

SPORTSTAF – 12/10/2010

Ziekte, immuniteit en sport

Return to play adviezen

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1. Bovenste luchtweginfecties

- Acute bovenste luchtweginfecties (URTI)

- ✓ frekwenste reden waarom sporters een arts opzoeken
- ✓ frekwenst voorkomend medisch probleem tijdens de Olympische zomer en winterspelen
- ✓ frekwente oorzaak van niet kunnen deelnemen aan competitie of verlies performantie
- ✓ potentieel gevaar voor besmetting andere teamleden

→ noodzaak accurate diagnose, snelle behandeling en sportadvies.

→ minimaliseren onderbrekingen van trainingen en/of competities

Algemeen: virale aandoening, zelflimiterend met symptomen zoals neusloop, neuscongestie, keelpijn, hoest, koorts, hoofdpijn, spierpijn en vermoeidheid.

✓ Diagnose:

Clinical and laboratory evaluation of upper respiratory symptoms in elite athletes.

Clin J Sport Med 18:438-445, 2008. Cox AJ. Et al.

70 elite-atleten met klachten bovenste luchtwegen (URS)

Klinische evaluatie sportarts: - 83% URTI virale origine

- 6% bacteriële infectie

- 11% allergie, asthma, inflammatie luchtwegen

Diagnose obv klinische biologie: - 30 % infectieus (26% viraal, 3% bacterieel, 1% EBV)

- 27 % suggestief voor infectie (WBC)

- 43 % ongekende oorzaak

→ URS ≠ URTI

→ Blijft klinische evaluatie gouden standaard bij evaluatie URS?

Virale en bacteriële pathogenen zijn gelijkaardig met URTI bij gewone populatie.

Pathogen identified by microbial and viral investigation	Triathletes (n=63) undertaking routine training and competitions	Elite athletes (n=70) presenting to a sports clinic	Elite athletes (n=41) with persistent fatigue and poor performance
	Spence et al. (2002)	Cox et al. (48)	Reid et al. (2012)
Rhinovirus	7	6	-
Influenzae (A & B)	7	1	-
Parainfluenzae (1, 2 & 3)	4	3	-
Adenovirus	0	2	-
Coronavirus	2	0	-
Metapneumovirus	1	0	-
Epstein Barr virus (primary infection)	1	1	3
EBV reactivation	-	1	8
Cytomegalovirus	0	0	5
Herpes simplex virus (types 1 & 2)	0	-	-
Ross River virus	-	-	1
Toxoplasmosis	-	-	1
Mycoplasma pneumoniae	0	1	1
Streptococcus pneumoniae	2	1	-
Staphylococcus pyogenes	0	1	-
Haemophilus influenzae	0	0	-
Moraxella catarrhalis	0	0	-
Enterococcus spp	0	0	-

bron: position statement part one: immune function and exercise

Clinical investigation of athletes with persistent fatigue and/or recurrent infections.

Br J Sports Med 2004;38:42-45. Reid VL. Et al.

Populatie: 41 elite-atleten met persisterende vermoeidheid en/of recurrenente infecties.

Doelstelling: onderzoeken naar onderliggende medische reden van vermoeidheid/infecties tijdens periodes van repetitieve zware training.

Methode: uitgebreid medisch onderzoek aangevuld met technische onderzoeken.

Table 1 Clinical conditions associated with fatigue or recurrent infections

Common conditions	Less common conditions
Immunodeficiency	Psychological factors
Acute or unresolved infections	Sleep disorders
Allergic disease	Diabetes mellitus
Autoimmune disease	Thyroid disease
Asthma	Cardiovascular disease
Airway dysfunction	Muscle dysfunction
Anaemia	Renal disorders
Nutritional deficiency	Liver failure
Depression	Malignancy

Table 3 Conditions with the potential to cause fatigue and/or recurrent infection identified in athletes

Condition identified	No of athletes
Partial humoral immune deficiency	11/40 (28)
Hypoglycaemia	10/36 (28)
Primary or unresolved infections	11/41 (27)
EBV reactivation	8/37 (22)
Allergic disease	6/41 (15)
Sleep disorder	6/40 (15)
Poorly controlled or undiagnosed asthma	3/40 (8)
Newly diagnosed exercise induced asthma	3/40 (8)
Upper airway dysfunction	2/40 (5)
Thyroid disorder	1/40 (3)
Low serum ferritin	1/40 (3)

Values in parentheses are percentage of athletes studied. EBV, Epstein-Barr virus.

