Neurological Altitude Decompression Sickness Among U-2 Pilots: 2002–2009

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Introduction: Compared to the previous 47 yr, U-2 pilots reported an increased number of altitude decompression sickness (DCS) incidents with central nervous system (CNS) manifestations during 2002–2009. Due to increasing incident severity during military operations, the U.S. Air Force initiated an investigation to prevent future mishaps. ***Methods:*** We retrospectively examined all neurological DCS cases observed among U-2 pilots during 2002–2009. Urgency to prevent further pilot losses limited this study to using existing, often incomplete data sources. ***Results:*** During 2002–2009, 16 confirmed incidents of CNS DCS occurred with 13 pilots, plus 4 possible incidents with 4 pilots. Significantly, 12 of 16 confirmed incidents occurred at 1 operating location, including 4 of 5 life-threatening cases. This series of cases were of a type and severity rarely found in flight operations and correlated temporally with increased sortie frequency/duration associated with combat operations. Multiple investigations confirmed no defects in aircraft, support equipment, or oxygen supplies. Nor were significant trends observed with age, habitus, environmental exposure, medication use, or cardiac defects. In 11 cases, symptom recognition occurred well after the 4-h point where clinical experience indicated risk should stabilize. Symptoms also recurred days later and responded to repeat hyperbaric oxygen therapy in three of four cases. Finally, neuropsychiatric symptoms persisted in six pilots for years and may represent permanent injury. ***Conclusions:*** An increase in U-2 CNS DCS cases probably resulted from more cockpit activity combined with longer, more frequent high-altitude exposures. Adjustments in preoxygenation, cabin altitude, exercise at altitude, and frequency of flights may reduce incidence.

Keywords: U-2, decompression sickness, neurological, exercise, risk mitigation.

THE U-2 (U-2S AND U-2ST variants) is the sole remaining manned high-altitude reconnaissance airframe in operational U.S. Air Force use. Since typical missions expose pilots to a pressure equivalent up to 29,500 ft (8992 m) of altitude for over 8 h while performing frequent movements in the cockpit, decompression sickness (DCS) remains an ever-present threat. In this sense, U-2 pilots operate at the limits of human and aircraft performance. While aircrew in other platforms (e.g., certain CV-22 and space missions) approach or exceed this risk at times (8), U-2 pilots deploy multiple times per year to fly high-altitude missions, normally every 3 or 4 days for months at a time. This sustained, frequent exposure to a high-risk altitude profile is unique in aerospace operations.

Two life support measures have been effective in preventing DCS during the program's history. These include preoxygenation (often referred to as prebreathe) with 100% oxygen at rest for at least 60 min before takeoff and wearing a full pressure suit (FPS) in case of sudden decompression. From the U-2 program's inception in 1955 to June 1998, there were no official reports of mishaps, deaths, or serious DCS symptoms [i.e., DCS incidents involving the pulmonary system, central nervous system (CNS), or both]. Reported operational cases involved predominantly joint pain with no reports of permanent injuries or significant mission impact (6,14). This is remarkable considering the significant risk of DCS to which U-2 pilots are routinely exposed. Studies from altitude chamber exposures dating to World War II indicate the potential for life-threatening and/or permanent damage from altitude DCS exists and may be expected based on statistical probability over the life of the U-2 (3,19). Also, predictions from the AFRL DCS Risk Assessment Computer (ADRAC) using an altitude profile identical to U-2 missions calculated a 73% risk of developing any DCS symptoms. [This program is based on statistical data from altitude chamber exposures and a bubble growth model which was subsequently validated in human subjects (4,8,12).] Thus, the true incidence of DCS in the U-2 program is probably higher than previously reported. Retrospective surveys of U-2 pilots revealed widespread under-reporting, possibly due to fear of grounding and subsequent negative career consequences. The surveys revealed 60–80% of respondents experienced DCS symptoms at some point in their careers, with 16–18% of these neurologic. In some cases, respondents reported symptoms severe enough to alter their missions (1). While the level of severity reported herein is greater than previously thought, the operational impact appears minimal throughout much of the U-2's venerable history. Unfortunately, this balance may have shifted.

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Following two severe cases of CNS DCS in early 2009, the 9th Reconnaissance Wing (9RW) Commander and Air Combat Command Surgeon General convened an expert panel from the U.S. Air Force School of Aerospace Medicine (USAFSAM), 711th Human Performance Wing, 99th Reconnaissance Squadron, and 9th Medical Group (9MDG). The command directed the panel to evaluate U-2 operations for potential causes behind the apparent increase in number of CNS DCS incidents between 2002 and 2009. This paper describes the results of the panel's investigation and discusses measures implemented to mitigate risk of DCS in future U-2 operations.

METHODS

This study protocol was approved in advance by the Institutional Review Board of David Grant Medical Center at Travis Air Force Base, CA. The protocol was exempted from providing written informed consent under U.S. Air Force Surgeon General-approved Clinical Investigation #FDG20100012H. The panel approached their task in the manner of a safety investigation following an aircraft mishap. The investigating team included pilots, flight surgeons, physiologists, flight safety officers, medical DCS experts, life support and aircraft systems engineers. Their purpose was to determine causal factors (human, materiel, environmental) directly or indirectly impacting U-2 neurological DCS events in order to prevent future incidents. Secondarily, the 9RW Commander asked the panel to address whether excessive body fat or medication use (specifically dexamphetamine "go-pills," an authorized pharmaceutical counter-fatigue measure) could have influenced DCS risk in U-2 pilots.

