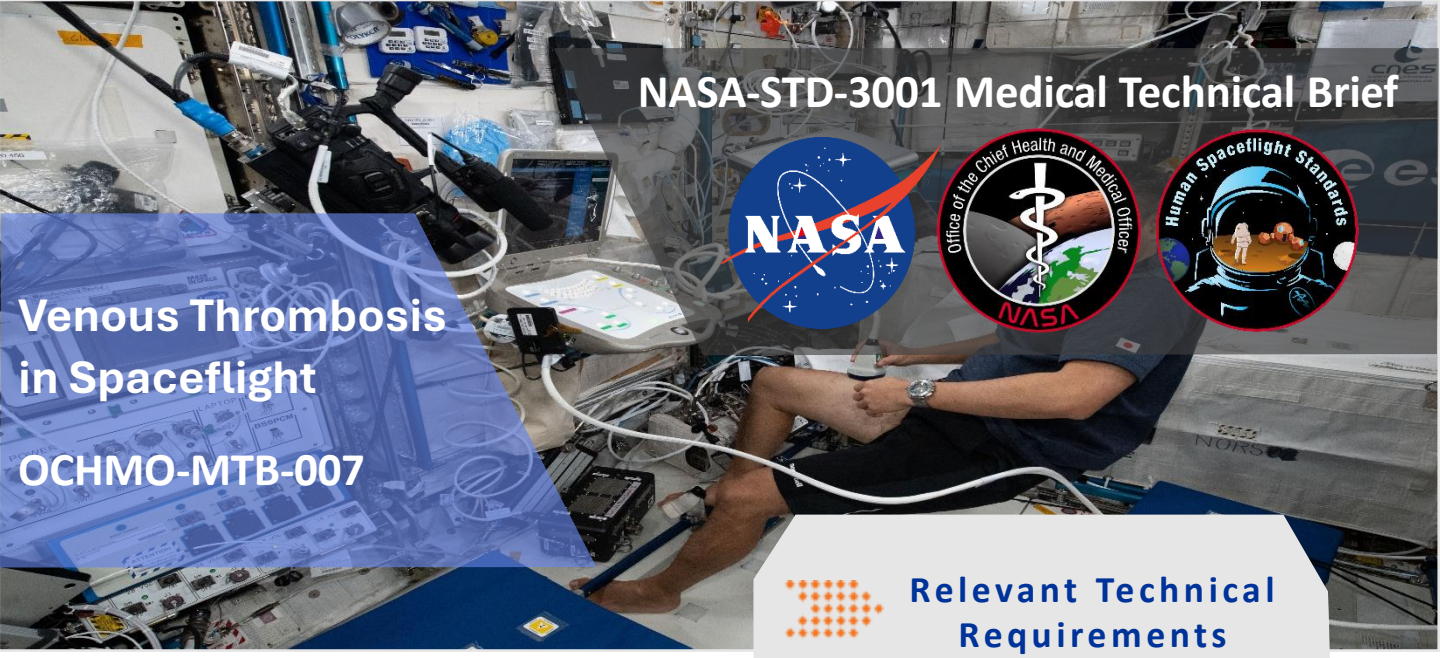


NASA-STD-3001 Medical Technical Brief

Venous Thrombosis in Spaceflight

OCHMO-MTB-007

Executive Summary

Altered blood flow has been identified in the internal jugular veins (IJVs) of crewmembers concomitant with vessel distension. Inflight ultrasound has revealed that flow in the left IJV may be: (a) antegrade but with lower rates than terrestrial norms, (b) stagnant, and/or (c) retrograde. In rare cases, a thrombus formation has been discovered in the left IJV of a crewmember.

NASA and the European Space Agency (ESA) convened technical interchange meetings (TIMs) with both internal and external experts in cardiology, vascular medicine and hematology, neurology, radiology, spaceflight medicine, obstetrics and gynecology, ophthalmology, and basic coagulation laboratory science to discuss diagnosed cases of venous thrombosis in spaceflight and to formulate recommendations. Based on the recommendations from these TIMs, NASA developed an algorithm to provide guidance for inflight assessment, prevention, and treatment of thrombus formation in weightlessness.

Relevant Technical Requirements

OCHMO-STD-100.1A *NASA Space Flight Medical Selection, Recertification and Mission Evaluation Standards*

[6041] Requirement: Every crewmember shall be screened for deep vein thrombosis (DVT) and flow anomalies of the internal jugular veins.

Laboratory Tests on Selection of NASA Astronauts - Hematology/ thrombophilia screen (Table 3)

NASA Astronaut Candidate (ASCAN) First Annual Exam - Venous Thromboembolism Panel (Table 4)

Mission Medical Examinations for Short Duration (< 30 days) Missions - Screening for deep vein thrombosis and venous flow anomalies (Table 7)

