



Defense Health Agency

PROCEDURAL INSTRUCTION

NUMBER 6025.14
December 6, 2018

Medical Affairs/Clinical Support Division

SUBJECT: Active Duty Service Member (ADSM) Erythrocyte Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency and Sickle Cell Trait (SCT) Screening

References: See Enclosure 1.

1. **PURPOSE.** This Defense Health Agency-Procedural Instruction (DHA-PI), based on the authority of References (a) and (b), and in accordance with the guidance of References (c) through (o), establishes Defense Health Agency's (DHA) procedures to implement Reference (d), for erythrocyte G6PD deficiency and SCT screening at the appropriate points: during entry to the Military Services (at appointment, enlistment, or induction (Reference (j))), at pre-deployment, and at other points as indicated for validation of results (per References (k), (m), and (n)).

2. **APPLICABILITY.** This DHA-PI applies to:

a. OSD, the Military Departments, the Defense Agencies, the DoD Field Activities, and all other organizational entities within the DoD (referred to collectively in this DHA-PI as the "DoD Components").

b. U.S. Coast Guard at all times, including when it is a Service in the Department of Homeland Security by agreement with that Department.

3. **POLICY IMPLEMENTATION.** It is DHA's instruction, pursuant to References (a) through (j), that the DHA will establish procedures for:

a. Erythrocyte G6PD deficiency screening of all personnel entering the Military Services and SCT screening done according to Service-specific operational requirements pursuant to Reference (d).

b. Ensuring validation of G6PD screening and SCT consistent with Service-specific operational requirements to include deployment and at selection for Service-specific special occupational training if required (References (e) through (g)).

c. Screening of SCT for at risk personnel at the appropriate point of care.

d. Screening of SCT if screening is deemed necessary for a particular assignment or duty based on the risk of the activity as related to SCT.

4. RESPONSIBILITIES. See Enclosure 2.

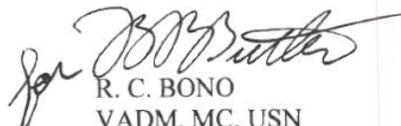
5. PROCEDURES. See Enclosure 3.

6. RELEASABILITY. **Cleared for public release**. This DHA-PI is available on the Internet from the Health.mil site at: www.health.mil/DHAPublications.

7. EFFECTIVE DATE. This DHA-PI:

a. Is effective upon signature.

b. Will expire 10 years from the date of signature if it has not been reissued or cancelled before this date in accordance with DHA-PI 5025.01 (Reference (c)).



R. C. BONO
VADM, MC, USN
Director

Enclosures

1. References
2. Responsibilities
3. Procedures

Glossary

ENCLOSURE 1

REFERENCES

- (a) DoD Directive 5136.01, "Assistant Secretary of Defense for Health Affairs (ASD(HA))," September 30, 2013, as amended
- (b) DoD Directive 5136.13, "Defense Health Agency (DHA)," September 30, 2013
- (c) DHA-Procedural Instruction 5025.01, "Publication System," August 21, 2015, as amended
- (d) DoD Instruction 6465.01, "Erythrocyte Glucose-6-Phosphate Dehydrogenase Deficiency (G6PD) and Sickle Cell Trait Screening Programs," July 17, 2015
- (e) U.S. Navy NAVMED P-117, "Change 156, Manual of the Medical Department of the U.S. Navy," March 10, 2016
- (f) Army Regulation 40-501, "Medical Services, Standards of Medical Fitness," June 14, 2017
- (g) Air Force Instruction 48-123, Medical Examinations and Standards, January 28, 2018
- (h) DoD Directive 5124.02, "Under Secretary of Defense for Personnel and Readiness (USD(P&R))," June 23, 2008
- (i) United States Code, Title 10
- (j) DoD Instruction 6130.03, "Medical Standards for Appointment, Enlistment, or Induction in the Military Services," May 6, 2018
- (k) DoD Directive 6200.04, "Force Health Protection (FHP)," October 9, 2004
- (l) DoD Instruction 6040.45, "DoD Health Record Life Cycle Management," November 16, 2015, as amended
- (m) DoD Instruction 6490.03, "Deployment Health," August 11, 2006, as amended
- (n) DoD Instruction 6490.07, "Deployment-Limiting Medical Conditions for Service Members and DoD Civilian Employees," February 5, 2010
- (o) DoD Instruction 6025.13, "Medical Quality Assurance (MQA) and Clinical Quality Management in the Military Health System (MHS)," February 17, 2011, as amended