Prior to visiting Beale Air Force Base, the panel compiled and analyzed data from multiple official sources describing U-2 DCS incidents. Since no comprehensive repository on U-2 DCS incidents existed, 9MDG flight surgeons collated data from individual records at the USAFSAM Hyperbaric Medicine Division (treatments, consults), Air Force Safety Center (mishap reports), 9MDG (narrative summaries, physiological support reports), and 9RW (flight records, aircraft inspections, equipment records.) This effort produced a database of reported DCS incidents dating from January 1991 to December 2009. Using this database, four panel members retrospectively reviewed the series of reported DCS incidents occurring in U-2 pilots between January 2002 and December 2009, using the cases between January 1991 and December 2001 for comparison. Confirmed cases of CNS DCS were defined based on narratives from official safety or medical records describing any CNS symptoms with onset during or after high-altitude flight. Probable cases were those in which official records denoted CNS DCS symptoms but provided incomplete details necessary for confirmation. Possible cases were those in which patients retrospectively reported CNS symptoms after high-altitude flight. Pilots in these cases either misrepresented or did not report to the flight surgeon at the time of the incident to avoid grounding (7,8,11). Thus, no official record existed for physician review and confirmation of diagnosis and treatment in these cases. Panel members then evaluated each case for common risk factors and operating characteristics.

The panel performed their main investigation at Beale Air Force Base during August 2009. Panel members conducted an exhaustive review of U-2 worldwide operations, life support equipment, and aircraft systems together with representatives from the 9RW Safety Office, 9MDG Physiological Support Division, U-2 Maintenance Depot, and supporting contractors. Additionally, the team interviewed four active case pilots to verify elements of their DCS incidents and subsequent treatment.

Ongoing military operations significantly constrained analysis. U-2 flights had to continue uninterrupted to support combat operations while the panel sought potential solutions which could be implemented quickly in order to prevent further pilot losses. This limited the team to using existing data, which was often inconsistent and incomplete. Even so, the increasing likelihood of adverse in-flight events and mission compromise required action. With these constraints, the panel members analyzed U-2 operations based on our current understanding of DCS physiology while closely examining each operating location for any unique environmental, material, or human characteristics.

Over 20 yr of human performance data based on altitude chamber exposures demonstrates the four most critical physiological factors for development of altitude DCS to be: level of denitrogenation (prebreathe), altitude attained, duration of exposure, and exercise at altitude (8,16). While other anthropomorphic variables and physical factors such as diet, sleep/rest cycles, and physical fitness may affect individual risk of DCS and should be optimized, their overall effect is small by comparison (12,17). Achieving any significant degree of DCS risk mitigation in the U-2 requires addressing the four main factors. At the conclusion of their investigation, the team briefed results to the 9RW Commander and recommended potential risk reduction measures.

RESULTS

U-2 pilots reported at least 67 DCS incidents of all types between 1991 and 2009. Given small numbers and the aforementioned tendency for under-reporting, these data are not all-inclusive and must be interpreted with caution. However, the trend for greater numbers of reported neurological DCS incidents since 1991 is apparent (**Fig. 1**). The panel looked closely at the series of incidents occurring between 2002 and 2009 because this was the period of concern to the operational commander and most events occurred at a single operating location during this period. Unfortunately, simple examination of numbers does not show the worsening severity of these cases, which provoked the greatest concern, particularly when the number of neurological DCS incidents spiked sharply upwards in 2009. Prior to 2002, the U-2 had performed without operationally significant problems due to DCS. However, 2002 coincided with marked changes in U-2 operations related to military campaigns in Afghanistan and Iraq (discussed later).

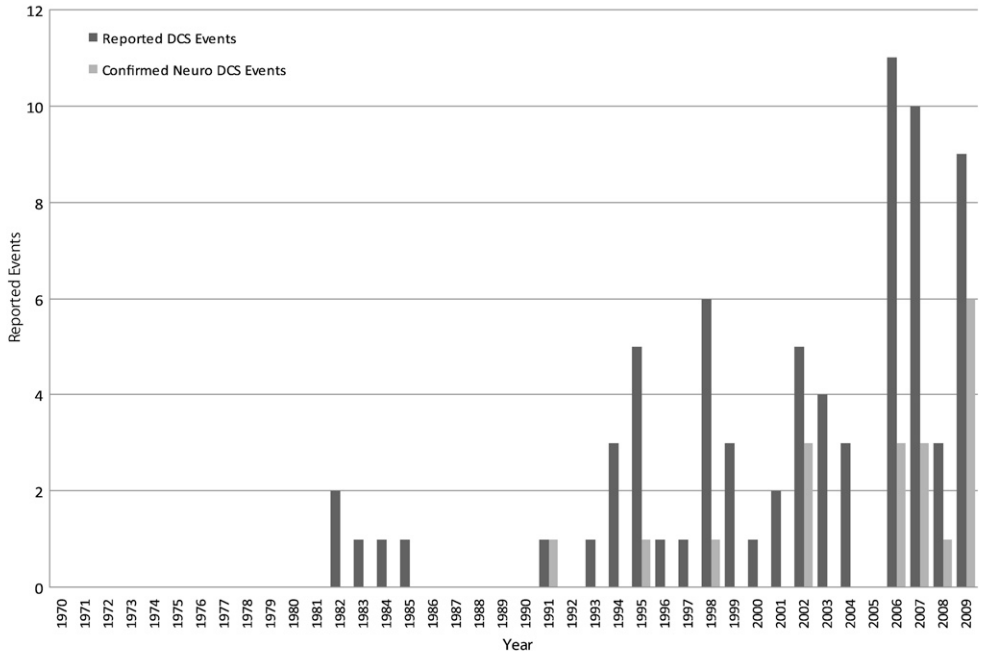

Fig. 1. Reported U-2 operational DCS incidents (1970-2009).

