Image Cover Sheet 96-00607

CLASSIFICATION	SYSTEM NUMBER
UNCLASSIFIED	155059

TITLE

DIABETES MELLITUS IN AIRCREW - TYPE I DIABETES IN A PILOT

System Number:

Patron Number:

Requester:

Notes:

DSIS Use only:

Deliver to:

AEROMEDICAL GRAND ROUNDS

Diabetes Mellitus in Aircrew—Type I Diabetes in a Pilot

G.W. GRAY, M.D., and JOHN DUPRÉ, M.D.

GRAY GW, DUPRÉ J. *Aeromedical Grand Rounds: Diabetes mellitus in aircrew—Type I diabetes in a pilot.* Aviat. Space Environ. Med. 1995; 66:449–52.

Diabetes mellitus has traditionally been considered disqualifying for flying duties. Increasingly, our understanding of both Type I and Type II diabetes permits identification of subgroups of diabetics with an acceptable aeromedical risk. A case is presented of a Canadian Forces pilot with Type I diabetes who continues on restricted flying duties. The pathophysiology of Type I and Type II diabetes is discussed, as well as aeromedical considerations for returning a diabetic to flying status. Within an envelope of defined geographic and operational flying limitations, diabetic aircrew may be safely and usefully returned to restricted flying duties.

CASE PRESENTATION

This 38-year-old military rotary wing Search and Rescue pilot enrolled in the Canadian Forces in 1980 at the age of 24. He had no significant past medical history at the time of enrollment. His family history was positive for diabetes; his mother and brother had insulin-treated diabetes.

He completed flying training in 1982 and was assigned to fly the CH-118 Iroquois helicopter at Base Flight (crash rescue). In April 1987, aged 31, he presented to the Flight Surgeon with symptoms of fatigue, increased thirst, polyuria and weight loss of about 4 kg over a period of several weeks. On admission to hospital, his blood sugar was 19.2 mmol • L^{-1}. There were no abnormal findings on clinical examination. His weight was 73 kg, height 184 cm.

Treatment was initiated with insulin. He was referred to the University of Western Ontario Diabetes Study Group, and was entered in a trial study of immunosuppressive therapy in newly diagnosed diabetics. Investigations included a glycosated hemoglobin of 15.5%, hemoglobin 13.7, creatinine 76 mmol • L^{-1}, and blood sugars ranging 7–12 mmol • L^{-1} on 18 units of insulin per day. His basal C-peptide level was 0.19, and glucagon-stimulated C-peptide 0.23.

He was started on cyclosporine 350 mg twice daily and, by day 65, insulin was discontinued. His self-monitored blood sugars showed quite stable euglycemia with no symptoms of hypoglycemia and no low blood sugars. After 6 months on cylosporine, his stimulated C-peptide level was 1.00, his self-monitored blood sugars were normal, and his glycosated hemoglobin 9.2%.* His creatinine had increased over the 6 months of cyclosporine treatment, requiring the dosage to be reduced to 360 mg daily.

His glucose metabolism remained stable, requiring small doses of insulin only during infrequent viral infections. His blood sugars were generally 4–8 mmol • L^{-1}. In October 1988, after a further reduction in the cyclosporine to 240 mg daily, a small daily dose of 5–10 units of insulin was started.

He faithfully monitored his blood sugars three to four times daily, and had no symptoms of hypoglycemia or recorded blood sugars below 4.0 mmol • L^{-1}. His glycosated hemoglobin was consistently in the normal range, and his stimulated C-peptide levels ranged from 0.40 to 0.80.

In 1989, 2 years after diagnosis, he was returned to restricted flying "to fly with or as copilot" with geographic restrictions to postings at fixed bases with physician's services available, with specialist and aeromedical follow-up every 3 months. He was assigned to a Search and Rescue squadron flying the Labrador helicopter.