Conclusie:

- Atleten met recurrenente infecties/vermoeidheid en prestatievermindering hebben baat bij uitgebreid medisch nazicht.
- Primaire virusinfecties, reactivatie virusinfecties en niet volledig genezen infecties worden frekwent

De accurate diagnose van een URTI vereist dus de identificatie van een pathogeen.

Klinische setting: niet haalbaar, niet kosten-efficiënt, resultaten vaak niet tijdig vooraleer genezing.

Wanneer:

- na 3 dagen bij persisteren van belangrijke symptomen
- klinisch beeld > klinisch onderzoek
- bevestiging klinische diagnose met belangrijke therapeutische consequenties (EBV,...)
- recurrenente URS in combinatie met vermoeidheid en prestatieverlies.

Welke onderzoeken:

- nasofaryngeale wisser of keelwisser: via PCR technieken (virologie)
- keelwisser: standaard microscopie, cultuur en antibiogram
- veneus bloedstaal: PBO, CRP, sedimentatie, detectie antistoffen (EBV Ig G en Ig M, CMV Ig G en Ig M, toxoplasmose Ig en Ig M), Ig E, allergietesten, ANF, humorale immuniteit, fe, vit B12, FZ, glycemie, CK, leverfunctie,

nierfunctie, SK

- speeksel: EBV DNA (reactivatie)

✓ Behandeling: symptomatisch, zz antibiotica

Clin Sports Med30 (2011) 575-590

www.dopinglijn.be

Olympic textbook of medecine in sport

✓ Return to play: - afwegen van risico op complicaties, risico op ongewild verlengen duur en intensiteit

infectie-episode, voorkomen besmetting team, conditieverlies,....

- complicatie: virale myocarditis (associatie plotse dood 5 tot 22% bij sporters), EBV

“neck check”

Symptomen beperkt tot locatie boven de hals (neusloop, neuscongestie, keelpijn,...)

→ 10 minuten test lichte inspanning

→ geen verergering symptomen: trainen subnormale intensiteit met geleidelijke opbouw naar volledige hervatting training.

→ verergering symptomen: training onderbreken.

Symptomen onder de hals of systemisch (overgeven, diarree, koorts, myalgie, gezwollen pijnlijke lymfadenopathie, thoracale pijn, tachicardie in rust, excessieve kortademigheid, excessieve vermoeidheid)

→ contra-indicatie sporten tot herstel van deze symptomen

Guidelines for exercise during episodes of URTI or GI in athletes

EIR 17 2011 – position statement part 2

•**First day of illness:** No strenuous exercise or competitions when experiencing URTI symptoms like sore throat, coughing, runny or congested nose. No exercise when experiencing symptoms like muscle/joint pain and headache, fever and generalized feeling of malaise, diarrhoea or vomiting. Drink plenty of fluids, keep from getting wet and cold, and minimize life-stress. Consider use of topical therapy with nasal drainage, decongestants and analgesics if feverish. Report illness to a team physician or health care personnel and keep away from other athletes if you are part of a team training or travelling together.

•**Second day:** If body temperature >37.5-38 °C, or increased coughing, diarrhoea or vomiting: no training. If no fever or malaise and no worsening of “above the neck” symptoms: light exercise (pulse <120 bpm) for 30-45 min, indoors during winter and by yourself.

Third day: If fever and URTI or GI symptoms are still present: consult your physician. In GI cases, antibiotics should be taken if unformed stools occur more than four times a day or for fever, blood, pus, or mucus in stools. Quinolones should be avoided whenever possible because of an increased risk of tendinopathy. If no fever or malaise and no worsening of initial symptoms: moderate exercise (pulse <150 bpm) for 45-60 min, preferably indoors and by yourself

•**Fourth day:** If no symptom relief: do not try to exercise but make an office visit to your doctor. Stool cultures or examination for ova and parasites should generally be reserved for cases that last beyond 10 to 14 days. If first day of improved condition, follow the guidelines below (186):

Guidelines for return to exercise after infections

- Wait one day without fever and with improvement of URTI or GI symptoms before returning to exercise.*
- Stop physical exercise and consult your physician if a new episode with fever or worsening of initial symptoms or persistent coughing and exercise-induced breathing problems occur.*
- Use the same number of days to step up to normal training as spent off regular training because of illness.*
- Observe closely your tolerance to increased exercise intensity and take an extra day off if recovery is incomplete.*
- Use proper outdoor clothing and specific cold air protection for airways when exercising in temperatures below – 10°C the first week after URTI.*