ENCLOSURE 2

RESPONSIBILITIES

1. DIRECTOR, DHA. Under the authority, direction, and control of the Assistant Secretary of Defense for Health Affairs, the Director, DHA, will:

a. Establish the implementation procedures for G6PD screening for Service members and for SCT screening as specified in this DHA-PI.

b. Monitor the implementation of procedures in Enclosure 3 of this DHA-PI.

c. Require establishment of standardized quality assurance and control monitoring metrics (Reference (o)).

d. Establish periodic audits which may also include Periodic Health Assessments (PHAs) for documented validation of G6PD screening.

2. DEPUTY ASSISTANT DIRECTOR, DHA MEDICAL AFFAIRS. Under the authority, direction, and control of the Director, DHA, and through instructing the Clinical Support Division to coordinate with the appropriate clinical communities, the Uniformed Services University of the Health Sciences, Connected Health, and other subject matter experts as appropriate, the Deputy Assistant Director, DHA Medical Affairs will:

a. Provide guidance regarding the provision of education related to G6PD deficiency and SCT.

b. Oversee patient safety and quality oversight monitoring to assess baseline incidence of ADSMs with G6PD deficiency mistakenly given Primaquine and assess the need for ongoing periodic audit.

c. Establish periodic audit of PHA documentation of G6PD screening.

3. SECRETARIES OF THE MILITARY DEPARTMENTS AND COMMANDANT OF THE U.S. COAST GUARD. The Secretaries of the Military Departments and Commandant of the U.S. Coast Guard will:

a. Disseminate this DHA-PI and implement procedures outlined in Enclosure 3, Sections 1.a.–1.m. for G6PD screening.

b. Implement procedures outlined in Enclosure 3, Sections 2.a.–2.i. for SCT screening.

ENCLOSURE 3

PROCEDURES

1. G6PD SCREENING PROCESS. Personnel in the Military Services are to be tested during the entry process (at appointment, enlistment, or induction), in accordance with References (d) and (j), and at a minimum will receive screening results prior to deployment (Reference (m)), permanent change of station to a malaria-endemic location, and when pregnant (if not previously validated). The Military Services may also require validation of screening results prior to selection for certain military occupation training programs. Results will be documented in the Service Treatment Record (STR), which includes the electronic health record (EHR) and the Adult Preventive and Chronic Care Flowsheet (DD Form 2766), as a subset of the Service member's health record, in accordance with References (l) through (n).

a. Personnel who have already been screened do not need to be retested, provided documentation is included in the Service member's STR, including the EHR and the Adult Preventive and Chronic Care Flowsheet (DD Form 2766), as a subset of the Service member's health record.

b. At any point, if a Service member is identified to have accessioned without documentation of G6PD testing, testing should be verified. In addition, the reviewer of the annual PHA (Reference (m)), validates that the Service member has G6PD results documented in their medical records. If no testing occurred or documentation cannot be located, medical staff should arrange for expeditious testing and documentation.

c. Prior to deployment or permanent change of station to a malaria-endemic location, results of G6PD screening will be reviewed with the Service member to ensure deficiency screening results in individuals who require treatment with or use of oxidant drugs including but not limited to dabrafenib, dapson, chlorpropamide, glipizide, glyburide, methylene blue, pegloticase, primaquine, quinine, and rasburicase, which are known to cause untoward events in those with G6PD deficiency, are not prescribed. G6PD documentation should be found in the STR, which includes the EHR and the Adult Preventive and Chronic Care Flowsheet (DD Form 2766), as a subset of the Service member's health record.

d. Personnel identified as having G6PD deficiency will receive patient education by trained medical personnel about remaining healthy through incorporating strategies to mitigate heat-related injuries, to avoid antioxidant medications, to avoid infection, and to avoid ingestion of fava beans or anything made from fava beans.

(1) Patient education information should include: G6PD diagnosis, causes, complications, treatment, and strategies to mitigate symptoms.