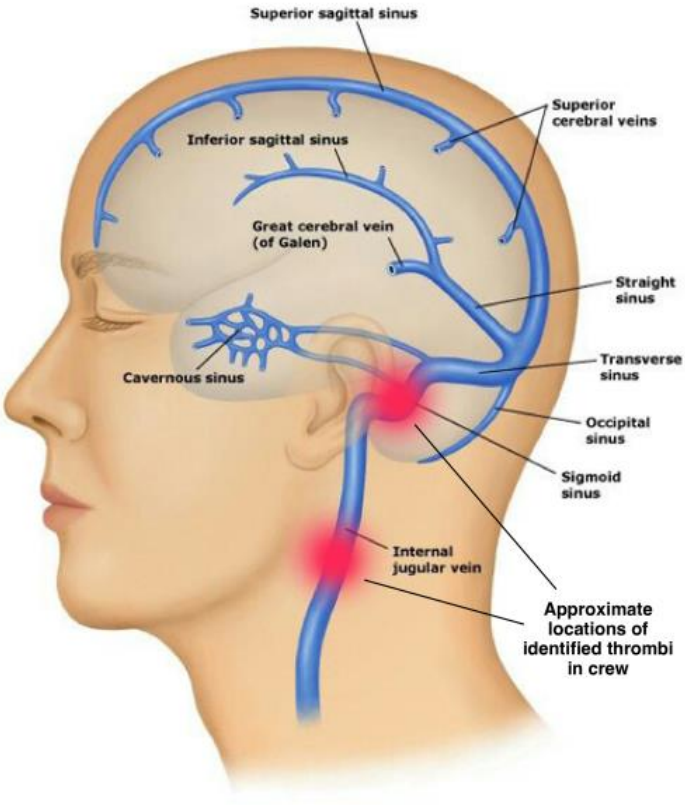
Mission Medical Examinations for Assigned Crew on > 30-day Missions - Screening for deep vein thrombosis and venous flow anomalies (Table 8)

Laboratory Tests for Private Astronauts with NO Critical Duties and on Missions <30 Days - Hematology/Thrombophilia Screen (Table 11)

Background

Venous thromboembolism (VTE) refers to blood clots in the veins and includes both deep vein thrombosis (DVT, blood clot in the deep veins, most commonly in the legs) and pulmonary embolism (PE, blood clot in the lungs). The precise number of people affected by either a DVT or PE is unknown, although as many as 900,000 people could be affected each year in the United States. Sudden death is the first symptom in about one quarter (25%) of people who have a PE. An estimated 60,000–100,000 Americans die of VTE each year (CDC, 2025).

Obstructive thrombi have been identified in a very small number of crewmembers and have been successfully treated with oral anti-coagulant pharmaceuticals. The first case of a left IJV DVT in an astronaut serving aboard the International Space Station (ISS) (Auñón-Chancellor, 2020) prompted NASA to host a vascular TIM in early 2019 to discuss VTE in spaceflight. External experts in hematology, radiology, pathology, vascular neurology, and obstetrics and gynecology were invited, as were medical representatives from NASA's international partners. Recommendations from the TIM led to on-orbit surveillance of all NASA astronauts for IJV DVT. Additional TIMs were hosted separately by NASA and ESA in late 2024. Recommendations included the use of prophylactic-dose anti-coagulation under certain circumstances and prompted the extension of vascular surveillance to all astronauts and cosmonauts (instead of just NASA astronauts) on board the ISS.



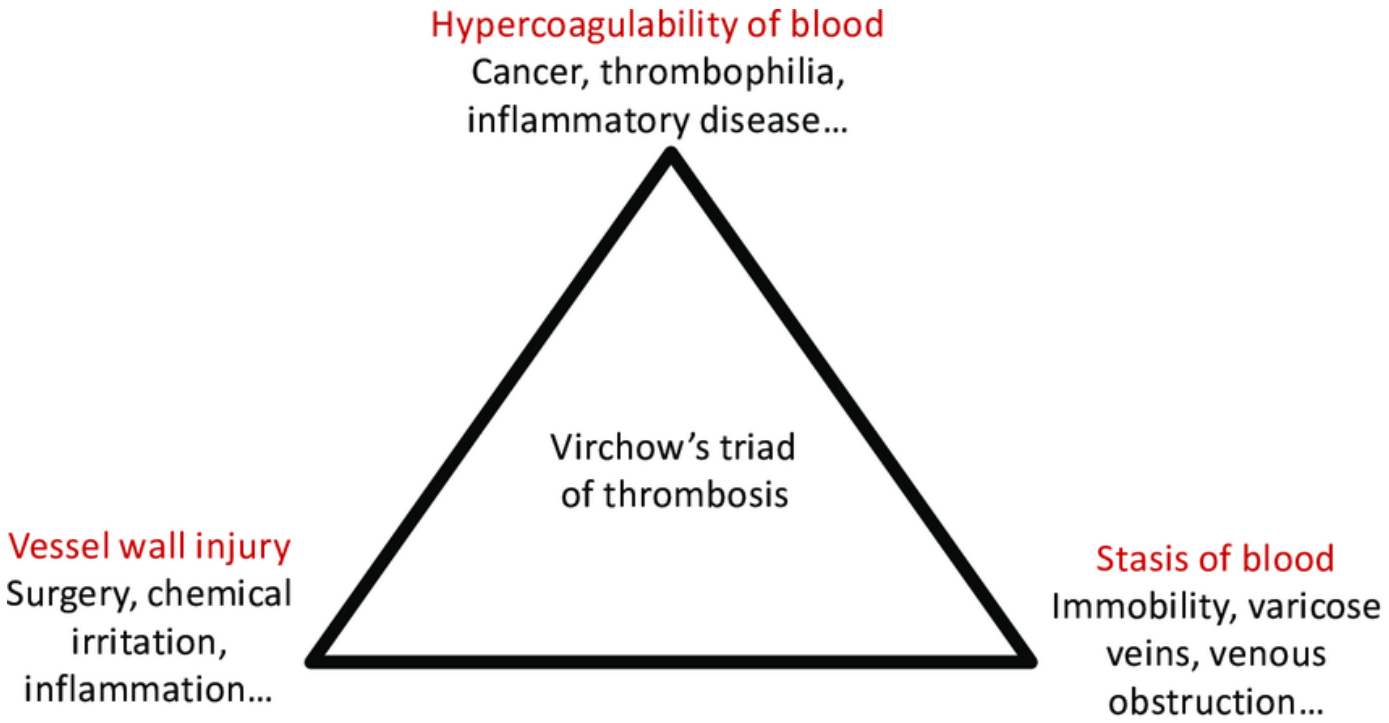
Approximate location of thrombi identified in crewmembers.
Source: Modified from Cerebral Sinus Venous Thrombosis – University of Colorado Denver

