

Cough and dyspnoea of an asthmatic patient at Mt. Kilimanjaro: A difficult differential diagnosis

K. Goebbels^a, U. Gieseler^{b,c}, Volker Schöffl^{c,d}, Thomas Küpper^{a,c,*}

^a Institute of Occupational and Social Medicine, RWTH Aachen University, Aachen, Germany

^b Department for Internal Medicine, Diakonissenkrankenhaus Speyer, Germany

^c Medical Commission of the Union Internationale des Associations d'Alpinisme (UIAA MedCom), Bern, Switzerland

^d Department of Trauma and Orthopaedic Surgery, Klinikum Bamberg, Germany

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Summary This case highlights the difficulties associated with the differential diagnosis of pulmonary symptoms in patients with pre-existing diseases in extreme environmental conditions. A 58-year-old man with child-onset allergic asthma developed dyspnoea and an acute non-productive cough during a trekking expedition on Mt. Kilimanjaro (5895 m) in Tanzania. The symptoms were believed initially to be linked to the high altitude exposure (high altitude pulmonary oedema (HAPE) or high altitude cough) or his pre-existing asthma. However, he was later diagnosed correctly with a reinfection of *Bordetella pertussis*. Pertussis is a highly communicable disease with potentially serious medical consequences that could have affected all of the expedition members. The effectiveness of a pertussis vaccine declines 4–12 years after the vaccination. Thus, it is suggested that the status of immunisation against pertussis should be checked along with those of other infections prior to travel.

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Introduction

Some of the most common disorders observed in mountain medicine are AMS (Acute Mountain Sickness) and HAPE (high altitude pulmonary oedema) with respective prevalence rates of 8–84% and 5–15%.^{1–8} Both AMS and HAPE are related directly to exposure to high altitude. Bronchitis and/or pharyngitis are experienced in approximately 12% of

all trekkers climbing for a short time period at altitudes higher than 4000 m.²

Access to appropriate medical diagnostic equipment and treatment during trekking tours will be limited, even if a medically qualified trekker accompanies the group. It is, therefore, important to be able to differentiate among the most common diagnoses using basic equipment and a sound knowledge base. The diagnosis is often unclear and the differentiation from disorders with similar symptoms causes regularly major problems for the travellers. We present a rare case study that was first assumed to be an altitude-related problem, and/or an acute worsening of pre-existing asthma. We discuss the differential diagnosis that should be taken into account in such situations where a mountaineer

* Corresponding author. Allmendenweg 52, D-40221 Düsseldorf, Germany. Tel.: +49 1520 1820256.

E-mail address: tkuepper@ukaachen.de (T. Küpper).

or trekker may also be suffering from potentially life-threatening HAPE.

Patient's medical/altitude climbing history

The patient was a 58-year-old healthy German male with the onset of asthma in childhood. The asthma was well-managed and stabilized over the years with the regular use of ipatropiumbromide/fenoterol spray (Berodual, Boehringer Ingelheim Ltd.) and beclometason/formoterol powder inhalator (Symbicort Turbohaler, AstaZeneca Ltd.).

His climbing experience included expeditions on mountains up to an altitude of 5000 m, and trips to Nepal lasting several weeks. His preparation for this particular trip included some recreational sport and endurance training once weekly, but no other specific training.

Altitude profile of the Mt. Kilimanjaro trekking undertaken

The patient planned to climb Mt. Kilimanjaro in Tanzania during the dry season, when the mean daily temperatures in the valley were between 20–35 °C, and –5 °C to about 6 °C on the mountain. There was no physician or medically trained trekker that accompanied his expedition.

The patient arrived at Arusha, situated at an altitude of 1400 m, where he stayed for one night. Here he was joined by the other expedition group members (10 mountaineers aged 40–60 years). The group then drove to Moshi, the formal beginning of the chosen trek up Mt. Kilimanjaro. Moshi is also situated at an altitude of 1400 m (Fig. 1).