By early 1990, increasing creatinine values required further tapering of his cyclosporine to 220 mg daily in divided doses. A DTPA renal scan demonstrated a mildly reduced GFR at 71 ml • min^{-1} (N 80–120). Daily insulin requirements increased to 15–20 units per day.

In April 1991, a renal biopsy showed evidence of mild early diabetic nephrosclerosis and so cyclosporine was tapered and discontinued. Based on studies indicating a

From the Defence and Civil Institute of Environmental Medicine, Toronto, and the University Hospital, London, Ont., Canada.

This manuscript was received for review and accepted for publication in November 1994.

Address reprints requests to: Commander G. W. Gray, M.D., DCIEM, 1133 Sheppard Avenue West, Downsview, ON, M3M 3B9, Canada. DCIEM No. 94-56

* Colorimetric method, upper limit of normal 8.8%.

slowing of pancreatic islet cell destruction, nicotinamide 1.5 g daily was started.

He was temporarily grounded and over the following 6 months his insulin requirements increased to 20–22 units per day. Blood glucose control remained extremely stable with readings 3–4 times daily in the 4–10 mmol • L^{-1} range. His creatinine levels returned to normal (96 mmol • L^{-1}) and his stimulated C-peptide levels remained in the range of 0.45–0.79. Retinal examination showed no evidence of diabetic retinopathy. An exercise thallium study and a DTPA scan of renal function were normal.

He returned to restricted flying duties in 1992 with geographic and flying restrictions as previously defined. He remains on active flying duties with regular 3-monthly check-ups at the University of Western Ontario and the Central Medical Board. His self-monitored glucose levels remain stable with no readings below 4.5 mmol • L^{-1}, and no symptoms of hypoglycemia. On flight duties, he self-monitors his glucose levels preflight, and at regular intervals on extended flights. He retains significant levels of basal and stimulated C-peptide indicating sustained secretion of endogenous insulin.

His performance as a pilot has been outstanding. In 1991, he was awarded a Governor-General's commendation for a sea rescue under adverse conditions.

DISCUSSION

Until recently, the term "diabetic pilot" was an oxymoron (and is still considered so by many). Over the past two decades there have been remarkable advances in our understanding of the genetics, pathophysiology, complications, and treatment of diabetes so that various aeromedical agencies have begun to consider criteria by which pilots with disturbed glucose metabolism might safely be allowed to fly.

The main concerns in returning diabetic aircrew to flying duties are firstly, hypoglycemia, and secondly, microvascular and macrovascular diabetic complications including coronary heart disease. Diabetic aircrew also present special logistic problems, including requirements for closer medical monitoring and provision of medical supplies that may limit their geographic employability.

The challenge for aeromedical physicians and licensing agencies/aeromedical boards considering reassigning diabetic aircrew to flying status is to identify the criteria for screening that acceptably minimize the risk of diabetic complications and eliminate as far as possible the risk of hypoglycemia. This requires an understanding of the mechanisms of diabetes.

Pathophysiology

It was first recognized in 1936 that diabetes manifests in two different patterns, which early-on were categorized as juvenile diabetes and maturity-onset, with clearly different patterns of clinical expression and complications (6).

Juvenile diabetes is now classified as Type I or Insulin Dependent Diabetes Mellitus (IDDM) (7). Maturity-onset diabetes is labeled Type II, or Non-insulin Dependent Diabetes (NIDDM). The genetic and metaboli features of the two diseases are distinct; patients wit IDDM ultimately develop an absolute deficiency of in sulin while NIDDM patients continue to secrete insulin the problem being tissue resistance to insulin combine with inadequate insulin secretion.

Type I IDDM

Type I diabetics require exogenous insulin to prever ketoacidosis. Type I diabetes is characterized by a grac ual autoimmune destruction of pancreatic islet bet cells progressing to a diminishment and eventual failur of insulin secretion (8). Genetic predisposition has bc come increasingly clarified, and operates through number of alleles on chromosome 6 within or near th major histocompatability complex. Disease expressio appears to be triggered in genetically susceptible indi viduals by an inciting event. Although specific trigge factors have not been definitively identified, drinkin cow's milk in infancy and certain Coxsackie viral infec tions have been cited as possible factors.

