

Mucegaiurile de interior un pericol pentru sanatate

17.12.2008

de Luke Curtis, MS, CIH; Allan Lieberman, MD; Martha Stark, MD; William Rea; Marsha Vetter, MD, PhD

[Articol extras din Nexus Magazine, Anul IV, Numarul 12 (decembrie 2008 - februarie 2009)]

Mucegaiurile si micotoxinele produse de catre acestea constituie o amenintare tot mai mare la adresa sanatatii, fiind necesara adoptarea pe scara larga a unor teste pentru detectarea si diagnosticarea lor.

Introducere

In ultimii ani, atentia publicului s-a concentrat tot mai mult asupra problemei reprezentate de mucegaiuri, prezente atat in interiorul caselor cat si al locurilor de munca si asupra pericolelor pe care o prezinta expunerea la acestea. Aceasta lucrare este prezentata de Academia Americana de Medicina a Mediului (American Academy of Environmental Medicine (AAEM)) si prezinta cunostintele pe care le avem in prezent in privinta efectelor adverse ale mucegaiului de interior.

Exista numeroase dovezi in literatura medicala care confirma efectele negative pe care le are aerul contaminat cu mucegai asupra sanatatii oamenilor. Expunerea la aerul contaminat cu mucegai de interior cauzeaza frecvent efecte adverse asupra sanatatii umane provocand leziuni si disfunctii ale multor organe si sisteme incluzand: 1) sistemul respirator, 2) sistemul nervos, 3) sistemul imunitar, 4) sistemul hematologic si 5) piele. Mucegaiul de interior este, de asemenea, o cauza comuna pentru infectiile sistemice ce pun in pericol viata pacientilor cu un sistem imunitar compromis.

Mucegaiurile sunt omniprezente in mediul interior

Ciupercile (sau mucegaiurile) sunt omniprezente atat in mediul interior cat si in cel exterior. Mucegaiurile sunt frecvent raspandite pe calea aerului, prin spori. Pentru a putea creste, mucegaiul si sporii de mucegai au nevoie de umezeala si de o sursa de hrana precum celuloza sau mancarea aflata in descompunere.

1. Din moment ce sporii de mucegai se umfla si cresc in prezenta apei, ei se alungesc, formand niste protuberante de forma unor baloane (hife) care secreta micotoxine si enzime digestive. Ciuperca digereaza apoi sursa de hrana pentru a-si sustine cresterea. Aproximativ 100000 de specii de ciuperci au fost deja identificate; de fapt, se estimeaza ca ciupercile reprezinta un uimitor procent de 25% din biomasa globala.

2. Cercetari variate realizate in casele din America de Nord si Europa au raportat ca mucegaiul vizibil si/sau pagubele datorate apei au fost descoperite in 23% pana la 98% din totalul caselor studiate.

3-6 In prezent nu exista standarde oficiale pentru concentratia de ciuperci de interior care se propaga pe calea aerului. Totusi, un nivel al ciupercilor de interior de peste 150 pana la 1.000 de unitati formatoare de colonii pe metru cub de aer (cfu/m³) este considerat a fi suficient pentru a cauza probleme de sanatate.[4, 7-9] Numeroase rapoarte au demonstrat ca aerul din interior poate fi adeseori contaminat cu niveluri de spori de mucegai mult peste 1000 cfu/m³. Cele mai comune ciuperci de interior sunt Cladosporium, Aspergillus si Penicillium. Speciile de Alternaria, Stachybotrys, Rhizopus, Mucor, Wallemia, Trichoderma, drojdii, Botrytis, Epicoccum si Fusarium sunt deseori descoperite si in interior.[10-17]

Prescrierile de ipoteci, procesele si cererile de asigurari datorate problemelor cauzate de mucegai sunt obisnuite.