The group stayed overnight at Moshi ("N1" in Fig. 2) and headed off towards Rongai the next day. This journey took 5 h in an open vehicle for 80 km on a very dusty gravel road at about 35 °C (Fig. 1). They passed through Rongai (1950 m), and they arrived at Kihelwea (2050 m) as

planned. Kihelwea marks the entrance point to the ascent planned. Up to this stage the patient did not experience any respiratory problems.

The expedition members decided to hike the so-called 'Rongai route' (for altitude profile, refer to Fig. 2). From Kihelwea the route begins from 2050 m with a 3.5 h walk to the first overnight stay at Cave Camp at 2830 m (Figs. 1 and 2, "N2"). The following day consisted of a 2.5 h walk up to the Second Cave Camp at 3450 m (Figs. 1 and 2, "N3"). Next day they took another 2.5 h to reach the next Cave Camp at 3850 m, though normally the hikes from days two and three are done in a single day. From Camp Three the route continued for another 4 h before reaching the School Hut at 4750 m. On the following day, Uhuru Peak (5896 m) could be reached within 4–6 h walking via Gillmans Point (5715 m), by walking 4–6 h.

To order to acclimatise properly (Fig. 2) and to avoid developing altitude-induced illnesses, it is strongly recommended that at least one night is spent at each of the huts.⁹ In reality, few trekkers acclimatise properly as they climb too high too fast by completing the walks from the 1st to the 3rd Cave Camp in a single day, and make themselves more susceptible to developing altitude-induced illnesses because of poor acclimatisation.

Medical situation at Mt. Kilimanjaro and later findings

The patient reported retrospectively his symptoms on Mt. Kilimanjaro when he returned to Germany. On the first day of his ascent, some hours above Kihelwea (2050 m), he developed a dry cough. This non-productive cough was described as "paroxysmal" by the patient, continued to worsen with increasing altitude exposure, and was accompanied by increasing dyspnoea. On the following day, these symptoms significantly worsened. On the third day when

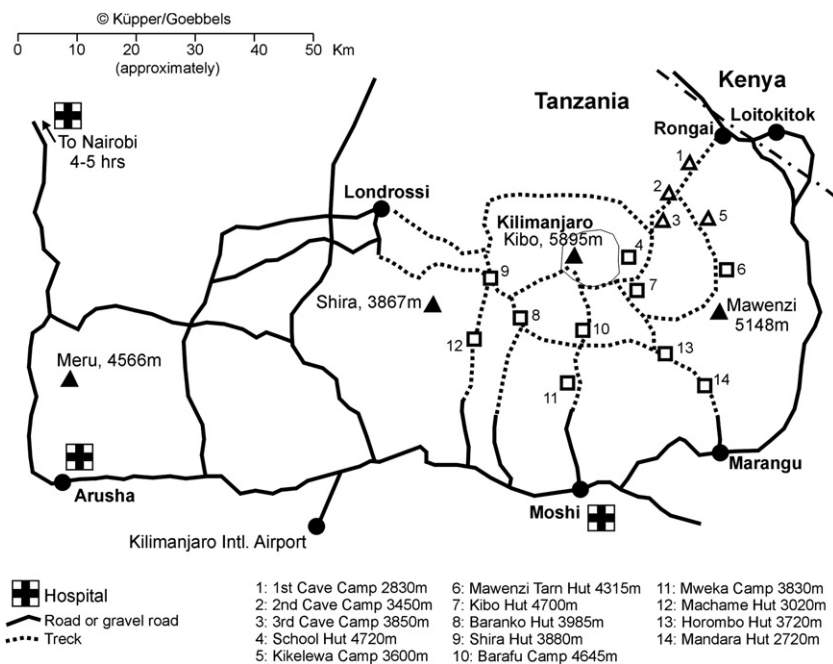


Figure 1 Sketch map of Mt. Kilimanjaro and the most important trekking routes.