(2) G6PD deficiency patient education must be documented in the STR (Reference (l)).

e. Upon receipt of an order from an authorized provider for a G6PD test on an ADMSM, the laboratory or medical section receiving the request will draw and test, or draw and submit the appropriate sample(s) needed to screen for G6PD deficiency to a reference laboratory.

f. G6PD screening can be accomplished by qualitative, semi-quantitative, and quantitative methods. Laboratories will follow manufacturer's guidelines to ensure accuracy in the diverse screening methodologies which are available to detect decreased levels of G6PD enzyme activity.

g. In accordance with the manufacturer's listed test limitations, if a Service member has decreased enzyme levels, and the manufacturer recommends confirmatory testing, laboratories will enter a comment recommending follow-on testing through appropriate confirmatory techniques.

h. Confirmatory testing through an appropriate confirmatory technique (quantitative/equivalent method) is required.

i. The submitting and testing laboratory has the responsibility of ensuring the results are accurately entered into the laboratory information system of record. Due to the key importance of this test for medical readiness, and in accordance with good laboratory practices, (if the test is cancelled or needs redraw, etc.), it is the expectation that laboratories alert the ordering provider of positive test results or an issue with the testing; however, a result of G6PD deficiency is not considered a critical/alert value and will not trigger direct verbal communication to the ordering provider.

j. DoD laboratories are regulated by the Clinical Laboratory Improvement Program to ensure patient safety and quality standards. If a laboratory refers testing to a different laboratory, it is the responsibility of the submitting laboratory to ensure that the reference laboratory complies with required regulations.

k. Quality oversight monitoring shall be conducted through periodic review of Sentinel Event Reports (SERs) (Reference (o)) submitted on Service members with G6PD deficiency prescribed Primaquine, or other medication that can cause untoward effects in G6PD-deficient individuals. All positive SER findings shall be reported through DHA governance.

2. **SCT SCREENING PROCESS.** SCT screening may occur at different points during entry to the Military Services, at appointment, enlistment or induction, or during military service for Service members who meet demographic, clinical, or operational criteria, as developed by each Service. The Military Services may require screening for high risk Service members prior to selection for certain military occupational training schools (e.g., Special Forces etc.), or prior to deployment. Results will be documented in the STR (Reference (l)), in the EHR, and/or in the Adult Preventive and Chronic Care Flowsheet (DD Form 2766), as a sub-set of the Service member's health record.

a. Prior to deployment, assignment to high risk environments, and/or selection for training schools for certain military occupations, results of SCT screening for those who meet Service criteria for screening will be reviewed to ensure fitness for duty and maintenance of optimal health while in military service (References (e) through (g), and (m)).

b. Pregnant female ADSMs will be offered SCT screening (if not already done), and will be advised that all newborns are screened for SCT.

c. At any point, if a Service member is identified to meet screening criteria for SCT without documentation of Hemoglobin S testing, testing should be verified. In addition, self-reported health concerns, including SCT, are addressed in the annual PHA (Reference (m)). The annual PHA validates that Service members at risk for SCT, or who report past SCT screening, have results documented in their confirmed STR, as indicated. If no testing occurred, or documentation cannot be located, medical staff should arrange for expeditious testing and documentation.

d. Personnel identified as having SCT will receive patient education by trained medical personnel, about remaining healthy through incorporating strategies to mitigate symptoms.

e. Patient education shall include: SCT diagnosis, causes of SCT, complications of SCT, treatment, mitigating symptoms (to include self-awareness assessments), and Service-specific restrictions. Service-specific associated risk factors and activities in all areas, including operational, occupational, environmental, and recreational, as well as the genetic implications to include considerations for family planning and screening of newborns shall also be discussed.

f. Upon receipt of an order from an authorized provider for SCT screening test on an ADSM, the laboratory or medical section receiving the request will draw and test or draw and submit the appropriate sample(s) needed to screen for SCT to a reference laboratory.

g. SCT screening is typically accomplished by qualitative methods. Laboratories will follow manufacturer's guidelines to ensure accuracy in the diverse screening methodologies which are available to detect SCT. If screening methodologies indicate SCT, in accordance with good laboratory practices, laboratories will enter a comment recommending follow-on testing with appropriate confirmatory methods to confirm that SCT is positive. The submitting and testing laboratory have the responsibility of ensuring the results are accurately entered into the laboratory information system of record.

h. In accordance with good laboratory practices, if there is an issue with obtaining accurate results for SCT (i.e., if the test is cancelled or requires a redraw), it is the expectation that laboratories alert the ordering provider; however, a result of SCT is not considered a critical/alert value and will not trigger direct verbal communication to the ordering provider.

i. DoD laboratories are regulated by the Clinical Laboratory Improvement Program to ensure patient safety and quality standards. If a laboratory refers testing to a different laboratory, it is the responsibility of the submitting laboratory to ensure that the reference laboratory complies with required regulations.