Summary Report from NASA TIM October 2024: Assessment of Risk of Venous Thromboembolism during Spaceflight

Pathophysiology

The proposed pathogenesis of VTE is referred to as Virchow's triad and suggests that VTE occurs as the result of:

1. Alterations in blood flow (i.e., stasis),
2. Vascular endothelial injury/changes, and/or,
3. Alterations in the constituents of the blood leading to hypercoagulability (i.e., hereditary predisposition [Bauer & Lip, 2024] or acquired hypercoagulability).



The Virchow's triad of risk factors for venous thrombosis. Source: Bouchnita, 2017

Blood stasis, or venous stasis, refers to a condition in which the blood flow in the veins slows down which leads to pooling in the veins. This slowing of the blood may be due to vein valves becoming damaged or weak, immobility, and/or the absence of muscular contractions. Associated symptoms include swelling, skin changes, varicose veins, and slow-healing sores or ulcers.

Risk Factors

The risk of VTE is multifactorial:

Risk Factors for Venous Thromboembolism

Acquired Risk Factors		Hereditary/Genetic Risk Factors	
Transient	**Persistent**	**Loss-of Function Mutations**	**Gail-of-Function Mutations**
Surgery (general/orthopedic) and hospitalization	Active malignancy	Deficiency of antithrombin III	Factor V Leiden
Pregnancy and the postpartum period Infections	Overweight/obesity	Deficiency of protein C	Prothrombin
Trauma	Chronic inflammatory diseases*	Deficiency of protein S	Mutation G20210A
Hormone replacement therapy (oral)	Increasing age	PNH	Elevation of factor VIII
Long-haul (air) travel	Immobilization		JAK2 V617F mutations
Oral contraceptive use	Malignancy	**Non-Mutation Related Hereditary Risk Factors**	
Certain medications**	IMIDs	Height	
	Adjuvant chemotherapy	Male Sex	

IMIDs = immunomodulatory agents, PNH = paroxysmal nocturnal haemoglobinuria.

*Chronic (inflammatory) diseases, including human immunodeficiency virus (HIV) infection, inflammatory bowel disease, systemic lupus erythematosus, hyperthyroid disease, among others.

**Including tamoxifen, raloxifene, and those containing estrogen.

Source: Mehta & Bhave (2023)

Risk Factors

Many of the terrestrial risk factors of VTE are not applicable to the astronaut population. When assessing VTE in spaceflight, the following risks should be considered along with ultrasound, physical, and alternative assessments.

Family History

A history of unprovoked venous thrombosis in immediate family members is considered a risk factor for VTE, as shown in the following table (Bostick et al., 2025).

Family History	*Relative Increase in Risk of Thrombosis*
First-degree relative with history of VTE < age 50	Up to 2-fold
Multiple first-degree relatives with history of VTE	Up to 4-fold
Family history combined with a genetic or environmental risk (i.e., surgery, injury, immobilization, pregnancy, use of oral contraceptives/hormone therapy, or malignancy)	Up to 64-fold

Relative increase in risk of thrombosis with family history. Source: Bezemer et al., 2009

Thrombophilias

Thrombophilias include a variety of genetic mutations that are associated with increased risk of VTE. The most routinely assessed hereditary thrombophilias include deficiencies of antithrombin, protein C, or protein S, and the gain-of-function mutations Factor V Leiden (FVL) and prothrombin G20210A (PGM). The table below shows the relative increase in risk of thrombosis for various thrombophilia conditions (Bostick et al., 2025).

Thrombophilia Condition	*Relative Increase in Risk of Thrombosis*
Factor V Leiden heterozygous	4.9-fold (3-8 fold)
Factor V Leiden homozygous	16-fold
Factor V Leiden with other thrombophilia conditions like a prothrombin gene mutation	20-fold
Protein C deficiency	7-fold
Protein S deficiency	7-fold
Antithrombin III deficiency	16-fold (up to 20-fold)
Prothrombin gene mutation, heterozygous	3.8-fold

Relative increase in risk of thrombosis with various thrombophilia conditions. Source: Albagoush, 2023

Risk Factors

Hormone Therapy

Hormone management or suppression is commonly used by crewmembers since the logistics of menstruating during spaceflight can be challenging (waste disposal, volume/mass hygiene products) (Jain, 2016). Therapeutic devices (e.g., levonorgestrel intrauterine device [LNG-IUD]), or treatment including combination oral contraceptive (COC) pill, transdermal patches, or depot medroxyprogesterone acetate can all be used to prevent menstrual flow. Currently, crewmembers may be on a variety of hormones (e.g., oral contraceptives to block or regulate menstruation, hormone replacement therapy, etc.) each of which pose different levels of VTE risk, as shown in the table below (Bostick et al., 2025).

