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Disclaimer: This content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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COMMENT & RESPONSE

Aircraft Cabin Hypoxia and Adverse Medical Events

To the Editor In their review of in-flight medical emergencies,[1] Dr Martin-Gill and colleagues outlined characteristics of the aircraft cabin environment, including mild hypoxia, that might precipitate or contribute to such emergencies, and provided recommendations for how to manage them medically. However, the underlying physiology that links routine cabin hypoxia to adverse medical events was not discussed. It is important to consider how physiological responses to cabin hypoxia might actually cause clinically significant effects in passengers, as this has implications for management of the most serious conditions in flight.

Of the classic physiological responses to hypoxia, the phenomenon of hypoxic pulmonary vasoconstriction is particularly relevant to passenger health as it is maladaptive at altitude. During commercial air travel, hypoxia causes an increase in pulmonary vascular resistance and pulmonary artery pressure that, in susceptible passengers, can result in flight-induced pulmonary hypertension.[2,3] Case reports have described progression to cardiac decompensation in airline passengers, and hypoxic pulmonary vasoconstriction may be an unrecognized contributing factor in many in-flight emergencies and in-flight deaths.[2,3] Mild hypoxia can also reduce myocardial oxygen supply while simultaneously increasing demand and reducing the ischemic threshold.[4]

Such mechanisms can harm vulnerable passengers by provoking or exacerbating in-flight cardiopulmonary emergencies. A key overriding principle of management should therefore be to normalize physiology as much as possible, including using supplementary oxygen to counteract the effects of the aircraft cabin environment.

In this context, we are concerned that the authors' management recommendations unnecessarily limited and thereby discouraged the use of oxygen. For example, in the management of cardiovascular symptoms, they advised oxygen only when dyspnea or respiratory distress is present and further qualified its use in other serious situations. We believe this is inappropriately restrictive for the in-flight setting, especially in older passengers in whom in-flight hypoxemia is more severe and pulmonary artery pressure response is greater[2] (and who are more likely to require an aircraft diversion for a medical event[5]). At cruising altitudes, low-flow nasal oxygen (approximately 2 L/min) corrects environmental oxygen deficiency without causing hyperoxia and has the potential to protect passengers from harm by safely and rapidly restoring physiology to a normal sea-level baseline.[4] We therefore recommend that low-flow oxygen should be commenced in any serious cardiopulmonary presentation in flight and that published guidance should encourage this.

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In Reply In our review,[1] we recommended supplemental oxygen for patients with dyspnea *or* another symptom of distress; we did not seek to restrict use of oxygen to only patients with dyspnea or hypoxia. Pulse oximetry is not commonly available aboard commercial aircraft, nor is it a required component of the emergency medical kit mandated

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by the Federal Aviation Administration, making clear identification of this finding infrequent. Because commercial airlines are not required to have oxygen stores to maintain passenger need for an entire flight, decision making led by the ground-based expert command physician allows the best use of any resources. Also, preflight screening to identify and plan for selected patients is wise, the latter often resulting in bringing on board an oxygen-concentrating device.

Patients with more severe cardiovascular compromise would reasonably be expected to have some degree of dyspnea if altitude imposes a burden. If resources to treat are not available, ground physician contact again can help weigh diversion to aid resolution of any suspected hypoxia or apparent respiratory distress from altitude. Roubinian et al[2] reported a small case series of patients with pulmonary hypertension who flew commercially, a higher-risk group than healthy volunteers reported in other studies of in-flight pulmonary vasoconstriction. Although some experienced in-flight hypoxia without symptoms, none experienced adverse cardiac effects. Whether clinically significant pulmonary vasoconstriction occurs aboard commercial aircraft absent any respiratory symptoms is unknown. Similarly, whether in-flight patients with no respiratory symptoms or hypoxia would have an outcome benefit from supplemental oxygen is also unknown.

Despite this paucity of data, we agree that administration of oxygen in any patient with cardiovascular symptoms is reasonable. Careful preflight evaluation and planning coupled with close expert contact, before and during the flight, is the best path.

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Approach to Evaluation of Multiple Liver Lesions

To the Editor Dr Mikolajczyk and colleagues presented a JAMA Clinical Challenge[1] of a 55-year-old man with a single-phase computed tomography (CT) scan demonstrating multiple liver lesions suspicious for malignancy, with the remaining liver morphologically normal. An elevated α-fetoprotein level was present. A triple-phase CT scan was obtained to evaluate the small bowel, and a pancreatic tail mass was discovered. The authors stated that the next step would be to perform endoscopic ultrasound-guided fine-needle aspiration of the pancreatic mass.

Why not perform a liver biopsy as the next step, possibly even before the triple-phase CT, instead of performing endoscopy to accomplish the pancreatic biopsy after the triple-phase CT? In my experience, a metastatic lesion, when approachable, is usually chosen for biopsy because it enables firm diagnosis of metastatic disease, commonly narrows the range of possible primary lesions, and even enables treatment when a primary lesion is not found. Furthermore, in approximately 5% of cases, liver lesions in patients with cancer may represent a second unknown primary cancer, rather than the suspected or known cancer, and in another 5%, the liver lesion may be benign.[2] Liver biopsy is safe and accurate.[2,3] One might argue the converse, then, that a biopsy of a liver metastasis does not mean that the patient may not have another different primary cancer—but in my experience, oncologists tend to treat the metastatic disease as the more important finding in the care of a patient.

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Conflict of Interest Disclosures: None reported.

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In Reply The patient in our case was noted to have intussusception of the small bowel on the single-phase CT scan.[1] Enteric malignancies are a well-recognized etiology for intussusceptions in adult patients.[2] Given the concomitant, innumerable liver lesions, there was initial concern for metastatic disease from an enteric malignancy. Thus, triple-phase CT enterography was pursued to evaluate for a primary malignancy involving the small bowel. Hypothetically, if liver biopsy had been performed first and the pathology had revealed neuroendocrine tumor cells, subsequent imaging would still have been needed to identify the primary neuroendocrine tumor. Therefore, performance of a biopsy of the liver lesion before triple-phase imaging, as suggested by Dr Ellis, would not have led to an overall change in the care or clinical course of this patient. Yet we do agree that liver biopsy of the metastatic lesions would have been an alternative approach to obtaining a pathologic diagnosis in this particular case. However, the purpose of the article was not to define the proper means of tissue acquisition but rather to inform readers of the importance of tissue sampling before treatment and to educate them on

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