Insulin secretion remains normal initially during the insidious destruction of beta cells, reflected by the pres ence of islet cell antibodies (ICA's), which may be present a decade before the development of diabetes The autoimmune beta-cell destruction is associated with lymphocytic infiltration termed "insulitis." As beta cel destruction continues, insulin secretion gradually de clines and eventually, when about 90% of the beta cel mass has been rendered non-functional or destroyed. overt symptoms of diabetes appear. Even after the development of diabetes, the pancreas continues to secrete insulin. Levels of endogenous insulin secretion can be assayed by measuring the level of insulin connecting peptide, or C-peptide.

Insulin is formed in the beta cell as proinsulin, connected to C-peptide. After release into the bloodstream, the C-peptide is cleaved by a protease, freeing the active insulin moiety. The presence of C-peptide thus reflects continuing insulin secretion by the beta cells. This is significant because the presence of even a reduced amount of endogenous insulin reduces the risk of hypoglycemia, and is thus an important marker in identifying Type I diabetics who might be considered for flying. Stimulated C-peptide levels assayed after glucagon infusion are an even more sensitive indicator of beta cell function.

The final stage of Type I diabetes is the complete destruction of beta-cells as manifested by the disappearance of C-peptide. At this stage, there is total dependence on exogenous insulin, and a significantly increased risk of serious hypoglycemic reactions and of ketoacidosis.

The demonstration of an autoimmune mechanism for beta cell destruction has led to a number of clinical trials of immunosuppressive agents in an attempt to induce remissions. Up to half of patients treated with cyclosporine, including this pilot, have had remissions lasting up to 1 year (1). But unfortunately, in the longer term, immunosuppression has not produced a lasting response. Complications of this immunosuppressive therapy have included nephropathy, which may limit dosage and sometimes requires discontinuation therapy.

The major complications of Type I diabetes are ketoacidosis, hypoglycemia, microangiopathic changes resulting in nephropathy, retinopathy and neuropathy, and macroangiopathy (coronary, cerebral and peripheral vascular disease). The effect of the level of control in Type I diabetes on diabetic complications, including hypoglycemia, was assessed by the Diabetes Complications and Control Trial (DCCT) recently published (3). The trial showed a significant reduction in the rate and progression of diabetic complications (nephropathy, retinopathy and neuropathy) in tightly controlled Type I diabetics (mean daily blood glucose 155, Hg A1C 7.2%) compared with conventional control (231, 8.9%). Intensive control reduced the progression of nephropathy by 35% in the primary prevention arm and 56% in the secondary prevention group. Neuropathy was reduced by 60%.

However, the trade-off for intensive control was an increased risk for hypoglycemia. Intensive control was associated with a 3.3-fold increase in the rate of severe hypoglycemia, a 3-fold increase incidence of coma/seizure, and a 2.3-fold increase in ER/hospital visits for hypoglycemia. This information is of considerable importance in the aeromedical consideration of Type I diabetes. While "tight" control regimens may reduce diabetic complications, they are probably unsuitable for aircrew because of the significantly increased risk of hypoglycemia. This may present an ethical dilemma; i.e., whether to treat a Type I diabetic aircrew optimally to minimize the risk of complications which will require removal from flying duties, or to allow less stringent glycemic control which minimizes the risk of hypoglycemia which might allow reinstatement.

Type II NIDDM

Type II diabetes is much more common than Type I, accounting for 90–95% of all diabetes (2). It is characterized by both an impairment of beta cell function and a diminished responsiveness to insulin, particularly in skeletal muscle. Remarkably, both these features are improved by any form of treatment which normalizes the fasting blood sugar including diet, exercise, exogenous insulin, or oral hypoglycemics.