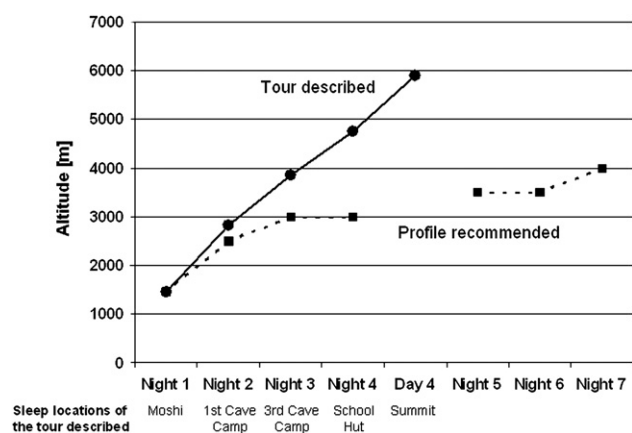


Figure 2 Altitude profile itinerary of the patient's trek (circles); and the suggested altitude profile according to evidence-based consensus recommendations (e.g. from UIAA MedCom, squares).

the patient arrived at an altitude of 4500 m, he experienced dyspnoea and a severe persistent cough. As these symptoms were also experienced during rest, he had to abandon the ascent. Before descending alone, he tried in vain to decrease his acute symptoms by administering his prescribed asthma medication as the only emergency medical treatment available to him at the time, but without any decrease in the symptoms. During his single day solo descent, he experienced severe coughing and dyspnoea. The dyspnoea decreased only minimally during the descent. During the entire expedition, he had no fever or other symptoms.

The paroxysmal cough persisted, even when the patient returned to Germany. One week after his return home, a chest X-ray showed normal results. He still had an acute, severe dry cough but normal breathing. His complete blood count, all other laboratory examinations and body temperature were normal except a leucocytosis of 12,800/ μ l. In the anamnesis a pertussis infection in his childhood attracted attention and as he did not receive any immunisation during childhood, or no further re-immunisation until the age of 40, a pertussis reinfection was the most probable diagnosis. To confirm this diagnosis, IgG, IgM, and IgA antibody titer against *Pertussis bordetella* were determined (anti pertussis toxin technique). IgG antibody titer was 78 U/ml (<20: no immunity; 20–30: suspicious/to be controlled; >30: definitive positive), IgM antibody titer was 6 U/ml (<9: no suspicion; 9–14: suspicious/to be controlled; >14: definitive positive), and IgA titer with 45 U/ml (<15: no suspicion; 15–22: suspicious/to be controlled; >22: definitive positive). The blood sample was obtained at day 17 after the onset of the first symptoms. The patient never suffered from the distinctive sound of the “whooping” cough which is typical for pertussis and facilitates the diagnosis. However, this “whooping” cough is more typical for infants and occurs only in some adults.

Discussion

This case is an extraordinary example of a respiratory tract infection that occurred during a trekking expedition to high

altitude, and then persisted at sea level. Reaching the correct diagnosis in a healthy individual would have been challenging enough, however it was more complicated in a patient with pre-existing health conditions. In addition, the patient did not follow the guidelines of the UIAA Medical Commission for proper acclimatisation,⁹ thus increasing his likelihood of developing altitude-induced illnesses. For example, the itinerary for UIAA planned route would have required sleeping in each of the camps, and spending at least one additional day at the Second Cave Camp and at the School Hut.

Both the diagnosis of HAPE, and presumably also the high altitude cough were very likely in this case – and both these conditions could have been avoided by a slower ascent. A slower ascent that facilitates acclimatisation is easy to plan when using the altitude profile guidelines listed in Fig. 1.

From the history of the medical problems, which the patient developed during his trip, one could hardly predict the final diagnosis. Normally the main differential diagnosis in the case described above would be high altitude cough or with regard to his dyspnoea HAPE (high altitude pulmonary oedema), followed by a broncho-pulmonary infection, or exacerbation of asthma. Other health issues such as cardiac insufficiency could have been excluded from his previous history of sport and medical examinations. Refer to Tables 1 and 2 for the differential diagnosis.