Changes in USAF aeromedical disposition regulations occurring circa 1999 probably influenced the reported number of U-2 CNS DCS cases. These changes essentially facilitated reporting of DCS without risking permanent grounding of pilots, thereby removing a policy which unintentionally prevented patients from receiving adequate medical care. Historically, pilots avoided reporting to a flight surgeon unless symptoms became severe and/or persistent. For example, literature reports noted cases in which U-2 pilots regularly experienced minor joint and skin DCS symptoms without reporting them for fear of grounding. This resulted in only the most severe and persistent cases of DCS joint pain being recorded by flight surgeons (1,14) and may explain some periods where no DCS incidents were reported (refer to Fig. 1). In contrast, research subjects in hypobaric chambers report and are treated at the onset of any suspected symptoms. Even with this apparent bias, the incapacitating nature of severe CNS symptoms makes it unlikely all pilots would have avoided reporting such disturbances prior to the 1999 regulatory changes.

Human and Medical Factors

Between January 2002 and December 2009, 37 U-2 pilots reported 45 DCS incidents of all types (some had multiple incidents). Of these, we confirmed 16 incidents of CNS DCS: 10 pilots with 1 incident each and 3 pilots with 2 incidents each. In addition, four probable incidents of CNS DCS occurred with four pilots. Importantly, 12 of 16 confirmed incidents occurred at 1 operating location, including 4 of 5 life-threatening cases. Five cases were considered life- and/or aircraft threatening because of the incapacitating nature of symptoms, their occurrence during flight, or both. Specifically, three extreme cases included severe neurological and pulmonary symptoms in which the pilots were incapacitated and exhibited symptoms of shock (7,11). The other two pilots experienced sudden-onset waves of vertigo, confusion, and depressed consciousness during flight so severe they considered ejecting. Fortunately, all pilots recovered their aircraft and received treatment.

The panel observed no significant trends with age, gender, body characteristics, or use of dexamphetamine during flight (**Table I**), which justified further analysis. Most cases occurred in men (one woman), consistent with the U-2 pilot population. No patent foramen ovale or other cardiac defect was detected among six case pilots tested using transesophageal or transthoracic echocardiogram with bubble study. Of nine case pilots tested with magnetic resonance imaging (MRI), one had significant brain lesions which corresponded with his neurological deficits (7).

By comparison, 13 U-2 pilots reported 24 DCS incidents of all types between 1991 and 2001 (some had multiple incidents; **Table II**). Of these, five pilots reported two confirmed incidents of pulmonary DCS and three confirmed, one probable, and one possible incident of CNS DCS (some pilots had multiple incidents and/or symptoms). All cases occurred in men (Defense Department regulations prohibited women in combat during most of this time). Data regarding age, body characteristics, and post-treatment tests were incomplete. Only one pilot underwent diagnostic imaging tests, with normal cranial MRI and transthoracic echocardiogram with bubble study. Operational use of dexamphetamine was not implemented during this timeframe.

Based on previous altitude DCS research, nearly all DCS incidents should occur within the first 4 h of exposure (8,12). However, in many cases, U-2 pilots recognized neurological symptoms late. Of 20 confirmed and

TABLE I. U-2 PILOT ANTHROPOMETRIC AND FLIGHT DATA (2002-2009).

Mission Pilot	Age	Body Mass Index	In-Flight Medication Use†	Physiological Altitude in meters (feet)	Exposure Time (hours)	Type of DCS Symptoms
MP1	35	24	No	8900 (29,200)	10.5	Confirmed CNS, pulmonary
MP2	37	32	No	8778 (28,800)	6.0	Confirmed CNS
MP3	43	NR	No	8992 (29,500)	11.7	Probable CNS
MP4	NR	NR	No	8992 (29,500)	NR	Probable CNS
MP5	30	NR	No	8717 (28,600)	7.3	Probable CNS
MP6*	35	24	No	>7620 (25,000)	6.0	Confirmed CNS, pulmonary
MP7	47	32	No	8534 (28,000)	11.1	Confirmed CNS, pulmonary
MP7	48	32	No	8697 (28,500)	2.8	Probable CNS
MP8*	33	23	No	8534 (28,000)	8.1	Confirmed CNS
MP9	39	27	No	8230 (27,000)	5.0	Confirmed CNS
MP10	37	28	No	8839 (29,000)	2.7	Confirmed CNS
MP11	36	25	Yes	8626 (28,300)	5.5	Confirmed CNS
MP12	35	21	No	8230 (27,000)	7.8	Confirmed CNS
MP13	36	29	No	8230 (27,000)	9.5	Confirmed CNS
MP14*	42	24	Yes	8809 (28,900)	9.6	Confirmed CNS
MP15	32	27	Yes	8077 (26,500)	7.0	Confirmed CNS
MP16	34	24	No	8687 (28,500)	9.5	Confirmed CNS