In America se primesc aproximativ 50 de telefoane pe saptamana de la asigurati a caror ipoteca a casei urmeaza sa fie prescrisa din cauza problemelor cu mucegaiul. [18] In 2002, in tribunalele din SUA se aflau pe rol aproximativ 10.000 de cazuri legate de mucegai[19], industria asigurarilor platind in Texas peste 2 miliarde de dolari numai in cazurile legate de acestea.[20]

Simptome datorate mucegaiului

Multi pacienti au raportat aparitia a o multime de efecte negative asupra sanatatii datorita expunerilor la mucegai. Studii efectuate asupra a mai mult de 1.600 de pacienti care sufereau datorita expunerii la fungii au fost prezentate la o intalnire in Dallas din 2003 (21st Annual Symposium of Man and His Environment, Dallas, Texas, iunie 2003 [19-22]).[21-25]

Pentru a cita cateva studii... Lieberman[21] a examinat 48 de pacienti expusi la mucegai care aveau urmatoarele probleme de sanatate: 1) dureri musculare si/sau de articulatii, 71%; 2) oboseala/slabiciune, 70%; 3) disfunctii neurocognitive, 67%; 4) sinuzite, 65%; 5) dureri de cap, 65%; 6) probleme gastrointestinale, 58%; 7) probleme de respiratie 54%; 8) anxietate/depresie/ iritabilitate, 54%; 9) probleme de vedere 42%; 10) senzatii de apasare in piept, 42%; 11) insomnie, 40%; 12) ameteala, 38%; 13) amorteala/furnicaturi, 35%; 14) laringita, 35%; 15) greata, 33%; 16) eruptii pe piele, 27%; 17) tremuraturi, 25%; si 18) palpitatii ale inimii, 21%. Studiul lui Rea asupra a 150 de pacienti expusi la mucegaiul de interior a identificat urmatoarele probleme de sanatate: 1) oboseala, 100%; 2) rinita, 65%; 3) pierderi de memorie si alte probleme neuropsihiatrice, 46%; 4) probleme respiratorii, 40%; 5) fibromialgie, 29%; 6) colita mucoasa, 25%; 7) vasculita, 4.7%; si 8) angioedem, 4.0%. Aceste rapoarte clinice demonstreaza efectele adverse ale mucegaiului raspandit pe calea aerului. Exista in prezent numeroase dovezi in literatura medicala de specialitate, ce arata ca expunerea la ciupercile de interior raspandite pe calea aerului poate cauza numeroase efecte adverse.

Mecanismele de actiune ale mucegaiurilor asupra sanatatii

Ciupercile pot exercita efecte negative asupra sanatatii prin intermediul a trei mecanisme: 1) infectie; 2) alergii si 3) toxicitate. Infectiile grave provocate de ciuperci precum Candida, Aspergillus si Pneumocystis sunt comune si cele mai multe apar la pacientii cu un sistem imunitar sever compromis.[26-28]

Ciupercile precum Candida, Histoplasmosis, Cryptococcus, Blastomyces si Coccidioides pot afecta intern persoanele cu o imunitate optima.[29] Ciupercile precum Trichophyton, Candida si Malasezia cauzeaza de obicei infectii minore ale pielii la oamenii cu un bun sistem imunitar.[28] Cel putin 70 de alergeni au fost pe larg clasificati dupa spori, parti vegetative si particule mici din ciuperci (0,3 microni si mai mici).[30, 31] Alergiile provocate de alergenii din ciuperci sunt foarte comune.

O revizuire a 17 studii a descoperit ca 6% -10% din populatie si 15%-50% dintre cei cu o predispozitie ereditara au prezentat o sensibilitate imediata a pielii la ciuperci.[32]

Ciupercile produc o mare varietate de substante chimice toxice numite micotoxine.[1, 33, 34] Printre micotoxinele comune se includ: 1) aflatoxinele: substante carcinogene foarte puternice si hepatotoxinele produse de unele specii de Aspergillus; 2) ochratoxinele: nefrotoxice si carcinogene; produse de unele specii de Aspergillus si Penicillium; 3) sterigmatocistina: o substanta represiva pentru sistemul imunitar si carcinogena pentru ficat produsa de specii de Aspergillus, in special A.multicolor; si 4) trichothecenele: produse mai ales de specii de Stachybotrys si Fusarium, si despre care s-a raportat ca inhiba sinteza proteinelor si cauzeaza hemoragii si varsaturi.