In support of the diagnosis of high altitude cough was the presence of cold, dry air that could have been a triggering factor and the dry, non-productive cough. To treat this condition, an antitussive drug such as noscapine would have been the usual treatment. One would expect a significant decrease of symptoms with this approach. However, in this situation, this treatment would have been the wrong “diagnosis” and would have continued to place the patient's trekking companions at risk of contracting the highly communicable infectious disease pertussis. With continuing symptoms, the situation would have been still unclear.

The diagnosis of HAPE may have been considered because of the altitude profile, poor acclimatisation, the continuing cough and dyspnoea that persisted during resting conditions. In this case the treatment would have required immediate descent, nifedipine, and (if available) treatment using an oxygen supply or portable hyperbaric chamber before descending. But the other HAPE symptoms, especially acute and extreme decrease of work capacity and breathlessness, were missing. Nevertheless, the diagnosis does not always include all of the typical textbook symptoms and it is therefore more difficult for laypersons to interpret the symptoms. Had oxygen or nifedipine been administered to treat the assumed diagnosis of HAPE, the most likely outcome would have been that there was no change in symptoms. By following this course of treatment, the diagnosis of HAPE might have been excluded. Although there are some data that suggest that acetazolamide may reduce the risk of HAPE, this drug is still most commonly used in high altitude medicine to prevent and treat AMS,^{10–12} although sufficient acclimatization is recommended instead of the use of drugs for prevention. Nevertheless, there is no evidence that the use or non-use of this drug may have had any influence on the case under discussion.

Table 1 Most important differential diagnoses to HAPE.

Diagnosis	Patient's history	Symptoms	Therapy	Remarks
"Physiological dyspnoea"	High altitude exposure	Tachypnoea without any other symptom	None (limit your workload!)	—
Hyperventilation syndrome	Agitation, massive fright	Tachypnoea, often combined with tingling sensations of the extremities, dizziness, sometimes collapse/unconsciousness	Calming down the patient, breathing controlled by counting seconds. Normally no drug therapy necessary	Self-limiting after collapse. Most important danger: injuries caused by fall
Aspirin intolerant asthma	History of nasal polyps and/or urticaria likely. Acute onset of asthmatic symptoms dependent on aspirin and/or salicylate dose (in foods or drug form)	Ronchus, dry rales, expiratory dyspnoea, <i>Note: anaphylaxis may occur</i>	Betamimetics, inhaled corticosteroids, corticosteroids i.v., theophylline. Adrenaline for anaphylaxis	Ask for aspirin tolerance/use! Genetically influenced disorder, therefore ask for symptoms at other family members too! <i>Note: Attack by cross-reactions with other non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen or diclofenac possible</i>
Sleep apnoea	High altitude exposure	Phases of dyspnoea or apnoea at night	Improve acclimatization. If symptoms persist, try theophylline slow release, 300–400 mg slow release in the evening	—
Cardiac insufficiency	Coronary heart disease/myocardial infarction? Cardiac insufficiency/vitium?	Dyspnoea, moist rales, pathological cardiac sound	Furosemide 40–80 mg i.v.	<i>Note: Acute cardiac problems are rare at high altitude</i>
Pulmonary embolism	Dehydration, immobilization (especially during flight!) varicosis	One-sided swollen leg, dyspnoea, tachycardia, split 2nd cardiac sound	Heparin 25,000 I.E., if available	<i>Note: Most important non-traumatic risk for fatal incidents at high altitude</i>
Pneumonia	Infection, fever, cough, expectoration	Cough, expectoration, chills, one-sided pulmonary rales	Antibiotics (macrolides or tetracycline)	<i>Note: Fever does not exclude HAPE from pneumonia</i>

The pre-existing asthma, when exposed to a possible triggering factor such as the dusty gravel road, may have led towards the diagnosis of "exacerbation of asthma" with the accompanying dyspnoea. It is important to note that it can never be assumed that asthmatic patients will carry their own prescribed bronchodilators to use in event of an acute asthmatic attack, as this is often not the case. But this patient was very compliant and used his medication regularly. To treat the exacerbated asthma, one could have tried a rapid-acting bronchodilator like salbutamol or terbutalin in combination with a topical steroid as a treatment option. But the topical steroid might have worsened an infectious disease such as bronchitis, although this risk is low if recommended dose is used.