NR = Not reported.
* These pilots each had two confirmed incidents of CNS DCS symptoms.
† Dexamphetamine is a counter-fatigue medication approved by USAF for operational use.

probable CNS DCS cases during 2002–2009, only 7 (35%) pilots recognized symptom onset during flight within 4 h of takeoff. Of the remaining pilots, three (15%) recognized CNS symptoms during flight but after more than 4 h at altitude. Another eight (40%) recognized onset of CNS symptoms well after landing, between 4.7 and 36 h later (i.e., no recognition of symptoms during flight). Time of onset for the remaining two pilots (10%) occurred at some unknown time during flight (see **Fig. 2**). Among these 20 incidents, 3 pilots recognized DCS symptoms while in flight but avoided reporting. This resulted in progression to life-threatening neurological and pulmonary symptoms in two cases (7,11) and severe neurological symptoms in the third.

At least nine case pilots reported long-lasting and/or permanent neurological symptoms, which is highly unusual for aviation neurological DCS. As expected with aviation-related DCS, symptoms on initial presentation varied considerably and affected only the brain. No spinal symptoms were reported. Signs and symptoms included visual problems, vertigo, memory problems, confusion, headache, weakness, altered consciousness, and inappropriate fatigue. Symptoms improved markedly with descent and subsequent hyperbaric oxygen (HBO) therapy in all cases. However, 9 of 20 pilots (45%) from 2002–2009 reported lasting symptoms after completion of indicated HBO therapy. The most severe cases reported permanent visual deficits, short-term memory difficulties, and personality changes with corresponding cranial lesions on MRI (7). Seven reported a consistent pattern of recurrent headaches, central fatigue, memory difficulties, "foggy thinking," and personality changes (i.e., irritability). These symptoms generally improved over time but persisted for several weeks to years. Three of four treated with additional HBO therapy reported partial improvement. Additionally, one pilot was diagnosed and successfully treated for post-traumatic stress disorder. Review of medical records showed a second case pilot reported symptoms consistent with post-traumatic stress disorder, but was unrecognized at the time and subsequently lost to follow-up. While persistent and/or permanent neurological deficits are common in diving-related DCS, their presence in aviation-related cases is rare (3,19). This pattern of symptoms and time course of illness is very similar to that seen in patients with mild traumatic brain injury (5).

TABLE II. U-2 PILOT ANTHROPOMETRIC AND FLIGHT DATA (1991-2001).

Mission Pilot	Age	Body Mass Index	In-Flight Medication Use†	Physiological Altitude in meters (ft)	Exposure Time (hrs)	Type of DCS Symptoms
AP1	32	NR	No	>7620 (25,000)	>8.0	Confirmed CNS
AP2	34	NR	No	8047 (26,400)	NR	Confirmed CNS
AP3	NR	NR	No	NR	NR	Possible CNS
AP4*	37	NR	No	>7620 (25,000)	7.5	Confirmed CNS, pulmonary
AP4	37	NR	No	>7620 (25,000)	6.5	Pulmonary, joint pain
AP5*	31	26	No	>7620 (25,000)	2.5	Probable CNS

NR = Not reported.
* These pilots had multiple DCS incidents and/or symptoms.
† Dexamphetamine was not approved for operational use during this timeframe.

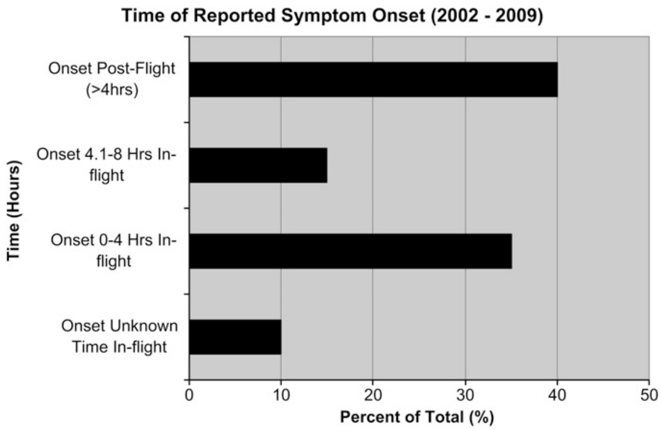

Fig. 2. Time of initial symptom onset.

Panel members concluded appropriate treatment was provided in all but one case (8). Medical records showed flight surgeons administered ground level oxygen and HBO therapy appropriately in 19 of 20 confirmed cases after consultation with USAFSAM hyperbaric medicine specialists. HBO therapy was delayed in one case, but subsequently initiated after return to home station with reported resolution of symptoms. However, symptoms recurred after completion of indicated HBO therapy in at least four other cases. Two case pilots reported recurrence of symptoms after mild changes in altitude (approximately 305 m or 1000 ft) while driving home after HBO therapy. Unfortunately, repeat HBO therapy did not take place in these cases because symptoms had resolved by the time patients reported to a physician (over 2 wk elapsed). Two more cases occurred during commercial airline flights taken 4-5 d after HBO therapy. Although these patients underwent repeat treatment within 24 h of landing with substantial improvement, both are among the pilots who reported persistent symptoms.