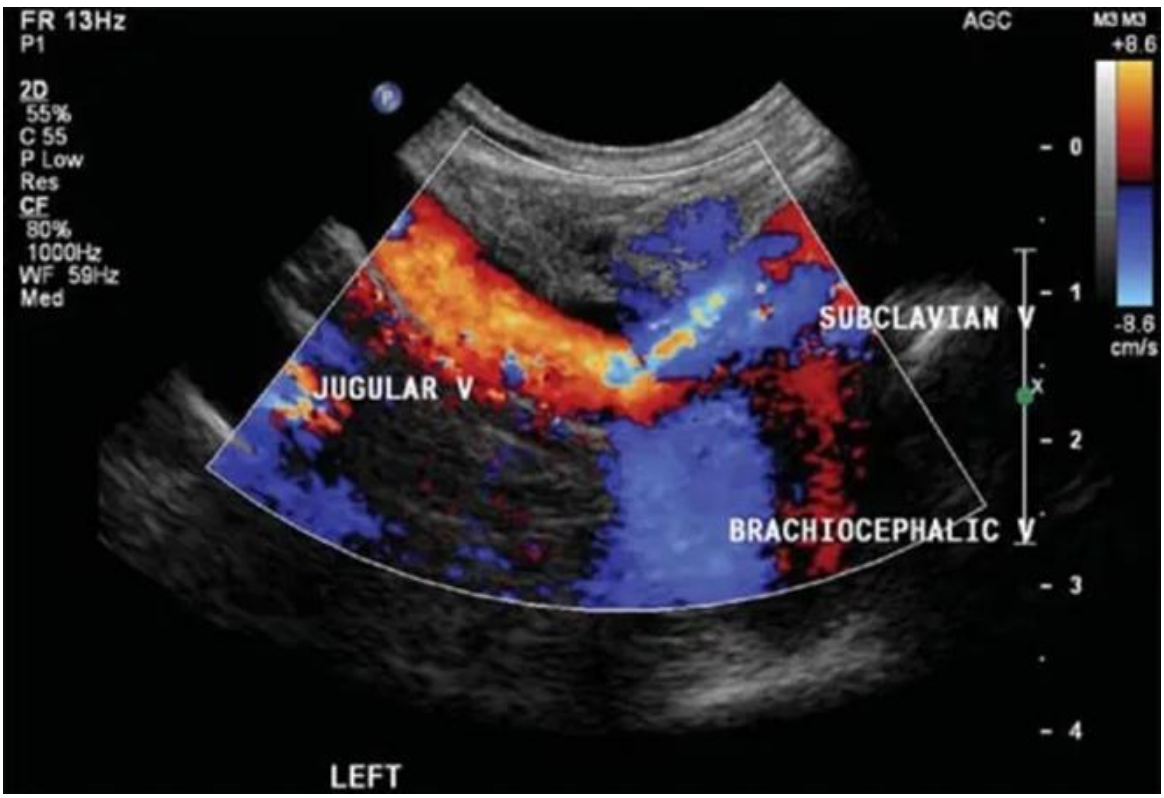
Hormone Comparison Table

Hormone Preparations	Progesterone	Estrogen (mcg)	VTE Risk
Progestin only pills	Norethindrone	None	Low/No increased risk[1]
LNG IUD	Levonorgestrel	None	Low/No increased risk[2]
Implant	Etonogestrel	None	Low/No increased risk[3]
Hormone Testosterone micronized 2mg	None	None	Low/No increased risk
Testosterone Cypionate injections	None	None	Low/No increased risk
Hormone Therapy Estrogen		Estradiol patch	Low/No increased risk[1]
		Premarin oral	2-fold increase[1]
Progesterone	Micronized progesterone 100mg (Oral)	None	Low/No increased risk[5]
	Medroxyprogesterone depot 150mg	None	2.6-fold increase[2]
2nd Generation Progesterone CoC	Levonorgestrel	Ethinyl estradiol (20,10)	2.8-fold increase[4]
		Ethinyl estradiol (20)	
		Ethinyl estradiol (30)	
		Ethinyl estradiol (20,25,30,10)	
		Ethinyl estradiol (20,10)	
1st Generation Progesterone CoC	Norethindrone acetate	Ethinyl estradiol (10,10)	3.2-fold increase[2]
		Ethinyl estradiol (20)	
		Ethinyl estradiol (30)	
		Ethinyl estradiol (20,30,35)	
	Norethisterone	-	
	Norethindrone	Ethinyl estradiol (35)	
	Ethynodiol diacetate	Ethinyl estradiol (35)	
		Ethinyl estradiol (50)	
	Norgestrel	Ethinyl estradiol (30)	
		Ethinyl estradiol (50)	
3rd Generation Progesterone CoC	Norgestimate	Ethinyl estradiol (35)	3.8-fold increase[4]
	Desogestrel	Ethinyl estradiol (20,0,10)	
		Ethinyl estradiol (30)	
	Gestodene	-	
4th Generation Progesterone CoC	Drospirenone	Ethinyl estradiol (30)	Similar to 3rd generation progesterone CoC[1]
		Ethinyl estradiol (30)	
		Estetrol (14.2 mg)	
1. LaVasseur et al., 2022; 2. Cockrum et al., 2022; 3. Perez et al., 1997; 4. Alsheef et al., 2022; 5. Bińkowska, 2014			
Key: Low/no increased risk of VTE Some increased risk of VTE Moderate increased risk of VTE			

Pathophysiology

In addition to the terrestrial risk factors of VTE, there are physiological changes associated with spaceflight that are hypothesized to potentially play a role in the development of VTE in weightlessness. Specifically, researchers have explored the effects of the microgravity environment and subsequent observed headward fluid shifts that occur, and the potential impact on blood flow (Lawley et al., 2017; Marshall-Goebel et al., 2019; Baran et al., 2021) Crewmembers onboard the ISS experience weightlessness due to the microgravity environment and thus experience a sustained redistribution of bodily fluids from the legs toward the head. The prolonged headward fluid shifts during weightlessness results in facial puffiness, decreased leg volume, increased cardiac stroke volume, and decreased plasma volume (Bostick et al., 2025).