■ Infectieuze mononucleosis

- ✓ EBV = herpesvirus
- ✓ Asymptomatische infectie/ acute infectieuze mononucleosis/ reaktivatie EBV
- ✓ Infectie van epitheliale cellen orofarynx en B-lymphocyten
- ✓ Levenslang aanwezig, EBV geïnfecteerde B-memory lymfocyten, gecontroleerd door EBV specifieke cytotoxische T-lymfocyten; bij wegvallen controle → reaktivatie van latente herpesvirussen.
- ✓ Klinisch:

Box 1. Symptoms and findings in adolescents and young adults with infectious mononucleosis^a

Common

Lymphadenopathy (cervical or generalized), 94%
Pharyngitis, 84%
Malaise, 82%
Fever, 76%
Splenomegaly, 52%
Atypical lymphocytosis (> 10%), 90%
Mild transaminitis (2–3× normal), 90%
Heterophile positive, 85%–90%
Lymphocytosis, 70%

Less common

Myalgia, 20%
Hepatomegaly, 12%
Rash, 10%
Jaundice, 9%
Arthralgia, 2%
Heterophile negative, 10%–15%

^a Adapted from [20–23].

Clin Sports Med 23 (2004)
485-497.

- Diagnose

- ✓ klinisch vermoeden
- ✓ verhoging WBC 12,000 tot 18,000 cellen/mm³, atypische lymfocyten
- ✓ stijging transaminasen
- ✓ serologie: monospottest (heterofiele antistoffen), 10 tot 15 % negatief

EBV Ig M (positief 1 tot 2 maanden)

EBV Ig G (levenslang positief)

EBV nuclear antigen antibodies (na 4 a 6 weken)

- Differentieel diagnose

- ✓ CMV
- ✓ HIV
- ✓ virale hepatitis

- Behandeling

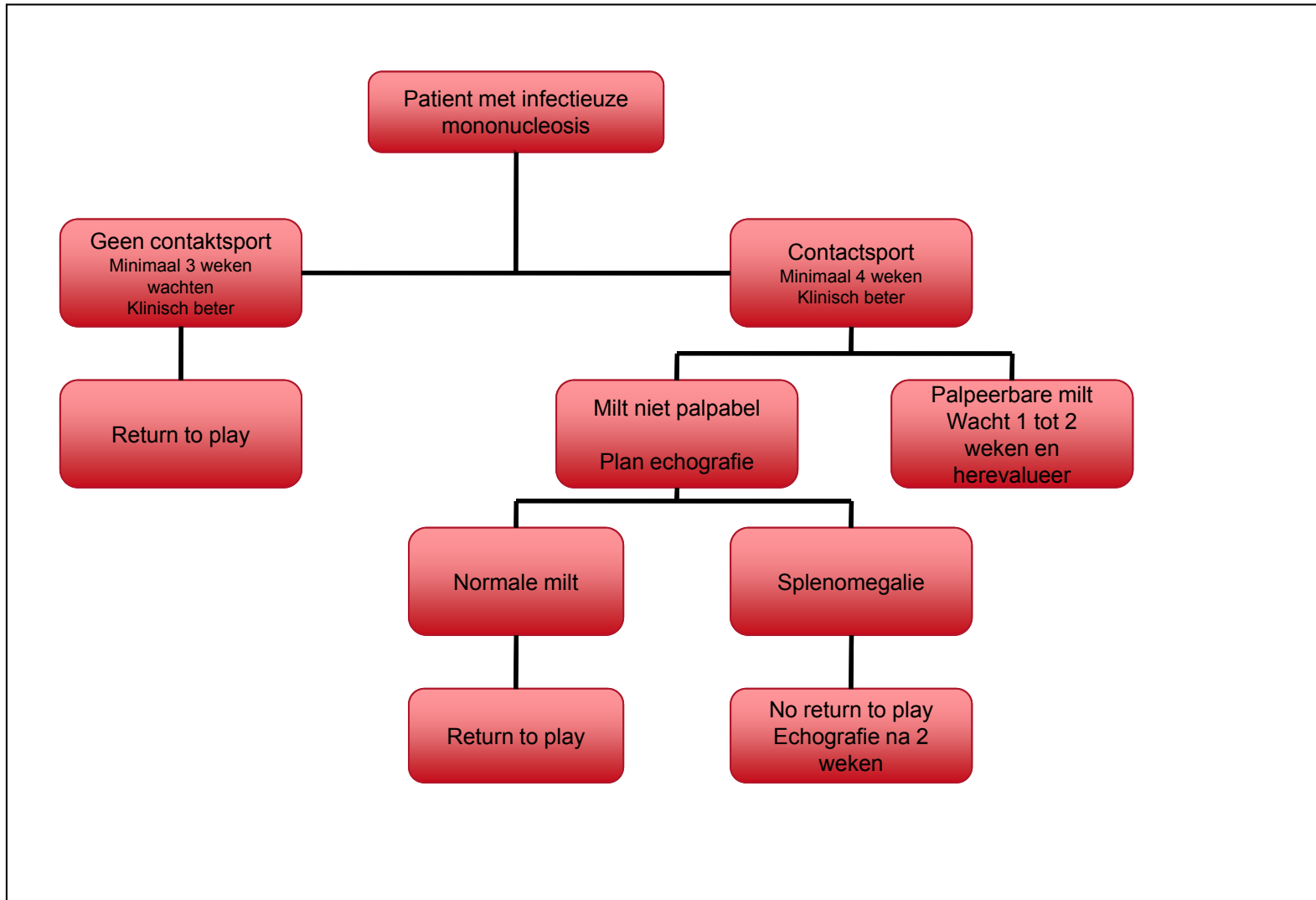
- ✓ Symptomatisch, lichte aktivering
- ✓ Antivirale therapie: inhibeert EBV replicatie en virale reactivatie, geen effect op symptomen.