Significant Operational Factors

Three changes in U-2 operations during the timeframe studied coincided temporally with the apparent increased number and severity of neurological DCS incidents. First, a change in aircraft sensors and a shift in mission emphasis resulted in greater pilot physical activity in the cockpit while at altitude. Prior to 1991, U-2 missions emphasized collection of strategic intelligence data for policy makers. Early U-2 missions involved flying a prescribed route using film cameras requiring few actions by the pilot. Film was downloaded after landing and flown to Washington, DC, for analysis and dissemination days later. In contrast, introduction of new sensors during 1990–1991 enabled real-time intelligence support to combatant commanders and dynamic interaction with ground forces (Mayse C, 9RW Historian. Personal communication; July 2009). Today's U-2 pilots operate multiple sensors and radio equipment while directing the aircraft to support tasks from ground commanders in real-time. As a result, present day U-2 pilots engage in more physical activity while at altitude. Though this is difficult to quantify, human research studies showed that even mild exercise increased risk of DCS from 57% (at rest) to 91% over 3 h at 35,000 ft (10,668 m) (8,16). From these data, it is suggested that even mild activities such as pushing ones heels against rudder pedals, raising ones arms to actuate flight instruments, or even repeated shifting of body position would significantly increase DCS risk over a resting condition.

Second, available data indicated present day U-2 pilots fly more frequently than in the past. Individual records and comments from operational commanders initially suggested a greater number of flight hours among case pilots. Unfortunately, military data sources for flying hours are inconsistent and incomplete, providing only aggregate flying hours for the entire U-2 program and only for certain fiscal years. Also, detailed individual military personnel records of flight hours are stored at the base level and move with the pilots when they change job locations or retire. The individual records are not systematically collected or analyzed on a consistent basis. Consequently, panel members were unable to obtain the statistical data needed to calculate incidence rates or make individual comparisons over time. Nevertheless, panel members were able to confirm an overall trend toward increasing sorties (number of flights) and total hours by using aggregate data for the U-2 program.

Available data showed the U-2 program flew an average of 13,195 h annually between fiscal years 1998 and 2009. During this timeframe, the program supported multiple, sustained combat-related operations in the Middle East in addition to standing requirements for intelligence collection and international treaty monitoring. By comparison, the program flew an average of 10,140 h annually between fiscal years 1979 and 1989, mainly in noncombat missions (Lt. Col. Heupel, AFSC/SEH. Personal communication; February 2010). This was a time of relatively routine military operations during the Cold War. Aggregate number of annual sorties followed a similar trend. Between fiscal years 1998 and 2009, U-2 pilots flew an average of 3457 annual sorties. By comparison, the program flew an average of 2039 sorties of all types annually between fiscal years 1979 and 1981. (Data regarding number of sorties was available only for fiscal years 1979–1981 due to inconsistent record keeping.) Again, the increase is attributable to sustained combat support missions added on top of stable, long-term operational support missions such as treaty monitoring. This information is more meaningful when one considers the number of available pilots (pilots actually flying combat missions and not unable to fly for health or administrative reasons). An average of approximately 49 available pilots flew missions annually from 1994–1997. Due to various personnel decisions, the U-2 program experienced a gradual decline in available pilots afterwards. From 1998–2009, an average of approximately 37 pilots flew missions annually, a 24% reduction (TSgt. Sibley, 9RW Historian. Personal communication; February 2010). Assuming a stable personnel situation between the periods 1979–1981 and 1994–1997 (historical records indicated manning levels remained stable or higher than 1994 during the latter part of the Cold War), U-2 pilots during that era flew approximately 207 h and 42 sorties annually. In contrast, U-2 pilots from 1998–2009 flew approximately 353 h and 92 sorties annually, an increase of 70% and 122%, respectively (**Table III**).

Third, present day U-2 pilots fly longer sorties. Records showed most serious DCS incidents, including 4 of 5 life-threatening incidents, occurred at a single overseas location (called Operating Location B for convenience). Not surprisingly, this was the primary support base for combat operations with the greatest number of assigned pilots. Analysis of the typical support mission for this operating location showed significant differences in duration and frequency of altitude exposures when compared to other U-2 operations (Operating Locations A and C). Unfortunately, the panel's initial analysis using aggregate data to derive average sortie durations was inappropriate and provided misleading results. For example, the foregoing data on flight hours and sorties from Table III shows a reduction in average sortie duration over time, from 4.9 h per sortie during 1979–1981 compared to 3.8 h per sortie for the period 2002–2009. This is both counterintuitive and contradicts individual flight records for this series of case pilots. The problem arose because aggregate data includes flights of all types, inappropriately combining both short-duration (typically 1-2 h) training missions with longer-duration (typically over 6 h) combat missions. Fortunately, Air Combat Command collected more complete information on average sortie duration during the period of interest. **Fig. 3** shows average combat sortie duration increased steadily from 8.2 to 9.3 h per sortie at Operating Location B between fiscal years 2002 and 2007 (last available year for comparison) (Lt. Col. Nasir, ACC/SGP; Personal communication; July 2009). While complementary data from the earlier 1979–1981 period were not available due to incomplete databases, Fig. 3 provides a more accurate indication of average exposure duration at the operating locations of interest.