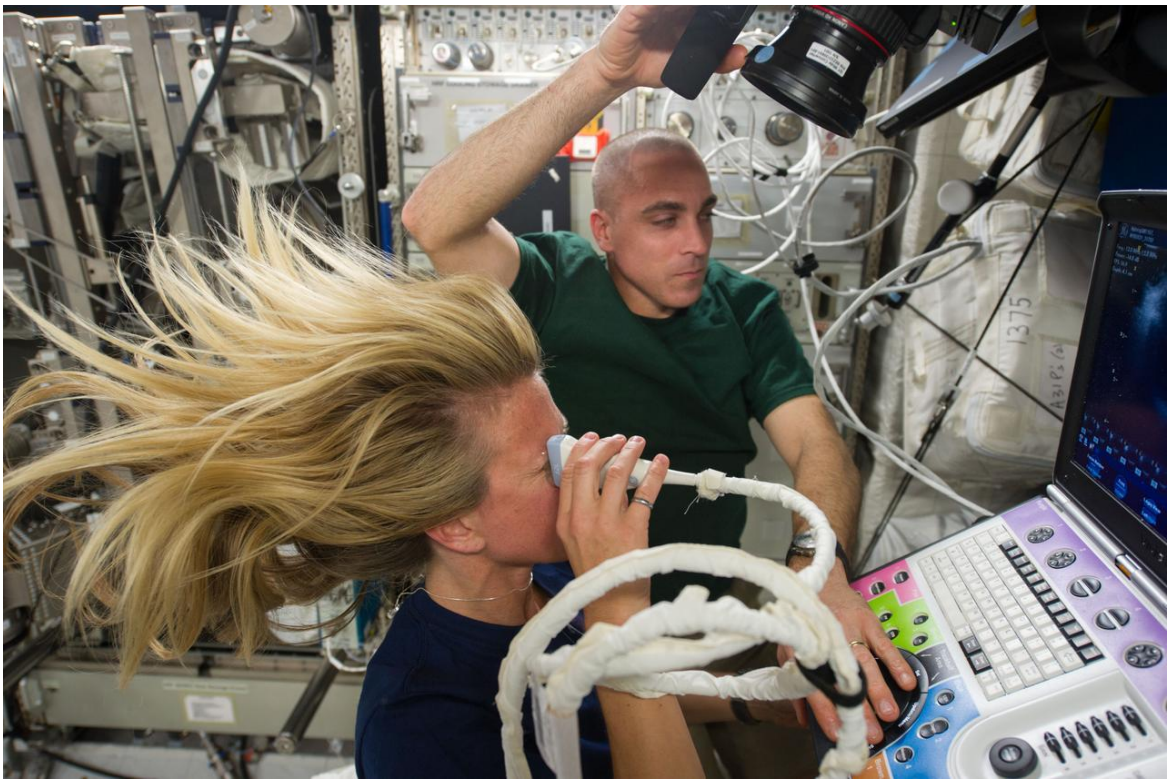
Crewmembers have also experienced altered blood flow during spaceflight, including retrograde venous blood flow (RVBF) (the backflow of venous blood towards the brain) or stasis (a stoppage or slowdown in the flow of blood) (Marshall-Goebel et al., 2019). While the causes of the observed stasis and retrograde blood flow in spaceflight participants is not well understood, the potential clinical significance of the role it may have in the development of thrombus formation warrants further investigation (Bostick et al., 2025).



Doppler imaging of a retrograde flow in the left internal jugular vein
Source: Yan & Seow, 2009

Pathophysiology

Other physiological concerns affected by fluid shifts are being studied to consider if any relation to VTE exists. Chronic weightlessness can cause bodily fluids such as blood and cerebrospinal fluid to move toward the head, which may be the cause of optic nerve swelling, folds in the retina, flattening of the back of the eye, and swelling in the brain that have been observed in many astronauts. This collection of eye and brain changes is called “spaceflight associated neuro-ocular syndrome,” or SANS. Some astronauts only experience mild changes in space, while others have clinically significant outcomes. The long-term health outcome from these changes is unknown but are actively being investigated. The risk of developing SANS is higher during longer-duration missions and remains a top research priority for scientists ahead of a Mars mission.



Astronaut Karen Nyberg, Expedition 37 flight engineer, assisted by astronaut Chris Cassidy, performs an Ocular Health (OH) scan using Ultrasound 2 in the Destiny laboratory of the ISS. Source: NASA

View OCHMO-MTB-001 Spaceflight Associated Neuro-ocular Syndrome (SANS) Medical Technical Brief.

NASA Screening Process

The *NASA Space Flight Medical Selection, Recertification and Mission Evaluation Standards* document (OCHMO-STD-100.1A) provides medical requirements and clinical procedures designed to ensure crew health and safety and occupational longevity of NASA career astronauts. This NASA Technical Standard is used for selection and annual recertification of astronauts and provides medical evaluation criteria for low-Earth orbit spaceflight missions. Subsets of screening and testing that may identify risk factors for VTE include:

Laboratory Tests on Selection of NASA Astronauts

Hematology/Thrombophilia Screen

- Complete Blood Count – to include hemoglobin, hematocrit, red blood cell count, differential count, platelet count
- Reticulocyte count
- Screening tests for thrombophilia: prothrombin time (PT) and partial thromboplastin time (PTT)
- Hemoglobin evaluation (A, A2, F, S, C, E)