Ciupercile produc de asemenea beta-glucani care au efecte imunologice.[35] Mirosul mucegaiurilor provine in special de la compusii organici volatili.[36] Efectele adverse asupra oamenilor si animalelor cauzate de alimentele contaminate cu micotoxina au fost recunoscute inca de la inceputul secolului al XX-lea.[33, 37] Dar daca micotoxina ne afecteaza doar atunci cand este inhalata, aceasta este o intrebare al carei raspuns este inca dezbatut.[38] In absenta unor studii controlate, efectuate asupra unor subiecti umani expusi inhalarii de micotoxina, numai cercetarile privind expunerea controlata de animale si cele de epidemiologie umana pot fi folosite. Studiile demonstreaza ca semnificative cantitati de micotoxine (inclusiv ochratoxina, sterigmatocistina si trichothecenele) si spori de ciuperci care pot fi absorbiti pe calea aerului.[34, 37, 44, 45] sunt prezente in praful de interior[39-43].

Pacientii expusi la Stachybotrys de interior au prezentat niveluri masurabile ale toxinei hemoragice de stacilisin.[46]

Nivelurile de micotoxine trichothecene din urina au fost semnificativ mai mari la pacientii expusi la niveluri mari de ciuperci de interior, in contrast cu un grup de control care nu fusese expus la niveluri ridicate de ciuperci de interior.[47]

Nivelurile de ochratoxina din sange au fost gasite in mod semnificativ mai ridicate la muncitorii din industria alimentara expusi la ochratoxina raspandita pe calea aerului fata de cei neexpusi.[43]

Aceste descoperiri demonstreaza in mod clar ca inhalarea este modul de intrare in organism a micotoxinelor.

Prelevarea probelor in cazul expunerii la mucegaiuri

Prelevarea probelor in cazul ciupercii de interior este cel mai adesea facuta prin masurarea nivelurilor de spori viabili (ce pot fi cultivati) sau totali (viabili si ne-viabili) din aer.[48, 49] Unele metode de luare de probe viabile din aer, precum esantionarele Andersen, colecteaza aer doar pentru cateva minute.

Metoda prin care particulelor li se permite sa se aseze pe un anumit suport este una

putin costisitoare si permite obtinerea unei masuri semi-cantitative a nivelurilor de ciuperca de interior raspandita pe calea aerului. Masuratorile de spori viabili si neviabili din aer pot varia considerabil in decursul unei perioade scurte de timp, astfel ca prelevarea de probe din aer pe parcursul catorva perioade de timp poate fi necesara pentru a caracteriza precis nivelurile de spori de ciuperca din aer.[48, 49]

Totusi, masuratorile de ciuperca din aer nu iau in considerare contaminarea cu mucegaiul care nu este prezent in aer, precum contaminarea cu mucegai din praf sau de pe suprafete (uneori vizibile cu ochiul liber) si cu micotoxinele din aer, praf si de pe suprafete.[48, 50] Astfel, testarea prafului depus pentru a vedea nivelul de ciuperci si micotoxine este deseori recomandata.[48, 49]

Pentru a se asigura o evaluare mai completa, se recomanda adeseori ca masuratorile din aer sa fie suplimentate de testarea mucegaiurilor si micotoxinelor din praful deja depus sau din aer.[48, 49] Alte tehnici precum PCR (reactia in lant a polimerazei), ELISA (incercarea de legare a unui anticorp de o enzima) si masurarea substantelor chimice organice volatile produse de ciuperci, polizaharide, ergosterol si beta-glucani poate de asemenea sa fie folositoare pentru a testa mediile interioare de mucegaiuri si de alergeni si micotoxinele lor.[48] Pentru o privire de ansamblu in legatura cu metodele de luare de probe, va rugam sa consultati Pasanen[48] si Macher.[51] Pentru un ghid informativ privind clasificarea, identificarea si biologia ciupercilor comune de interior, vezi Samson.1 Exista cateva ghiduri bune pentru prevenirea si remediarea problemelor cauzate ciuperci de interior.[51-53]