While long missions were never uncommon for the U-2, flights over 8 h were the exception prior to 2001 rather than the rule as they are today. Today's U-2 missions are designed to maximize time over target in order to provide persistent, responsive intelligence, surveillance, and reconnaissance support to ground forces. As shown in Fig. 3, the greatest pressure to perform longer missions occurs with pilots at Operating Location B. Not surprisingly, pilots at this site experienced both the highest number and most severe cases of CNS DCS incidents. By comparison, average sortie durations at Operating Locations A and C are significantly lower (between 6-7 h) during the same time period. These results accurately reflect the long-term and generally less intensive nature of typical operational missions at these two locations.

Other Factors Analyzed

Review of operational and medical records indicated dehydration was not a contributory factor in any incident. Though there is little research, dehydration is believed to increase susceptibility to DCS. In theory, hemoconcentration may increase DCS susceptibility by promoting nitrogen bubble growth and/or impairing the circulatory system's ability to eliminate nitrogen. Thus, current best-practice based guidelines recommend hydration as a DCS preventative measure (9). All case pilots prevented dehydration by drinking mixed water/electrolyte solution during flight through a helmet port designed for this purpose. Inspections also showed all integrated aircraft/FPS urine collection systems functioned properly.

Given the high number of severe, life-threatening events occurring at a single location, the panel carefully scrutinized the operating environment and equipment used at deployed locations. Internal and external agency inspections confirmed no defects in aircraft, life support, or oxygen supplies. Aircraft maintenance and safety personnel routinely inspected all aircraft systems, life support equipment, and oxygen supplies after each incident. Aircraft mechanical failures were rare, involving only one or possibly two cases of joint pain due to loss of cabin pressure. No mechanical failures occurred with any case of neurological DCS. Likewise, the cabin oxygen supply was designed as a separate, closed system to prevent cross-contamination from other aircraft systems. Tests showed no contamination in either aircraft or ground-level oxygen supplies. Finally, safety personnel recorded tail numbers for most reported DCS incidents and there was no correlation with specific aircraft.

No significant changes occurred in prebreathe procedures or life support equipment design during the study period. Life support equipment and integration procedures were standardized and implemented identically at each operating location worldwide. Each case pilot conducted a standard resting prebreathe for denitrogenation lasting at least 1 h. Physiological Support Division personnel inspected each FPS and helmet after every incident. There was no evidence of suit malfunction or improper use.

TABLE III. COMPARISON OF U-2 MISSION DURATION AND FREQUENCY.

	Previous Generation Pilots (1980s – 1997)	Present Generation Pilots (1998 – Present)	Percent Change
Number of Pilots Available	49	37	24% fewer pilots
Average Annual Hours per Pilot	207	353	70% more hours
Average Annual Sorties per Pilot	42	92	122% more sorties
Time to Achieve "1,000-Hour" Status	7-10 yr	3-5 yr	

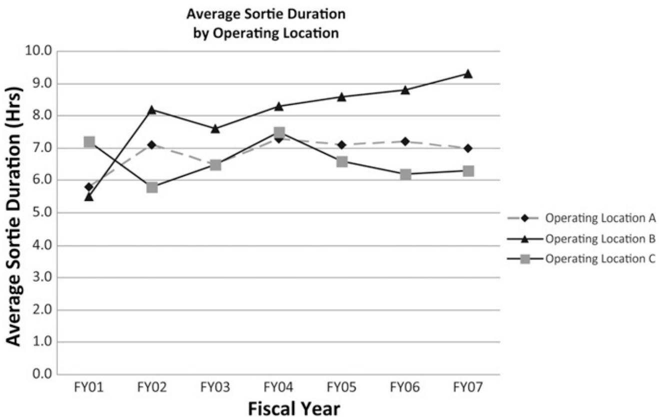

Fig. 3. Average sortie duration by location.

DISCUSSION

This case series showed U-2 pilots reported an increased number and severity of neurological DCS incidents during 2002–2009 compared to earlier periods. No readily apparent cause was identified by the expert panel's investigation. Eliciting causal factors is difficult due to the unique nature of the altitude exposures, inadequate databases, and limits to our current understanding of DCS pathophysiology. The increase in U-2 CNS DCS cases corresponded temporally with increased sortie duration and frequency associated with military operations. In particular, 12 of 16 severe cases occurred at the operating location with the highest frequency and duration of altitude exposures. Additionally, these U-2 case pilots engaged in more physical activity at altitude than their predecessors due to evolution in sensor capabilities and mission emphasis. Based on our current understanding of altitude-related DCS physiology, these are the most likely causes behind the increased number of U-2 DCS incidents. No other environmental, mechanical, equipment, procedural, or medical factors explained the increased number of cases, nor the preponderance of severe, life-threatening cases which occurred at a single operating location.

Operationally, this analysis was sufficient to demonstrate a trend toward more frequent high-altitude exposure for longer periods of time than the historical norm for the average U-2 pilot between 1998 and 2009. Military commanders often must act in the face of uncertainty based on trends or partial information. In this instance, action was needed to prevent further loss of pilots and potential loss of life while maintaining a vital wartime mission. Scientifically, however, the foregoing is statistically flawed and unsuitable for determining exposure rates or predicting risk of DCS for individual pilots. Caution must be taken in drawing conclusions from these data as the inherent limitations of any retrospective observational series apply. These include small numbers, potential selection bias, confounding variables, and lack of controls. Collecting consistent operational data over decades for individuals was not possible due to personnel moves and poor databases. Additionally, prospective studies were not possible given the urgent need for preventative action. Nevertheless, study of these individuals subjected to the same uniquely dangerous environment adds valuable new insight to our understanding of human high-altitude exposure.