- Complicaties

- ✓ Luchtwegobstructie
- ✓ Miltruptuur (0,1 tot 0,5 %), significante abdominale pijn li bovenste kwadrant, teken van Kehr; spontane ruptuur zonder trauma, splenectomie/conservatief
- ✓ Neurologische complicaties: encephalitis, Guillian-Barre
- ✓ Cardiale, hematologische, pulmonale en renale complicaties
- ✓ Persisterende vermoeidheid: langer dan een maand tot 6 maand

- Return to sport

- ✓ Miltruptuur vermijden
- ✓ Trainingshervatting bij atleten met persisterende vermoeidheid
- ✓ Geen goed uitgevoerde studies beschikbaar



Opm: bepaald % jonge volwassene heeft een lichte vorm van splenomegalie: klinisch oordeel voor sporthervatting na 7 tot 8 weken.

Vermoeidheid:

- ✓ welzijnsgevoel atleet
- ✓ herstart 50% normale trainingsniveau, opbouwen volgens reactie lichaam, periode tot 3 maand nodig om op pre-ziekte niveau te geraken.

■ Virale myocarditis

- ✓ Inflammatoire aandoening van het myocard
- ✓ Virale etiologie:

Enterovirussen (Coxsackie B)

Parvovirus

Adenovirus

Humaan Herpes Virus 6

EBV

CMV

(rhinovirus, coronavirus)

Etiology	Cell type	Clinical type
Virus	Lymphocytic type	Acute
Bacteria	Giant cell type	Fulminant
Fungi	Eosinophilic type	Chronic
Rickettsia	Granulomatous type	(prolonged)
Spirochetes		(latent)
Protozoa, parasites		
Other causes of infection		
Drugs, chemical substances		
Allergy, autoimmune		
Collagen disease, Kawasaki disease		
Sarcoidosis		
Radiation, heat stroke		
Unknown cause, idiopathic		

