Panel Meeting
Preliminary Research Proposals
October 10, 2008

An expert panel of Polycythemia Vera (PV) researchers, environmental scientists, and public health officials met on August 25, 2008, to evaluate possible research projects. The panel identified 4 major research areas: epidemiology, genetics/biomarkers, toxicology, and environmental analysis. Within these four areas, 11 separate projects were discussed. All of the projects have the potential to provide new information about PV. However, each project differs in scope as some are specific to the PV cluster in the Tamaqua area while others provide more general information about this and closely related diseases. The validity and usefulness of some projects may be affected by the results of others, thus sequencing of projects and coordination among groups with varying expertise are important considerations.

Each panel member provided written commentary on the proposed projects based on their area of expertise. The Agency for Toxic Substances and Disease Registry (ATSDR) and the Pennsylvania Department of Health (PADOH) are currently working with the expert panel to prioritize the research proposals by evaluating the:

- comments of individual panel members
- scope and potential benefits of each proposal
- resources and time required for each proposal

ATSDR and PADOH will then determine which recommendations fit the mandate and mission of their organizations and identify the institutions or agencies that could most effectively address the remaining research. ATSDR will post this information on the PV web site (http://www.atsdr.cdc.gov/sites/polycythemia_vera/index.html) and make it available to all stakeholders as soon as the evaluation is complete.

Proposed Research Projects

EPIDEMIOLOGIC STUDIES

1. **Conduct a case-control study of PV cases from the Tamaqua area and a suitable control group.**
   Justification: This purpose of this study would be to identify potential risk factors associated with the disease by comparing area patients with the disease (cases) to community members without the disease (controls).
2. **Locate and describe the other myeloproliferative diseases (MPDs) in the area, including essential thrombocythemia (ET), primary myelofibrosis (PMF), and chronic myeloid leukemia (CML).**
   Justification: MPDs are closely related and share elements in common, thus evidence of elevated rates could provide additional useful epidemiological data. As with the initial PV studies, the diagnosis would need to be validated and genetic markers assessed. This study would also provide useful information regarding the correct diagnoses and reporting of the other MPDs to the state cancer registry.
3. **Perform a longitudinal study to determine the clinical outcomes of patients with MPD in the study area and compare them to MPD patients from other locations**
   Justification: If MPD cases in the cluster area have a similar and unique cause, the course and outcome of the disease may also be different than cases from other areas.
4. **Compare the Tamaqua area cluster with populations in other locations with similar environmental risk factors, such as West Virginia or other parts of Pennsylvania.**
   Justification: This project would help evaluate the association between PV and potential environmental risk factors and might identify additional PV clusters. It would also provide additional information on the correct diagnoses and reporting of PV to state cancer registries.
5. **Continue to monitor and document the incidence of MPDs in the study area.**
   Justification: It is important to follow the PV incidence in the area since a return to expected levels would indicate that any presumptive causative exposures are no longer present. This project will also help monitor improvements in PV diagnoses and reporting to the state cancer registry.

GENETIC/BIOMOLECULAR STUDIES

6. **Test the existing blood specimens from the current PV patients for specific morphological and/or genetic alterations related to toxic exposures.**
   Justification: This project could help support the hypothesis that there is an environmental cause for PV and/or the current cluster.
7. **Conduct gene profiling analyses of the MPD patients from the study area and control patient populations from other geographic sites.**
   Justification: This research would help determine if there is a genetic or hereditary component for PV and if unique attributes exist in the Tamaqua area population.
8. **Establish a tissue bank for specimens from patients with MPDs in the involved area.**
   Justification: A tissue bank provides a repository for biological specimens which might be invaluable in future studies if unique biomarkers are identified.
9. **Compare the prevalence of the JAK2 mutation and related genetic abnormalities in local blood bank specimens to those from other areas.**

Justification: This project would determine the burden of the JAK2 mutation and possible pre-clinical cases in the general population and provide a comparison of the JAK2 occurrence in the cluster area to other areas.

TOXICOLOGICAL STUDIES

10. Develop a physiological in-vitro toxicological assay using stem-cell cultures.
Justification: This research would provide a valuable tool to evaluate the potential for suspected toxic chemicals to cause PV

11. Evaluate specimens from PV patients and healthy individuals in the study area for specific biomarkers known to occur with polycyclic aromatic hydrocarbon (PAH) exposure.
Justification: PAHs are common to waste coal plant emissions and the Superfund sites found in the study area and are known to cause bone marrow toxicity in mice. This research would evaluate the role of PAHs in the current PV cluster and could possibly lead to new therapeutic/preventive agents.

ENVIRONMENTAL STUDIES

12. Further analysis of historical residences and documented potential exposures from Superfund or other sites.
Justification: This research could determine if PV cluster cases shared common potential exposure risks in space and/or time.