GLOSSARY

PART I. ABBREVIATIONS AND ACRONYMS

ADSM	Active Duty Service Member
DHA	Defense Health Agency
DHA-PI	Defense Health Agency-Procedural Instruction
EHR	electronic health record
G6PD	glucose-6-phosphate dehydrogenase
PHA	Periodic Health Assessment
SCA	Sickle Cell Anemia
SCT	Sickle Cell Trait
SER	Sentinel Event Report
STR	Service Treatment Record

PART II. DEFINITIONS

These terms and their definitions are for the purposes of this DHA-PI.

G6PD. A red blood cell enzyme that catalyzes the first step in a metabolic pathway that serves as precursor for important molecules. The red blood cell is particularly dependent on G6PD for protection against oxidative stress because, unlike other cells in the body, red blood cells lack a nucleus, mitochondria, and other organelles necessary to produce the proteins involved in alternate pathways that can generate nicotinamide adenine dinucleotide phosphate, responsible for cellular respiratory, oxidative, burst. Red blood cells deficient in G6PD are therefore susceptible to oxidation and hemolysis under conditions of oxidative stress.

G6PD deficiency. The most prevalent human enzyme deficiency in the world, the disorder stems from an intrinsic metabolic defect of the red blood cells. The majority of people with G6PD deficiency are unaware of their status, living out their lives with no anemia, no symptoms, and no complications although symptomatic individuals may experience acute hemolytic anemia, chronic hemolytic anemia, or neonatal hyperbilirubinemia. The condition is rarely fatal. G6PD is an X-linked inherited genetic disorder that most commonly affects persons of African, Asian, Middle Eastern, or Mediterranean descent. The disorder becomes recognized when an episode of acute hemolysis (rupture of the red blood cell) is triggered by exposure to oxidant drugs, infection, ingestion of fava beans or products containing fava beans or in rare cases to exposure to austere environmental conditions of heat or altitude.

G6PD screening. Employs a population-based screening method to identify G6PD deficiency in a large number of individuals such as military members. Positive G6PD results require definitive follow-on testing to confirm an abnormal result.

SCA disease. A hereditary condition, SCA disease, causes a type of faulty hemoglobin in red blood cells. Some red blood cells can become hard, change shape, and don't move well through the smallest blood vessels. This can stop or slow blood flow to parts of the body, causing less oxygen to reach these areas. The sickle cells also die earlier than normal blood cells, which can cause a shortage of red blood cells in the body. For most people, there is no cure for sickle cell disease.

SCT. All conditions in which an individual carries the sickle hemoglobin gene mutation on only one beta globin gene. If the other beta globin gene is normal, the individual has SCT, which is not a disease and does not alter the individual's life expectancy. Individual knowledge of carrier status is important for family planning to assist in the prevention of new cases of Sickle Cell Anemia (SCA) disease. SCT is generally a benign carrier condition, usually with none of the symptoms of SCA. In rare instances, some individuals with SCT, when subjected to the extremes of exertion, in particular when compounded by the environmental challenges of altitude or heat, have been shown to possess an increased relative risk for organ infarct, fulminant exertional rhabdomyolysis, and exertional non-traumatic sudden death. Those with SCT usually have no signs of disease and live a normal life. In the U.S., SCT is more common in African Americans.

SCT screening. Screening for SCT involves a blood test that checks for the presence of hemoglobin S, the defective form of hemoglobin that underlies SCA disease. If the screening is negative, then there is no sickle cell gene present. If the screening is positive, then future testing is done to determine whether the individual has one or two S genes present. Those with two genes present have SCA disease, while those with one sickle cell gene and one normal hemoglobin gene have SCT. SCT screening is included in all newborn screens in the United States.

SERs. Reports that are voluntarily submitted to The Joint Commission by The Joint Commission-accredited healthcare organizations when a sentinel event occurs. Sentinel events are defined as a patient safety event(s) that reaches a patient and results in death, permanent harm, or severe temporary harm and require intervention to sustain life. These events are called sentinel because an immediate investigation and response is required. SERs result in lessons learned from the event and are intended to improve patient safety.