Insulin resistance was recognized to be a key feature of NIDDM in the 1960's, but insulin resistance is not exclusive to NIDDM, occurring also in IDDM as well as in obese persons, acromegaly and Cushing's disease without diabetes.

The feature that appears to convert insulin resistance to frank Type II diabetes is a decompensation of pancreatic beta cells with a decline in insulin secretion in the presence of insulin resistance. Insulin resistance appears to be an inherited defect in Type II NIDDM, with greater than 90% concordance in identical twins. Insulin resistance can be demonstrated in high risk individuals well before impaired glucose tolerance develops.

The majority of Type II diabetics are obese, and with a diet/exercise program and weight loss, good diabetic control can frequently be achieved without resorting to pharmacological treatment.

The major complications of Type II diabetes are macroangiopathic (i.e., coronary artery, cerebrovascular and peripheral vascular disease), although Type II diabetics may also develop microangiopathic complications. With sustained, albeit diminished, insulin secretion, Type II diabetics have a low risk for hypoglycemia unless secondary to pharmacologic treatment with insulin or oral hypoglycemic agents; certain OHA's have a much greater predilection to cause hypoglycemia.

AEROMEDICAL CONSIDERATIONS

Clearly, not all diabetic aviators can be considered for flying status, yet neither are all diabetics universally unsuitable for flying duties. Blanket policies which ground all diabetics are no longer justifiable, and are under increasing challenge from human/civil rights organizations. In considering returning aircrew to flying duties, the task for aeromedical physicians and agencies is to identify diabetics at minimal risk of hypoglycemia, and who are free from diabetic complications. An additional consideration is the logistical problem posed by diabetic aircrew.

Hypoglycemia

Aeromedically, hypoglycemia is the diabetic complication of greatest concern. Features that characterize a low risk of hypoglycemia in diabetics include an educated awareness of the disease with an established pattern of stable glycemic control based on sustained compliance to a diabetic diet and exercise program. Stable control must be documented by regular self-monitoring with a memory-chip glucometer. Awareness of hypoglycemia and lack of previous episodes are also important features.

Type II diabetics controlled by diet and exercise alone have almost no more risk of hypoglycemia than non-diabetics. If oral hypoglycemics are required, the risk of hypoglycemia is increased, but varies with the medication prescribed. Risk is minimal with metformin, and lower with tolbutamide and gliclazide than with glyburide (glibenclamide) or chlorpropamide (5), which should not be used in aircrew.

In general, Type I diabetics are at greater risk of hypoglycemia because of the requirement for exogenous insulin. However, certain characteristics identify a subset of Type I diabetics who are at low risk of hypoglycemia. These features include:

a.) stable control with an absence of previous history of hypoglycemia/neuroglycopenia. The DCCT trials identified this as a major risk factor and predictor of further hypoglycemia;
b.) continued endogenous insulin secretion evidenced by near normal basal C-peptide levels;
c.) strong level of diabetic understanding and education; and
d.) consistent compliance with diet, exercise and self-monitoring.

Type I diabetics assigned to flight duties must be prepared to self-monitor glucose levels immediately before and at regular intervals during the duty period, and to take corrective action in the form of a snack for glucose levels below 6 mmol $\cdot L^{-1}$.

By selecting diabetics at low risk for hypoglycemia,

and with regular monitoring during the duty period, the risk of hypoglycemia, even in Type I diabetics, is minimized to an aeromedically acceptable level.

Other Diabetic Complications

Diabetics are at increased risk of a number of complications of significant aeromedical concern including ophthalmologic (cataracts, retinopathy, acuity changes due to osmotic changes in lens water) and cardiovascular (coronary and cerebrovascular disease). More stringent and frequent monitoring of potential complications is required in diabetics returning to flying duties. However, increased risk need not automatically translate to medical disqualification. As evidenced by this pilot, the cost of increased frequency of monitoring for these complications is more than compensated by the additional years of flying derived.