Based on our current understanding of DCS pathophysiology, achieving any significant degree of DCS risk mitigation in the U-2 required addressing four critical factors: level of denitrogenation (prebreathe), altitude attained, duration of exposure, and exercise at altitude (12,16). While other anthropomorphic variables and physical factors such as diet, sleep/rest cycles, and physical fitness may affect individual risk of DCS and should be optimized, their overall effect is small by comparison (12,17).

Weight constraints forced engineers to originally design an inadequate partial pressurization system in the U-2, which resulted in high altitude cabin pressures. Technological advances may enable better pressurization of the U-2 cockpit in the future. However, redesigning the pressurization system at this stage may be too costly, too lengthy to implement, and/or technically infeasible, so alternative preventative measures must be used until further engineering analysis can be completed. Exercise-enhanced prebreathe (EEPB) was the most effective DCS countermeasure available not regularly used by the U-2 program. Originally designed and tested operationally with U-2 pilots, the procedure underwent further human testing and use by NASA in space extravehicular operations (6,18). The standard EEPB protocol involves 10 min of moderate upper and lower body exercise at the beginning of a 60-min total prebreathe period. The protocol is proven to reduce DCS risk in the U-2 altitude profile by approximately 35%, is readily available, and inexpensive to implement. Operationally, there may be limitations to using EEPB in hot environments due to thermal loading since further stress, fatigue, and discomfort for pilots would be counterproductive. Alternatively, increasing the current 60-min resting prebreathe is inefficient: each additional hour after the first reduces DCS risk by only about 10%. Therefore, the expert panel recommended pilots who developed any DCS symptoms should use EEPB for all subsequent high altitude flights (8). Further operational testing and evaluation is ongoing to address concerns with thermal loading and may lead to continued use of EEPB by U-2 pilots.

Altering U-2 flight altitude parameters may seem inconceivable. However, modeling demonstrated relatively minor variations in physiological altitude (altitude the pilot's body experiences in the FPS) significantly altered U-2 DCS risk. ADRAC calculations show DCS risk steadily declines with decreasing physiological altitude below 30,000 ft (9144 m) and drops markedly below 24,000 ft (7315 m). This suggests modest operational measures to reduce the pilots' physiological altitude could reduce overall risk of DCS for the U-2 population. With the U-2's differential cabin pressurization system, this can be accomplished by a combination of flying lower and/or inflating the FPS (8,18). Mission requirements dictate operating altitudes—some missions require maximum altitude to optimize sensor collection or avoid threats while others may allow lower altitudes. In any case, the pilot is generally not required to operate at maximum altitude for the entire sortie. Given operational flexibility in this area, ADRAC results indicate significant DCS reduction can be expected with modest altitude reductions (**Table IV**). Additionally, pilots have some control over physiological altitude through FPS inflation. Many U-2 pilots reported inflating the suit for comfort or after DCS symptoms occurred (attempted treatment). By turning a knob, the pilot can adjust suit inflation through a range, producing minimal pressure (0.5 psi) with no restriction in movement to a high pressure (2.0 psi) requiring considerable exertion for movement. Together, using these two measures (lower altitude plus partially inflated suit) could significantly increase protection from DCS. In practice, implementing such changes in U-2 operations requires a shift in thinking since altitude differences of these magnitudes were previously considered inconsequential. Additionally, U-2 pilots need to be educated to fly with the suit partially inflated for the entire flight as a preventative measure, not just when symptoms appear.

The increased number of reported U-2 neurological DCS cases coincident with increased frequency and duration of altitude exposure suggests a causal relationship. Unfortunately, there is no recorded history of similar problems with aviation DCS for comparison in either the U-2 or other military high-altitude reconnaissance programs based on our literature review (14). Such a long period of sustained high operations tempo is unprecedented in the U-2. Anecdotally, senior members of the U-2 community reported times during the Vietnam War when flying schedules were adjusted to allow more rest between flights because of increased DCS incidence. If so, no record of these actions remained in the 9RW archives (Mayse C, 9RW Historian. Personal communication; July 2009).

Unfortunately, misperceptions persist among many flight surgeons and pilots regarding DCS. For example, early studies suggested gender, age, and body characteristics played a significant role in aviation DCS susceptibility. Recent research by Webb et al. showed gender was not a factor in DCS susceptibility and level of fitness is a more appropriate measure of susceptibility than weight alone (17). This cohort of U-2 pilots with CNS DCS included one woman. Since only six female pilots served in the U-2 program since these combat positions were opened in the 1990s, the authors felt this case was consistent with demographics. Likewise, this series did not show any tendency for more frequent or severe DCS with increased age or body mass index (BMI). Ages and BMI of the U-2 pilots described herein were consistent with current and historical norms. Though BMI is a poor measure of fitness, it is a widely used clinical marker that correlates with poor health when elevated. U-2 pilots in this series were relatively fit based on military standards and consistent with their unaffected peers.