Circ J 2011;75:734-743

- ✓ Oorzaken van plotse dood tijdens sport bij jonge competitieve atleten

→ 1-2 /100 000 atleten < 35 jaar

→ myocarditis 6 – 22 %

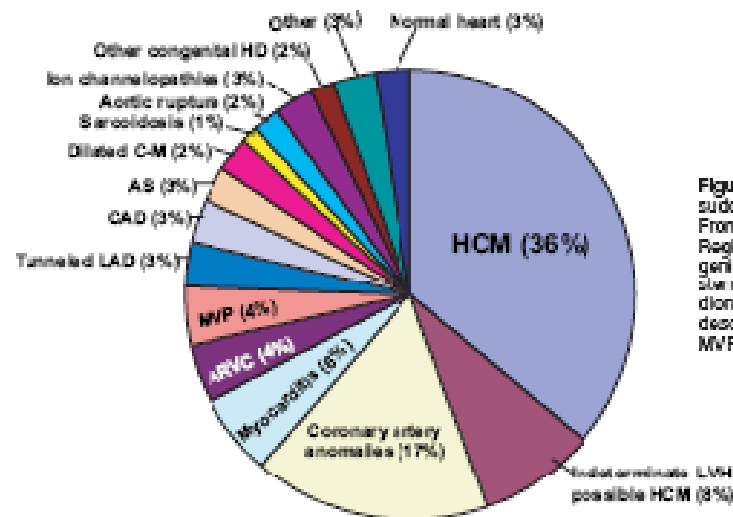


Figure. Distribution of cardiovascular causes of sudden death in 1435 young competitive athletes. From the Minneapolis Heart Institute Foundation Registry, 1980 to 2005. ARVC indicates arrhythmogenic right ventricular cardiomyopathy; AS, aortic stenosis; CAD, coronary artery disease; CM, cardiomyopathy; HD, heart disease; LAD, left anterior descending; LVH, left ventricular hypertrophy; and MVP, mitral valve prolapse.

Maron et al: circulation 2007

- ✓ Evolutie: volledig herstel (50%), chronische myocarditis (20%), gedilateerde myopathie (20%)

✓ Symptomen

- Griepale symptomen (koude rillingen, koorts, hoofdpijn, spierpijnen, malaise)
- Gastro-intestinale symptomen (verminderde eetlust, nausea, overgeven, diarree)
- Cardiale symptomen (enkele uren tot enkele dagen na initiële symptomen)

- geen → fulminant
- thoracale pijn (pericardiale irritatie)
- dyspnee
- hartfalen



- symptomen arritmieën, heart block (palpataties, syncope)

Febriele patient, recent infectieus verhaal en subtiele klinische tekenen.

- ✓ Diagnose
 - 1 Kliniek
 - 2 Biochemie: CRP, CK MB, troponine, LDH, AST, serologie// PCR nasofaryngeaal, speeksel
 - 3 ECG: sensitief, herhaald worden, geleidingsstoornis, abnormale ST-T golven, arritmieën
 - 4 Echocardiografie: transiente verdikking hartspier, beperkt volume ventrikel, pericardiale effusie, verminderde mobiliteit hartspier
 - 5 MRI en biopsie

Table 2. Diagnostic Guidelines for Acute Myocarditis

1. In acute myocarditis, flu-like signs and symptoms[¶], gastrointestinal signs and symptoms[¶], skin rash, joint pain, or muscle pain may occur before cardiac signs and symptoms[¶]. However, sudden death may occur without preceding clinical signs.
2. Cardiac findings such as tachycardia, bradycardia, arrhythmia, weakened heart sounds, gallop rhythm (III, IV), pericardial rub, and systolic murmur occur.
3. Generally, an abnormal ECG is observed during the course of myocarditis. ECG manifestations are diverse, and include atrioventricular block (I to III degree), intraventricular conduction delay (widened QRS complex), reduced R wave height, abnormal Q waves, ST-T segment changes, low voltage, frequent premature beats, supraventricular tachycardia, atrial fibrillation, sinus arrest, ventricular tachycardia, ventricular fibrillation, and asystole.
4. Localized or diffuse wall thickening, reduced wall motion, reduced cardiac chamber size, and pericardial effusion are found on echocardiography.
5. In myocarditis, myocardial constitutive proteins (cardiac troponin T and creatine kinase-MB) are detected in serum. C-reactive protein and white blood cell count are elevated. Early detection of troponin T using whole blood enables immediate diagnosis of myocarditis.
6. Since the conditions in items 2 and 5 above may progress within a few hours, changes over time in these conditions should be followed. If a patient has bradycardia, widened QRS complex, frequent premature beats, wall thickening, exacerbation of reduced wall motion, elevated troponin T, and continuous increase in troponin T level, the patient may have a cardiopulmonary emergency.
7. Definitive diagnosis of myocarditis requires that acute myocardial infarction be excluded.
8. The presence of abnormal histological findings on endomyocardial biopsy[¶] makes the diagnosis of myocarditis definite. However, the absence of such findings does not exclude the possibility of myocarditis.
9. Elevation of viral titer in a sample collected in the acute phase to at least four times that in a sample obtained in remission is useful for identify viral infection as the cause. Polymerase chain reaction is often used to demonstrate the presence of viral infection and to detect the viral genome. Separation of virus or identification of virus by antibody titer in throat swabs, urine, feces, blood, and especially pericardial effusion or cardiac muscle tissue provides direct evidence of myocarditis.