Logistic Considerations

Diabetic aircrew pose special logistic problems for operators whether military or civilian, including medication provision and storage, self-monitoring equipment, regularity of meals and special dietary requirements. These problems are not insurmountable, but do require geographic limitations on employability. Such aircrew are not deployable world-wide in a military setting, but can be usefully employed with specific geographic limitations.

Diabetic aircrew require close medical monitoring, with frequent joint review by a flight surgeon and an internist or endocrinologist. Regular ophthalmologic evaluation and screening for coronary heart disease are required, as well as monitoring for diabetic nephropathy. These requirements for close medical supervisio also mandate geographic limitations.

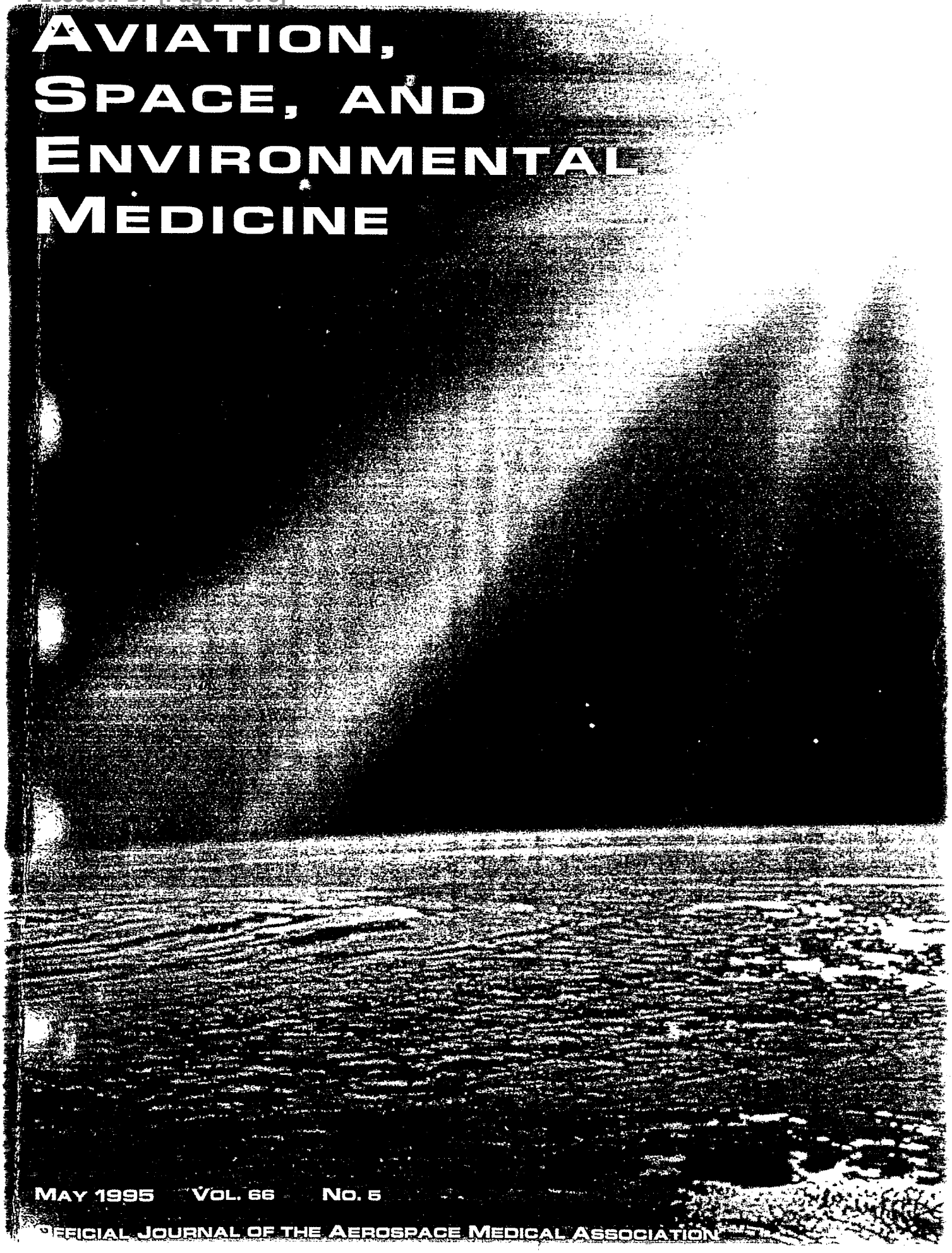
SUMMARY

Diabetes mellitus presents a spectrum of disease se verity. Increasingly, our understanding of both Type and Type II diabetes permits identification of subgroup with an acceptable aeromedical risk. The pathophysiol ogy of IDDM and NIDDM is discussed, as well as aero medical considerations for returning a diabetic to flying A case is presented of a Canadian Forces pilot wit Type I IDDM who continues on restricted flying duties Within an envelope of defined geographic and opera tional flying limitations, diabetic aircrew may be safel and usefully returned to restricted flying duties.

REFERENCES

1. The Canadian-European Randomized Control Trial Group. Cy closporin-induced remission of IDDM after early intervention Diabetes 1988; 37:1574.
2. Diabetes Care Review Issue. 1992; 15:737–805.