Expunerea la mucegaiul de interior si problemele respiratorii

Multe studii epidemiologice au mentionat ca expunerea la domiciliu la mucegaiuri si/sau umezeala cronica poate creste incidenta si morbiditatea asociate astmului/respiratiei dificile atat la copii cat si la adulti.[4-6, 54-67] Astmul si starile legate de acesta sunt foarte comune in SUA, cu o incidenta totala de aproximativ 5,4% la toate grupele de varsta si incidente de pana la 27% la copiii din orase.[68]

Studiile pe copii cu o varsta de pana la sapte ani au aratat ca expunerile de durata la ciuperci au fost asociate cu o prezenta mai ridicata a respiratiei dificile, a tusei si a bolilor aparatului respirator.[69, 70]

Nivelurile mai ridicate ale beta-glucanului de interior au fost asociate cu niveluri semnificativ mai ridicate de senzatii de strangere a pieptului si de dureri la nivelul articulatiilor.[71] S-a raportat ca expunerea profesionala la mucegai a fost asociata cu niveluri semnificativ mai ridicate de astm, sinuzita, piele si ochi iritati, si oboseala cronica.[72-76]

Un studiu a descoperit ca pacientii expusi la niveluri ridicate de ciuperci de interior aveau o functie a plamanilor semnificativ mai scazuta decat cei neexpusi.[24]

Concentratiile mai ridicate de ciuperci din mediul exterior au fost considerate ca avand legatura cu ratele mai ridicate de mortalitate datorate astmului[77] si cu incidenta crescuta a astmului[78, 79] la copii si la tineri.

Expunerile in scop experimental la extracte de *Penicillium* si *Alternaria* echivalente unor niveluri ridicate de expunere la ciuperci exterioare au fost mentionate ca reducand functia pulmonara foarte mult la astmatici.[80] Sensibilitatea pielii la *Alternaria* a fost legata de un risc mai ridicat de oprire a respiratiei.[81] Variate studii

epidemiologice au asociat sensibilitatea pielii la ciupercile de interior si incidenta sau severitatea mai mare a astmului[82-86] si ratele mai ridicate de sinuzita.[87]

Expunerea la ciupercile raspandite prin aer poate cauza sinuzita, aspergiloza bronhopulmonara si hipersensibilitate la pneumonita.88-89 Aproximativ 14% din populatia SUA sufera de rinosinuzita si de diverse conditii inrudite cu aceasta.[90]

Sinuzita alergica fungala a fost diagnosticata pe baza cresterilor concentratiei de ciuperci din secretiile nazale si dupa prezenta mucinului alergic la 93% din 101 pacienti ce urmau sa faca o operatie la nivelul sinusurilor.[90] In cadrul unui alt studiu s-a reusit recuperarea unor ciuperci (si cultivarea lor ulterioara) din sinusurile a 56% dintre 45 de pacienti care urmau sa faca o operatie endoscopica a sinusurilor pentru rinosinuzita cronica.[91]

Un studiu indelungat efectuat asupra a 639 de pacientii cu sinuzita alergica fungala a demonstrat ca pasii facuti pentru a reduce expunerea la ciuperci (prin utilizarea de exemplu a filtrelor de aer, a ionizatoarelor, sistemelor de control ale umiditatii si a spray-urilor antimicrobiale nazale) au redus rinosinuzita semnificativ si au imbunatatit morfologia mucoasei nazale. Acest studiu a concluzionat ca neputinta de a reduce nivelurile de ciuperci din aer la mai putin de patru pe ora pe placuta de depunere inseamna nerezolvarea sinuzitei.[22] Desi, din punct de vedere istoric, medicamentele fungicide nu au fost in general recomandate pentru tratamentul sinuzitei fungale,88-89 studii recente au descoperit efectele benefice ale medicatiei orale si nazale asupra pacientilor cu sinuzita.[22, 92] Cateva studii au facut legatura dintre expunerea rezidentiala la ciuperci cu hipersensibilitatea la pneumonita.[93-95]