Circ J 2011;75:734-743

- ✓ Behandeling: verwijzing cardiologie en opname
- ✓ Return to sport:

Recommendations for participation in competitive sport and leisure-time physical activity in individuals with cardiomyopathies, myocarditis and pericarditis

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Athletes with active myocarditis or pericarditis	History, PE, ECG, Echo		No competitive sports	
Athletes after resolution of myocarditis	History, PE, ECG, Echo, ET, Holter (6 months after clinical onset of the disease)	No symptoms, normal LV function, no arrhythmias	All competitive sports	Every 6 months
Athletes after resolution of pericarditis	History, PE, ECG, Echo, ET, Holter (3 months after clinical onset of the disease)	No symptoms, normal LV function, no arrhythmias	All competitive sports	Every 6 months

ARVC, arrhythmogenic right ventricular cardiomyopathy; BP, blood pressure; DCM, dilated cardiomyopathy; ECG, electrocardiogram; Echo, echocardiography; EF, ejection fraction; ET, exercise testing; HCM, hypertrophic cardiomyopathy; Holter, 24-h ECG monitoring; LV, left ventricular; LVH, left ventricular hypertrophy; PE, physical examination; SD, sudden death; Sport type, see Table 6.

- ✓ Preventie:
 - Stop elite sport voor 4 weken na een niet-specifieke bewezen infectie
 - atleten hebben tot 6 infecties/jaar → zelden toegepast
 - Stop sport and CV evaluatie igv subtiele symptomen bij virale infecties
 - welke verder onderzoeken?
 - cost-benefit ratio diagnose myocarditis in atleten?

Richtlijnen return to exercise after infections

Walsh NP et al Exerc Immunol Rev. 2011;17:64-103

- 1 dag zonder koorts en verbetering van URTI en GI symptomen
- progressieve opbouw trainingsintensiteit
- opvolgen individuele tolerantie, bij onvold herstel extra rustdag
- stop sportactiviteiten en raadpleeg arts indien opnieuw koorts of toename symptomen

2. Gastro-enteritis

- ✓ Frekwente aandoening bij sporters
- ✓ Erg besmettelijk, overdracht persoon tot persoon, voeding, omgeving
- ✓ Symptomen: 3 of meer episodes van platte stoelgang in 24 uur, nausea, overgeven, koorts, abdominale krampen, bloederige stoelgang?
- ✓ Etiologie: virus, bacterieel, parasitair

Table 2 Common gastrointestinal pathogens					
Agent	Typical transmission	Likely symptoms	Diagnosis (stool studies)	Duration of symptoms	Outpatient treatment
Escherichia coli ETEC (traveler's diarrhea)	Contaminated food or water	Acute watery large-volume diarrhea	Stool culture	Self limited (1–4 days)	Empiric ATBX treatment shortens course
Escherichia coli EIEC	Contaminated food	Fever, abdominal pain, low-volume diarrhea	Stool culture	Varied	Definite ATBXs based on resistance patterns
Escherichia coli EHEC	Undercooked ground beef, human contact	Diarrhea, HUS	Stool culture	Symptoms begin after 1–8 days of incubation	Supportive, ATBXs thought to worsen disease course.
Salmonella typhi	Human contact, prepared food, contaminated water	Fever, abdominal pain, diarrhea	Blood culture, stool culture	1–2 weeks incubation	Definite ATBXs based on resistance patterns
Salmonella (nontyphoidal)	Poultry, eggs, meat, dairy	Diarrhea (watery or bloody), fever	Stool culture	1–4 days	Treat only with ATBXs in immunocompromised and asplenia
Shigella	Human contact, prepared food, contaminated water	Diarrhea (watery or bloody), fever	Stool culture	Varied; Some self-resolve in 7 days, others last weeks	Definite ATBXs based on resistance patterns
Campylobacter	Poultry, meat, dairy products, tap water	Diarrhea (watery or bloody), fever	Stool culture	1–7 days	Supportive only
Calicivirus	Human contact (feces, vomitus), contaminated food and water	Fever, vomiting, diarrhea	PCR	1–2 days	Supportive only