Astronaut Candidate (ASCAN) First Annual Medical Examination

Venous Thromboembolism Panel

- Cardiolipin IgG Antibody
- B2 glycoprotein 1 IgM/IgG Antibody
- Activated Protein C (APC) Resistance
- Prothrombin Nucleotide 20210 G/A Gene Mutation (Factor II)
- Protein C
- Protein S
- Antithrombin
- Anti-phospholipid antibodies
- Factor V Leiden

Laboratory Tests on Annual Recertification of NASA Astronauts

Hematology/Thrombophilia Screen

- Complete Blood Count – to include hemoglobin, hematocrit, red blood cell count, differential count, platelet count
- Reticulocyte count
- Screening tests for thrombophilia: prothrombin time (PT) and partial thromboplastin time (PTT)
- Hemoglobin evaluation (A, A2, F, S, C, E)

Urinalysis

- Routine (specific gravity, glucose, protein, pH, ketones, blood), microscopic

Special Assessments for Selection and Annual Recertification of NASA Astronauts

Neurology

- MRI of brain
- MRI angiogram
- Carotid Ultrasound Study (to include intima medial thickness and/or carotid plaque area)

Cardiopulmonary

- Resting 12-lead electrocardiogram (ECG)
- Direct or indirect measurement of cardiorespiratory fitness (CRF) in ml/kg/min on maximum exercise stress test
- 24-Hour ECG monitoring
- Pulmonary function testing
- Atherosclerotic Cardiovascular Disease Risk Calculation
- Coronary calcium scoring

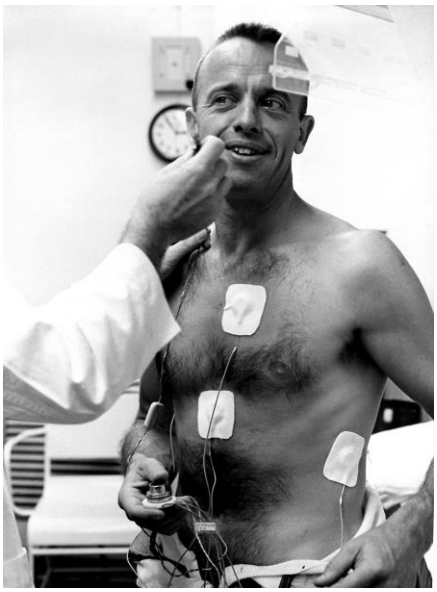
NASA Screening Process

Mission Medical Examinations for Assigned Crew on > 30-day Missions

Clinical Assessment and Monitoring	Pre-Flight (L-)	In-Flight	Post-Flight (R+)
Pre-and Post-flight Physical Exam for Short Duration Crews	AME L-12/6 m, L-21/14 d, L-2/1 d		R+0 d and R+3/7 d, PEX ACI – labs and PEX ID swab
Ultrasound Imaging (Sonography)	Carotid ultrasound AME 21/18m unless within last 5 years, AME L-12/6m	ACI	ACI
MRI Brain and MR Angiography	AME L-21/18m, if > 2 years since selection		ACI
Laboratory Testing	AMT L-12/6m	Blood and urine testing in-flight L+180d and ACI	Blood and urine R+0/1, R+3/7, R+14/30
Screening for deep vein thrombosis and venous flow anomalies of the internal jugular veins	L-12/3m	L+30 days; L+60 days	R-42 days, R+0/45d, ACI

Source: NASA Space Flight Medical Selection, Recertification and Mission Evaluation Standards document (OCHMO-STD-100.1A REV A)

Acronyms:
AME = annual medical exam
L-/+ = days or months from launch
R-/+ = days or months from return to earth
ACI = as clinically indicated



Astronaut Alan Shepard underwent a physical examination prior to the first manned suborbital flight. Source: NASA

Risk Assessment and Spaceflight Venous Thrombosis Management

Based on expert opinion and the assessment of each of the risk factors for thrombosis, the following algorithm was developed to provide guidance for inflight assessment, prevention, and treatment of thrombus formation in weightlessness (Bostick et al., 2025). The algorithm is based on early in-flight ultrasound surveillance to determine the flow characteristic of the left IJV.

Risk Factors

Family history (unprovoked thrombosis in immediate family members) and thrombophilia which increases thrombosis risk by 4-20X (Albagoush, 2023; Bezemer et al., 2009) are considered factors.

First- and second-generation estrogen-progestin combination oral contraceptive (COC) use which increases the thrombosis risk up to 3.2X (see table on page 6) (Cockrum et al., 2022; LaVasseur et al., 2022; Pérez Gutthann et al., 1997) are considered factors.

Age was evaluated and based on the data that include many comorbidities that astronauts do not have, it was not a factor in the algorithm. Incidence rates of VTE in patients aged ≥65 years are 3-fold higher than in patients aged 45–54 years (Akrivou et al., 2022; Cushman et al., 2004) and may be a factor to consider for commercial space flyers who may have comorbidities.

Preflight Considerations

Preflight assessment should include consideration of the type of oral contraceptive to minimize risk of VTE. The choice of a progesterone-only contraceptive (such as an IUD or the Nexplanon rod) may be preferred due to their lower risk for VTE over an estrogen-containing contraceptive to suppress/minimize menstrual bleeding on orbit. See table on page 6.

Crewmembers who have a history of unprovoked thrombosis in an immediate family member should consider not using oral estrogen therapy, and crewmembers positive for thrombophilia should not use combination oral contraception pills (COCPs).

Inflight Considerations

Based on expert opinion, stasis/stagnant flow was the most concerning as a pre-thrombotic indicator. Retrograde flow was not considered to be a main contributor to the formation of a thrombus but may be a concern if a thrombus does form.