Stachybotrys si efectele hemoragice

Expunerea la niveluri ridicate de Stachybotrys, Aspergillus si alte ciuperci de interior a fost epidemiologic asociata cu hemoragia la nivelul plamanilor la copiii sub sapte ani. [96-100] Desi s-au ridicat diverse intrebari asupra modului in care a fost descoperita aceasta asociere,[101] ea indeplineste multe criteriile epidemiologice pentru cauzalitate.[102]

Hemoragia pulmonara acuta la copiii sub sapte ani poate deveni rapid fatala; cand copilul supravietuieste, apar leziuni ale vaselor de sange din plamani si depozite de hemosiderina vor ramane in macrofagele plamanului, putand fi ulterior observate in tesutul obtinut in urma bronhoscopiei.[97]

Ciupercile Stachybotrys produc o gama larga de trichothecene, micotoxine (inclusiv satratoxine), cativa epimeri roridini, verucarina J si B si hemolizina.[34, 99] O proteina hemoragica numita stacilisina a fost izolata din Stachybotrys colectat din casele copiilor cu hemoragie pulmonara[103, 104] si din serul pacientilor expusi la Stachybotrys.[46] S-a emis ipoteza ca copiii mici, cu plamanii aflati in crestere sunt mai susceptibili la efectele toxice ale micotoxinelor de Stachybotrys.[105]

Studiile efectuate asupra unor adulti expusi la Stachybotrys au mentionat o incidenta mai mare a unor probleme de sanatate precum: afectiuni ale cailor respiratorii, respiratie dificila, iritarea pielii si a ochilor, simptome asemanatoare gripei si oboseala cronica.[106] Stachybotrys a mai fost izolat si din plamanii unui copil cu hemosideroza pulmonara.[107]

Schimbari imunologice

Expunerea la fungi poate altera parametrii imunologici. Unele studii au raportat ca pacientii expusi la ciupercile de interior au niveluri mai ridicate in ser, de anticorpi IgG, IgA si IgM la ciupercile comune, trichothecene si satratoxine.[108-110]

Intr-o scoala infectata cu mucegai, la subiectii ce sufereau de sinuzita anticorpii IgG la noua specii comune de ciuperci de interior erau semnificativ mai ridicati decat la subiectii sanatosi.[111] Alte studii nu au evidentiat nici o crestere semnificativa a IgG fungal[112,113] sau IgE fungal[108] la pacientii expusi la ciuperci. Expunerea la ciupercile de interior a fost asociata cu niveluri modificate de celule T4, T8 si NK si cu niveluri mai ridicate de auto-anticorpi.[23, 114, 115]

Expunerea la glucanul din interior a fost asociata cu o proportie mai mica de celule T citoxice (CD8+SF61+) si cu un factor de secretie de necroza tumorală mai ridicat decat in casele cu niveluri mai scazute de beta-glucani.[116] Studiile pe animale carora li s-au administrat pe cale orala astfel de micotoxine comune precum aflatoxine, ochratoxine si trichothecene arata o considerabila deteriorare a sistemului imunitar, inclusiv scaderea imunitatii celulelor T, B si a macrofagelor.[117]

Studii ale liniilor de celule (cultura de celule care prolifereaza la infinit daca traieste intr-un mediu proaspat si intr-un spatiu potrivit, n.ed.) au descoperit ca multe micotoxine pot suprima celulele T, B si activitatea NK la concentratii ale serului similare cu cele descoperite la pacientii expusi la mucegaiul de interior.[118]

Prin urmare, expunerea la micotoxinele ce se raspandesc pe calea aerului este considerata a cauza efecte daunatoare asupra sistemului imunitar.

Disfunctii neurologice

Expunerea la mucegaiul de interior raspandit pe calea aerului cauzeaza disfunctii neurologice si deficiente cognitive.