3. The Diabetes Control and Complications Trial Research Group The effect of intensive treatment of diabetes on the develop ment and progression of long-term complications in insulin dependent diabetes mellitus. N. Engl. J. Med. 1993; 329:977-86.
4. Expert Committee of the Canadian Diabetes Advisory Board Clinical practice guidelines for treatment of diabetes mellitus Can. Med. Assoc. J. 1992; 147:687–712.
5. Harris MI, Hadden WC, Knowler WC, et el. Prevalence of dia betes and impaired glucose tolerance and plasma levels in U population aged 20–74 yr. Diabetes 1992; 41:1503.
6. Himsworth HP. Diabetes mellitus: its differentiation into insulin sensitive and insulin-insensitive types. Lancet 1936; 1:117.
7. National Diabetes Data Group. Classification and diagnosis o diabetes and other categories of glucose intolerance. Diabete 1979; 28:1039–57.
8. Ziegler AG, Herskowitz RD, Jackson RA, et al. Predicting Type I diabetes. Diabetes Care 1990; 13:762.

AVIATION, SPACE, AND ENVIRONMENTAL MEDICINE



MAY 1995 VOL. 66 NO. 5

OFFICIAL JOURNAL OF THE AEROSPACE MEDICAL ASSOCIATION

155059

NO. OF COPIES NOMBRE DE COPIES	COPY NO. COPIE N°	INFORMATION SCIENTIST'S INITIALS INITIALES DE L'AGENT D'INFORMATION SCIENTIFIQUE
1	1	
AQUISITION ROUTE FOURNI PAR ▶ DCIEM		
DATE ▶		
DSIS ACCESSION NO. NUMÉRO DSIS ▶		

National Defence / Défense nationale

DND 1158 (6-87)

PLEASE RETURN THIS DOCUMENT TO THE FOLLOWING ADDRESS:

DIRECTOR
SCIENTIFIC INFORMATION SERVICES
NATIONAL DEFENCE
HEADQUARTERS
OTTAWA, ONT. - CANADA K1A 0K2

PRIÈRE DE RETOURNER CE DOCUMENT À L'ADRESSE SUIVANTE:

DIRECTEUR
SERVICES D'INFORMATION SCIENTIFIQUES
QUARTIER GÉNÉRAL
DE LA DÉFENSE NATIONALE
OTTAWA, ONT. - CANADA K1A 0K2