Any observations such as IJV swelling, facial edema beyond “nominal” spaceflight adaptation, and/or eyelid edema, mydriasis, headache, and SANS symptoms should be considered as part of the risk assessment.

Risk Assessment and Spaceflight Venous Thrombosis Management

Medical Management

In-flight Ultrasound Assessment – Thrombosis Discovered

For those crew found to have thrombosis on orbit via ultrasound, treatment consists of administering an anticoagulant regardless of stasis status. Apixaban has been successfully used in past cases when a thrombus was detected in a crewmember; this medication is carried in the in-flight medical kit, but alternates may be used. The recommended dosing is as follows:

- Treatment: Apixaban 10 mg twice a day for 7 days; afterwards 5 mg twice a day

Couturaud et al. (2024) provides evidence that reinforces the approach of transitioning to reduced doses of DOACs once the highest-risk period has passed.

Crewmembers using an estrogen-based COC should not discontinue its use if direct oral anticoagulants (DOACs) are administered to treat a suspected or confirmed thrombus due to the risk of abnormal uterine bleeding (AUB) (Baglin et al., 2012; Martinelli et al., 2016).

In-flight Operational Considerations for Crew with Thrombosis

- Restrict crew from both EVA and ARED for at least 30 days.
- Use of T2 and CEVIS can be considered, but harness shoulder straps should be removed.
- If crew is clinically stable, generally favor remaining on orbit for at least 30 days to complete uninterrupted therapy.

In-flight Ultrasound Assessment – No Thrombosis Discovered

Crew with no thrombosis but who have stasis with family history, thrombophilia, and/or who are taking any hormones that increase the risk of VTE (see Hormone Comparison Table on page 6) should be provided prophylaxis:

- Prophylaxis dose: Apixaban 2.5 mg twice a day

Crew with no thrombosis but who have stasis and no family history and/or thrombophilia and who are not taking any hormones that increase the risk of VTE should be monitored more often, and hydration should be ensured.

Medical System Considerations

- Tranexamic acid should be added as part of an in-flight medical system to be used in case of menorrhagia.
- Thrombolytics such as Tenecteplase should be considered for inclusion to treat a pulmonary embolism if it were to occur.

Risk Assessment and Spaceflight Venous Thrombosis Management

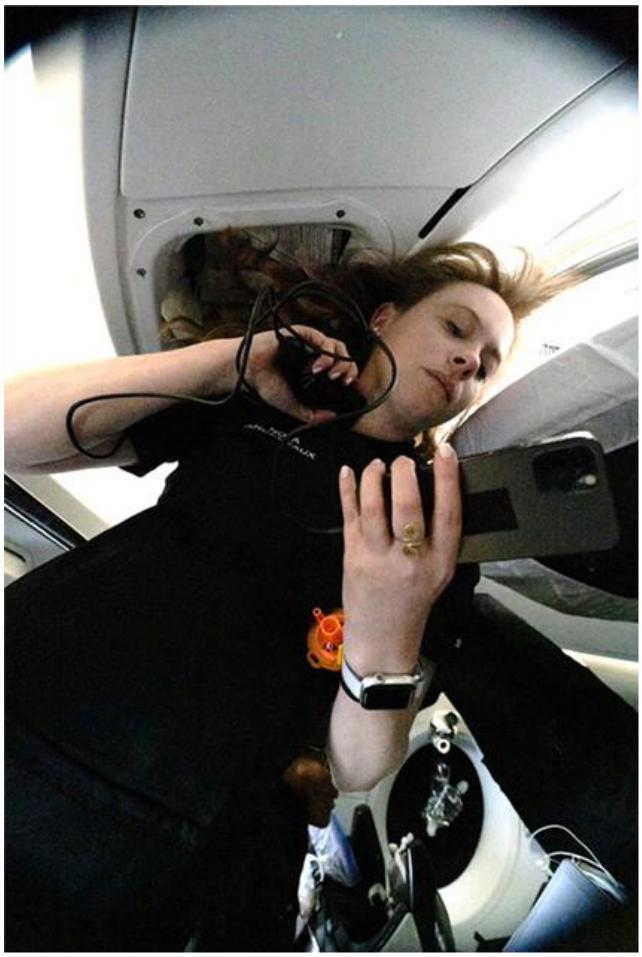
Landing Considerations

Apixaban has a half-life of roughly 12 hours (with wide interpersonal variation) and if trauma (bleeding) does occur, the wound can be compressed, and the next dose(s) may be skipped until the trauma is under control. Reversal agents are difficult to administer in space, and if other anticoagulants are used, this should be considered.

If a crewmember is taking a treatment dose of Apixiban, it is recommended to stop taking it least 48 hours prior to landing in case of significant trauma during the landing event. If a crewmember is taking a prophylactic dose of Apixiban, it is also recommended to stop taking it least 24 hours prior to landing.

NOTE: These are guidelines, and each case presents differently. Treatment must be adjusted accordingly.

Refer to the diagram on the following page for treatment guidelines.