Rapoarte clinice privitoare la un numar mare de pacienti expusi la mucegai au descoperit simptome de oboseala si slabiciune la 70%-100% din cazuri si disfunctii neurocognitive inclusiv pierderi de memorie, iritabilitate, anxietate si depresie la peste 40% dintre pacienti. De asemenea s-au constatat la un numar semnificativ de pacienti ameteli, furnicaturi si tremuraturi.[21, 23] Aceste semne si simptome constituie manifestari clasice de neurotoxicitate.[119]

Un studiu efectuat asupra a 43 de pacienti expusi la mucegai a descoperit ca acestia aveau rezultate semnificativ mai slabe (in raport cu 202 valori normale, de control) la multe teste neuropsihiatrice ce includeau echilibrul, reflexul de clipire, perceptia culorilor, timpii de reactie si puterea de strangere cu mana stanga ($P < 0,0001$ in fiecare caz).[120]

Studii cantitative ale unor electro-encefalograme au mentionat de asemenea latente semnificativ mai mari la pacientii expusi la ciuperci.[120] O imagine scanata a creierului SPECT a relevat pattern-uri neurotoxice la 26 din 30 (87%) dintre pacientii expusi la mucegai.[121] Un studiu al functiei nervoase vegetative la 60 de pacienti expusi la mucegai a descoperit ca 95% aveau raspunsuri vegetative anormale ale pupilei.[23] Studiile privind sensibilitatea vizuala de contrast erau de asemenea anormale la pacienti expusi la mucegaiul de interior.[23]

Studii aditionale au raportat ca pacientii expusi la mucegai au rezultate semnificativ mai slabe la testele de atentie, echilibru, timp de reactie, memorie verbala, concentrare, memorie si miscare ritmica a degetelor.[24, 122-124]

Majoritatea acestor pacienti prezentau de asemenea o gama larga de probleme de sanatate, inclusiv oboseala cronica, dureri de cap, insomnie, concentrare si atentie scazute. Studiile a 10 copii expusi la mucegai de interior si a 378 de adulti expusi la mucegai de interior au descoperit semnificativ mai multe anomalii neurofiziologice; acestea includeau EEG-uri anormale si potentiale vizuale si somatosenzoriale anormale.[25, 125]

Numarul mare de constatari neuropsihologice obiective, efectuate asupra unor pacienti simptomaticii, sustin ideea ca expunerea la mucegaiurile de interior poate avea efecte adverse asupra sanatatii.

Disfunctii renale

Expunerea la ciuperci poate de asemenea cauza disfunctii la nivelul rinichilor. Este bine cunoscut faptul ca alimentele contaminate cu ochratoxina sunt nefrotoxice.[126, 127] Expunerea la ochratoxina de interior poate fi si ea nefrotoxica.

Exista de asemenea un studiu efectuat asupra unei familii care prezenta simptome de sete crescuta, tendinte de urinare frecventa, letargie si eruptii pe piele. Cantitati considerabile de ochratoxina au fost descoperite in praful din casa in care locuia aceasta familie. Membrii familiei si-a revenit imediat dupa ce s-au mutat intr-o alta casa.[38]