Similarly our experience with these cases also suggests flight surgeons must reconsider the previous maxim that DCS rarely presents after 4 h when evaluating flyers for potential treatment. Previous empirical data and human research indicated DCS risk increased with duration, but symptom recognition seldom occurred after 4 h (8,10) These conclusions were based on over 3000 subject altitude chamber exposures during 1983–2005 (8). Butler et al. also noted that 60% of 1153 subjects manifested symptoms at altitude or within 2 h of exposure in USAF altitude DCS cases treated between 1941 and 1999 (3). Though small in number, 58% of U-2 pilots in our study presented after more than 4 h in flight, including 42% presenting over 24 h after landing. However, operational U-2 pilots are a markedly different population than the test subjects in the earlier studies. Of note, 93% of exposures examined by Butler et al. and 100% of those examined by Pilmanis came from altitude chamber operations (3,8). Altitude chamber subjects are monitored specifically for any suspected symptoms, with ready access to immediate medical treatment. Conversely, in addition to fear of grounding, operational pilots and astronauts tend to delay medical reporting for many practical reasons, such as pressing mission needs and extreme distances to treatment facilities. The protean nature of DCS symptoms also makes it difficult for physically stressed pilots to recognize nonspecific symptoms such as headache and inappropriate fatigue until severe or worsened. Thus flight surgeons must maintain a high degree of clinical suspicion for at least 72 h following any significant operational altitude exposures.

TABLE IV. ADRAC PREDICTION OF U-2 DCS RISK BY PHYSIOLOGICAL ALTITUDE (6).

Physiological Altitude in meters (feet)*	Predicted Risk (%) – Historical U-2 Exposure Profile§	Predicted Risk (%) – Current U-2 Exposure Profile†	Predicted Risk (%) – Current U-2 Exposure Profile with EEPB‡
9144 (30,000)	74	88	65
8534 (28,000)	52	76	32
7925 (26,000)	45	71	27
7315 (24,000)	34	54	18
6706 (22,000)	5	5	1

EEPB = exercise-enhanced prebreathe.
* Actual altitude experienced by the pilot's body in the full pressure suit.
§ Includes 60-min resting prebreathe and mild exercise at altitude.
† Includes 60-min resting prebreathe, more exercise at altitude, longer exposure at altitude, more stress and fatigue.
‡ Includes same exposure profile, but using 10 min of mild exercise within a 60-min total prebreathe.

Research regarding the effects of repeated high-altitude exposures for long durations (greater than 8 h) on DCS risk is unclear. A 2002 review by Pilmanis et al. showed inconsistent and contradictory results regarding the effects on DCS of repeated altitude exposures. The same study showed four consecutive, short-term (30 min) high-altitude exposures actually reduced incidence of DCS compared to a single 2-h exposure (13). No studies made further differentiation on the basis of exposure duration and most cases involved altitude chamber exposures less than 8 h. A more recent series by Brandt et al. noted a possible dose response relationship with higher rates of DCS among inside observers with more frequent altitude chamber exposures (2). Consequently, the U-2 and other operational programs have imposed various ground interval requirements between flights based primarily on operational factors (i.e., mission needs, duty restrictions, past experience, etc.).

Finally, some animal and human performance studies suggest it is possible to become acclimatized by repeated decompression exposures, thereby reducing the risk of altitude or diving DCS in some individuals (13,15). These studies suggest that variability in individual stress response to pressure changes or to nitrogen gas emboli could result in some pilots being more susceptible to DCS, whereas others become acclimatized. Indeed, within the U-2 program many pilots never experienced any DCS during the past 10 yr, while at least three case pilots experienced severe CNS DCS within their first few operational sorties. Current research does not enable prediction of individual susceptibility to DCS. However, this case series suggests an increased risk of CNS DCS with frequent long-duration high-altitude flights. Further research would be helpful regarding the influence of both exposure duration and frequency on risk of altitude DCS. Ideally, flyers would benefit from guidelines similar to dive tables in providing standards for safe intervals between flights based on frequency, duration, and altitude of exposure. As the difficulties depicted by the authors in this analysis illustrate, consistent operational records of individual altitude exposures and medical treatment would greatly facilitate statistical analyses required to develop better exposure guidelines.

In conclusion, our investigation did not uncover a single causal factor which could explain the apparent increased number of neurological DCS cases in U-2 pilots during 2002–2009. The cause is probably multifactorial, with both operational factors and individual susceptibilities influencing results. Conceptually, it appears U-2 pilots crossed a heretofore unrecognized physiological line in meeting the demands of current combat operations with the available manpower. In the absence of a single correctable problem and with only incomplete data, U-2 commanders have made incremental changes in controllable variables to mitigate DCS risk. Further research regarding the effects of frequency, duration, and activity of altitude exposure are also being undertaken. Given mission needs, there is little flexibility regarding physical activity at altitude beyond educating pilots to avoid unnecessary movements. Likewise sortie (altitude exposure) duration is driven by the need to maintain support to vital ground operations. However, the commander has increased the number of available pilots in order to both reduce the frequency of altitude exposure and increase rest cycles between flights while deployed. Time and further analysis with improved data collection may alter our scientific understanding of the relationship between frequency and duration of operational altitude exposure. Together, these measures may succeed in reducing the overall number of DCS incidents experienced by the U-2 program.

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