Rotavirus	Human contact, contaminated food and water	Fever, vomiting, diarrhea	EIA, latex agglutination	Diarrhea 3–8 days; Vomiting 1–5 days	Supportive only
Astrovirus	Human contact	Diarrhea, vomiting	EIA (not commercially available)	1–14 days	Supportive only
Adenovirus types 40 and 41	Human contact (feces, possibly vomitus)	Fever, vomiting, diarrhea	EIA (not commercially available)	1–7 days	Supportive only
Giardia	Tap water, mountain streams, human contact	Abdominal discomfort, bloating, diarrhea, malaise, low-grade fever	Microscopic examination of feces; EIA	3–4 days acute diarrhea then transition to subacute symptoms	Metronidazole
Cryptosporidium	Tap water, human contact	Large-volume diarrhea, abdominal pain, headache, fever	Microscopic examination of feces	5–6 days typically; (range 2–26 days)	In immunocompromised cases, consider antiparasitic/antibiotic treatment
Entamoeba histolytica	Human contact (feces), contaminated food or water	Fever, bloody diarrhea	Microscopic examination of feces	Mild symptoms may be present weeks to months	Use both luminal amebicide (for cysts) and tissue amebicide (for trophozoites)

Abbreviations: ATBX, antibiotics; EHEC, enterohemorrhagic; EIA, enzyme immunoassay; EIEC, enteroinvasive; ETEC, enterotoxigenic; HUS, hemolytic uremic syndrome.

Data from Adachi AA, Backer HD, DuPont HL. Infectious diarrhea from wilderness and foreign travel. In: Auerbach PS, editor. Wilderness medicine 4th edition. St. Louis (MO): Mosby; 2001. p. 1237–70; and Musher DM, Musher BL. Contagious acute gastrointestinal infections. N Engl J Med 2004;351 (23):2417–27.

Clin Sports Med 24 (2005):477-506

Stoelgangsculturen: > 7 dagen diarree

koorts

colitissymptomen: koorts, tenesmus, urge, krampen, bloederige diarree

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- ✓ Behandeling: - rehydratatie
 - antibiotica te overwegen bij ernstige diarree, koorts, bloed, pus, mucus in stoelgang
 - loperamide: omzichtig gebruik, ev tijdens competitie of langdurige reis
 - motilium?

- ✓ Return to sport: - neck check
 - hydratatie
 - infectierisico

3. Preventiemaatregelen



- ✓ Vaccinaties: influenza, kinkhoestvaccin, hepatitis A en b vaccinaties, f(reisbestemming).
- ✓ Minimaliseer contact met infectieuze/zieke mensen of potentieel gecontamineerde objecten
- ✓ Afstand houden van mensen die lopende neus hebben, niezen, hoesten.
- ✓ Regelmatig handen wassen voor eten, na contact met mogelijks besmettelijke mensen, publieke plaatsen. Alkoholgels bij de hand hebben.
- ✓ Papieren zakdoekjes gebruiken voor 1-malig gebruik, limiteer handcontact met neus en mond tijdens GI of URT infecties.
- ✓ Deel geen drinkflessen, tassen, glazen, handdoeken,...
- ✓ In buitenland: drink van gesloten flessen, eet geen rauwe groenten en vlees, fruit wassen en pellen.



- ✓ Isoleer een teammaat bij infectie en verplaats zijn roommate naar een andere kamer.
- ✓ Bescherm de luchtwegen tegen blootstelling aan extreme koude tijdens intensieve inspanning.
- ✓ Voorzie voldoende vocht en koolhydraatname voor, tijdens en na lange of intensieve duuractiviteiten om de duur en de lengte van de immunodepressie na inspanning te verkorten.
- ✓ Draag voldoende kledij, vermijd koude en natheid na inspanning.
- ✓ Minstens 7 uur slaap/dag.
- ✓ Vermijd crash diëten en snel gewichtsverlies.
- ✓ Draag slippers in douches, zwembaden om dermatologische aandoeningen te vermijden.
- ✓ Beperk algemene stress tot een minimum.

4. Take home messages

- ✓ Noodzaak van snelle diagnose, juiste behandeling en correct sportadvies.
- ✓ Zonder diagnose spreekt men beter van URS dan over URTI.
- ✓ Bijkomend onderzoek aangewezen bij klachten > 3 dagen en bij recidiverende infecties/chronische vermoeidheid.
- ✓ Return to sport advies obv “neck check”
- ✓ Voorzichtigheid bij EBV.
- ✓ Denken aan virale myocarditis.
- ✓ Preventie