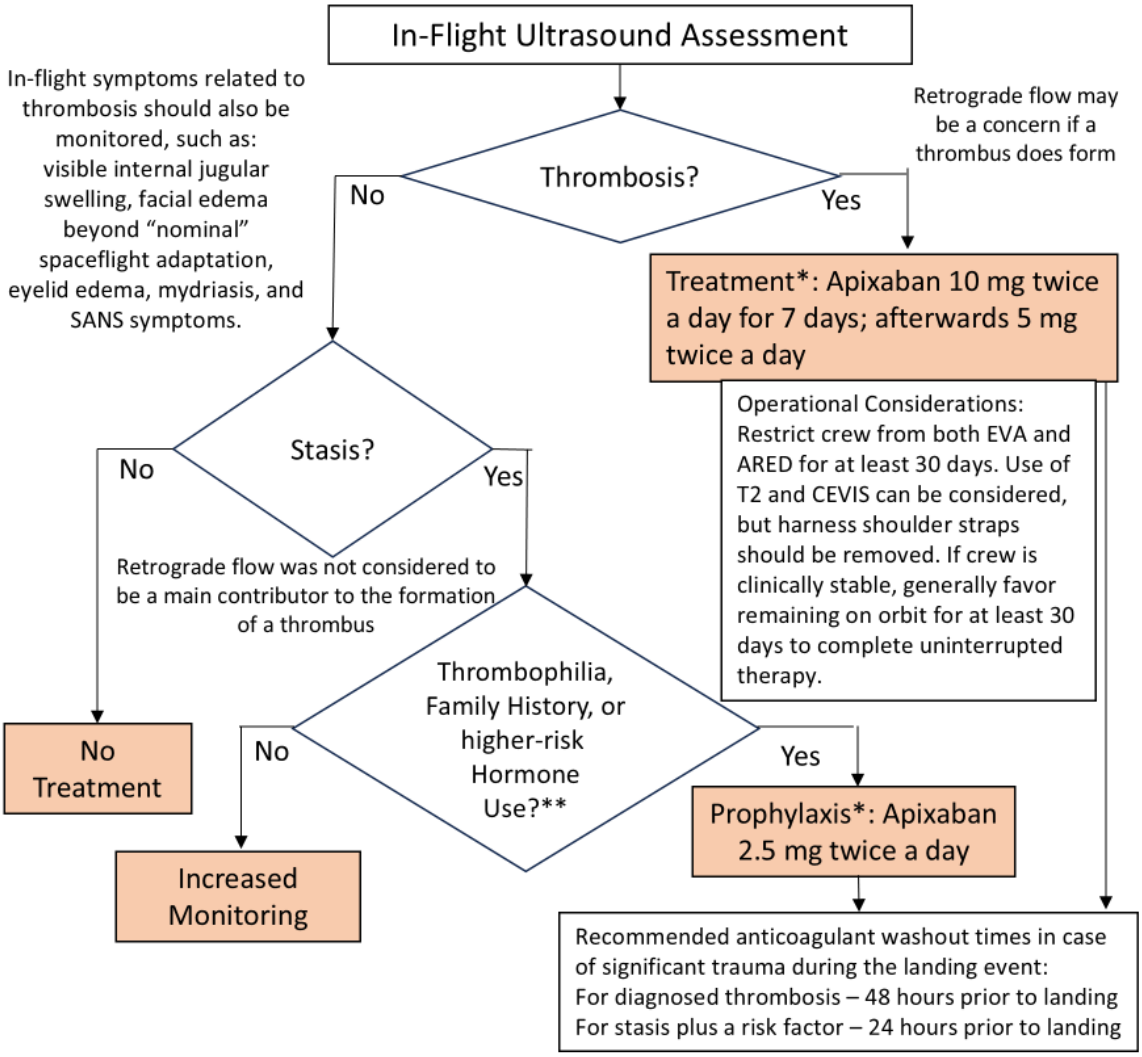


Private astronaut Hayley Arceneaux of the all-civilian Inspiration 4 crew takes ultrasound images of the jugular. Source: Twitter

Spaceflight Veinous Thrombosis Management

Preflight Considerations

- Subsets of preflight assessments screening and testing that may identify risk factors for VTE are listed on pp. 9-10.
- Medical history and hormone use evaluations are conducted pre-flight. Crewmembers are counseled on low and higher-risk hormone options and the potential implications for prophylaxis decisions.
- Crewmembers who have a history of unprovoked thrombosis in an immediate family member should consider not using oral estrogen therapy, and crewmembers positive for thrombophilia should not use hormone therapy or should use lower-risk hormone therapy.



*Crewmembers using an estrogen-based COC should not discontinue their use if DOACs are administered due to the risk of abnormal uterine bleeding (AUB) (Baglin et al., 2012; Martinelli et al., 2016).
**Unprovoked thrombosis in immediate family members; hormones that increase the risk of VTE (see Hormone Comparison Table on p. 6)

Source: Modified from Bostick et al., 2025

Back-Up

Referenced Technical Requirements

View the current version OCHMO-STD-100.1 on the OCHMO Standards website

OCHMO-STD-100.1A Revision A

6.3.2 Screening for Deep Vein Thrombosis and Venous Flow Anomalies

[6041] Requirement: Every crewmember **shall** be screened for deep vein thrombosis (DVT) and flow anomalies of the internal jugular veins.

Rationale:

- Primary DVT of the left internal jugular vein has been observed at elevated rates in microgravity. Flow anomalies are observed in a significant subset of crewmembers examined for both research and surveillance purposes and likely represent a risk for DVT development.
- DVT is associated with significant mission impact and poses an acute risk to crewmember health.
- Early diagnosis of abnormality will help identify crewmembers at risk for DVT formation and may allow the provisioning of early treatment before DVT becomes symptomatic or results in a life- or mission- threatening complication such as pulmonary embolism.

Description: Using an ultrasound device, duplex ultrasound of the bilateral extracranial internal jugular veins, with breathing and compression maneuvers, is performed with teleguidance and/or autonomously with just-in-time training. An onboard ultrasound device will be used for in-flight DVT and venous flow anomaly screening.

Example Schedule based on 180-day ISS mission: L-12/3 m, L+30 days; L+60 days; R-42 days, R+0/45d, as clinically indicated (ACI).

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