The diagnosis of broncho-pulmonary infection (bronchitis) might also have been considered because of the pre-existing

asthma combined with poor hygienic conditions and the high prevalence of bronchitis among the locals porters, local guides and the local population.² The influence of smoking, preparing and cooking food over open fires in small rooms as a possible additional risk factors for infection of the respiratory system has not been fully investigated, although this too may have served as a possible trigger to worsen the symptoms.

Throughout the time the patient spent in on Mt. Kilimanjaro, and subsequently when at home in Germany, he never developed any symptoms of fever, headache, cold, sore throat or difficulty in swallowing. But the absence of these symptoms does not exclude any of the above-mentioned diagnoses. To treat a broncho-pulmonary infection, a broad-spectrum antibiotic would have been useful in case of pneumonia, or in a case of a bacterial bronchitis a macrolide such as clarithromycin.

Table 2 Rarer differential diagnoses to HAPE.

Diagnosis	Patient's history	Symptoms	Therapy	Remarks
Asthma	Strain/stress? Infection? Aspirin? Cold air?	Ronchus, dry rales, expiratoric dyspnoea	Betamimetics, inhaled corticoides, corticoides i.v., theophylline, cromolyn sodium	First asthma episode at altitude is a very rare event! Ask for history of asthma! Peak flow can be an easy way to monitor symptoms, especially with heavy exercise at high altitudes ^a
CO intoxication	Cooking or fuel powered lights inside of the tent or a snow cave	Headache, confusion.	Oxygen (if available) or fresh air (open tent or cave!)	<i>Note:</i> No cyanosis
CO ₂ narcosis	Very tight closed tent or snow cave	Sluggishness, somnolence, dyspnoea	Oxygen (if available) or fresh air (open tent or cave)	—
Pneumothorax	Spontaneous or traumatic	Acute dyspnoea, one- sided reduced or missing respiratory sounds	Puncture/drainage (severe cases only)	—
Neurogenic pulmonary oedema	High altitude exposure, unsuccessful therapy of HAPE	Symptoms of HACE, signs for intracranial pressure, pulmonary oedema	Massive therapy of the HACE (high dosages of corticoides and oxygen)	—
Drug induced pulmonary oedema	Heroin? Cocaine?	Miosis (heroin) or mydriasis (cocaine) of both pupillae	Diuretics, no nifedipine	Rare event at high altitude!
Aspirin induced pulmonary oedema	Headache and aspirin intake	Typical pulmonary oedema	Cortisone, diuretics, no nifedipine!	Rare event at high altitude, especially since aspirin is not recommended at altitude
Pertussis	Pertussis infection, contact to infected patients	Cough, dyspnoea	Macrolide (preferable during catarrhal state), if necessary cortisone	Rare event at high altitude

^a Note: Peak flow meters under-read at high altitude. A decrease of ambient air pressure of 100 mmHg, corresponding to about 1200 m of altitude, needs +6.6% of the reading.²⁴

Aspirin intolerant asthma was never considered in this case, although up to 40% of all asthmatics are at risk.^{13,14} The patient may have taken these painkillers to treat an altitude-related headache. In general, the use of aspirin at high altitude is not recommended due to the increased risk for side effects such as gastrointestinal bleeding in hypoxic conditions.

As we know now after the diagnosis “reinfection by *P. bordetella*” was made, an antibiotic would have been the best option for treatment. Of course, by treating “bronchitis” in the field with antibiotics, the correct diagnosis would never have been reached.

This case demonstrates the difficulties posed when diagnosing medical problems at altitude and in a remote setting away from comprehensive health care, regardless of whether the diagnosis was made by a medically trained person or layman. And even if the right diagnosis was made, the next question would be, did anyone in the group bring

a complete first-aid kit that included antibiotics, a broncho-dilatating drug in case an asthmatic patient forgot to bring their prescription, a steroid drug, and painkillers. A first-aid kit is critical to have in such a remote region where there are no hospitals and where emergency helicopter rescue is not an option. In fact, the Rongai Route is one of the most isolated treks on Mt. Kilimanjaro, and so no one can expect immediate help.

Another problem presented by this case was the infectious risk of the patient's condition. It is not known whether there was another case of pertussis in the group. In general, any unidentified highly contagious disease could potentially endanger all those members who are in close contact during a longer trip. With respect to pertussis, about 80% of susceptible persons become infected with the bacterium after close contact with an infected person.¹⁵ Immunity against pertussis will last for years, but immunity may be reduced around 40–50 years of age.

Immunity can also be reduced in a younger person who was vaccinated against pertussis previously (but never suffered from the disease); it should be recognised that their immunity begins to decline 4–12 years after vaccination, and this results in increased adolescent and adult susceptibility.¹⁶ We do not have any information on the vaccination status of the other group members, but with a very low percentage of persons >40 years vaccinated against pertussis it can be expected that at least some of the group members were at risk. With an estimated effectiveness of pertussis vaccines of about 85% these people would have had a sufficient protection if they would have been vaccinated previously.^{17,18} Therefore before embarking on any trekking tour, every expedition member should seek medical advice from their normal physician to thoroughly review their medical history, including immunisation status. Special precautions or additional medications may be needed in foreign countries and as a result of altitude exposure or geographical setting, and so this too should be reviewed by the trekker's physician. More details on such medical pre-screening are available on the homepage of the UIAA Medical Commission (www.theuiaa.org/medical_advice.html).

Another important aspect of this case and any trekking advice is the altitude profile. It should be checked well in advance, and before booking. Many altitude profiles are "too aggressive" and result in the travellers sleeping 'too high too early' into the expedition.¹⁹ For example, the typical itinerary for a trek to Mt. Kilimanjaro (5895 m) normally spans 5–6 days, with the summit attempted on day four. Such an altitude profile averaging 1000 m+ per day is not advised as this promotes the development of altitude-induced illnesses. International medical recommendations on altitude pursuits state that beginning at about 2500 m, the sleeping altitude should not be increased for more than 500 m every second day.⁹

However, for several reasons a compromise often has to be accepted to bridge the gap between the "ideal" altitude profile that fulfils the international recommendations, and those of external factors (geography, time, costs etc.). When climbing Mt. Kilimanjaro such a compromise could have been to reach the summit on day six and descend as far as possible the same day. Another possibility would be to pre-acclimatise either by spending a few nights at a mountain location about 2500–3000 m, or alternatively spending a few nights in a hypoxia facility (isobaric hypoxia) with an inspiratory oxygen partial pressure (piO₂) corresponding to 2500–3000 m (~15% O₂). A third option might be to climb a lower mountain nearby (e.g. Mt. Meru, 4566 m) before attempting the higher summit.

Conclusions

Any diagnosis of disease of the respiratory system at high altitude will be difficult and requires as much medical knowledge as possible if these special circumstances are taken into account. To provide evidence-based medical information and to support such a diagnosis, the Medical Commission of the Union Internationale des associations d'Alpinisme (UIAA MedCom) updated recently its guidelines for the diagnosis and treatment of AMS, HAPE and HACE,^{9,20}

medical precautions for people with pre-existing conditions²¹ and of the use of drugs in extreme environments.^{22,23} Any first aid or medical training of trekkers or mountaineers, and especially that of the expedition doctor if present, should consider this topic. They should also consider carefully all the medical equipment needed for each specific trek separately based on the individual group members, and access to medical support or hospital.

Conflict of interest

The authors declare no conflicts of interest.

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