Infectii fungale potential fatale

In ultimii ani, a crescut incidenta infectiilor ce ameninta viata la pacientii cu un sistem imunitar compromis din cauza lui *Aspergillus* si a altor ciuperci comune.[128, 129] Aspergiloza invaziva este foarte comuna la pacientii cu un sistem imunitar compromis, cel mai des fiind intalnita in urmatoarele cazuri: transplanturi de plaman, 17%-26%; transplanturi alogene de maduva osoasa, 5%-15%; leucemie acuta, 5%-24%; si transplanturi de inima, 2%-13%.[130, 131] Chiar si atunci cand sunt utilizate medicamente fungicide puternice si sunt efectuate tratamente intense intraspitalicesti, ratele de mortalitate datorita aspergiliozei invazive sunt intre 50% si 99% in cazul celor cu un sistem imunitar compromis.[132, 133] Controlul mediului inconjurator joaca un rol cheie in prevenirea infectiilor cu *Aspergillus*. Cateva studii au asociat lucrarile de amenajare ale spitalelor cu o rata crescuta a cazurilor de aspergiloza invaziva.[134-137] S-a demonstrat ca incercarile de control al mediului inconjurator, precum folosirea filtrelor HEPA, sigilarea incaperilor, curatarea camerelor in mod regulat si folosirea de vopsea fungicida cu quinolat de cupru 8 reduc semnificativ nivelurile de *Aspergillus* din aer si ratele de aspergiloza invaziva la pacientii din spitale cu un sistem imunitar compromis.[135-141] Alta cercetare recenta a aratat faptul ca un numar mare de spori de *Aspergillus* pot fi transmisi prin rezervele de apa[142] si ca o dezinfectare eficienta a dusurilor poate reduce semnificativ nivelurile de *Aspergillus*. [143]

Diagnosticarea si tratarea problemelor de sanatate cauzate de mucegaiuri

O examinare atenta a mediului si a istoricului medical este un prim pas esential in evaluarea unui pacient cu probleme de sanatate datorate mucegaiului.[52, 144-146]

O atentie speciala ar trebui acordata oricarei expuneri la orice forma vizibila de mucegai si/sau la pagubele datorate umiditatii, in casa sau la locul de munca. Prelevarea de probe din mediu de spori viabili, spori totali si micotoxine din aer si praf poate furniza informatii importante despre expunere.

Pentru pacientii suspectati de a fi fost expusi in mod substantial la ciuperci, o baterie de teste sofisticate de laborator a fost dezvoltata, ce analizeaza: 1) prezenta in serul acestor pacienti a unor anticorpi la mucegaiuri si micotoxine;[108, 109] 2) factori imunologici;[115] 3) micotoxine in urina si sange;[47] si 4) cativa parametrii importanti (inclusiv electrolitii, zaharul din sange si starea rinichilor) folosind un panou metabolic de baza. De asemenea, toti pacientii expusi la mucegaiuri ar trebui sa fie supusi unor teste de sensibilitate la contrastul vizual. Folosirea unei baterii de teste neuropsihologice standard[23, 122-124] precum si testarea nervilor vegetativi, electroencefalograma si tehnicile de vizualizarea a creierului precum SPECT si MRI pot fi instrumente foarte folositoare in documentarea leziunilor neurologice datorate mucegaiului.[25, 120, 121, 125, 144] Testarea functiei pulmonare este si ea utila pentru pacientii cu simptome respiratorii.[24, 120] Daca simptomele pacientului si/sau o examinare sugereaza afectarea urechilor, nasului, gatului, sistemului gastrointestinal, ochilor sau inimii, atunci consultarea unor medici specializati in expunerile din mediu inconjurator (fie un specialist in otorinolaringologie, un gastroenterolog, un oftalmolog sau un cardiolog) poate fi de mare folos. Neefectuarea unor testari obiective care sa permita evaluarea disfunctiei unui sistem sau a unui organ explica pozitia acceptata in prezent, ca expunerile la mucegaiul raspandit pe calea aerului nu au efecte adverse semnificative pentru sanatate.[38]

Factori comuni, non-fungali, ai mediului interior includ slaba ventilatie, monoxidul de carbon provenit de la surse de caldura defecte, pesticidele, fumatul pasiv, substantele petrochimice precum acelea ce se gasesc in produsele de curatat, materialele de constructie si solventii, formaldehida din materialele de constructie, bacteriile si alergenii din blanuri, penele si saliva unor animale care traiesc in casa precum gandacii de bucatarie, acarienii din praf, pisicile, cainii, pasarile din colivii si porumbelii. Expunerea la ozon, fumatul pasiv, formaldehida, alergenii proveniti de la gandacii de bucatarie si infectiile virale pot de asemenea avea un efect sinergic cu expunerea la ciuperci, contribuind la inrautatirea astmului si rinitei.[147-151] Cea mai importanta parte a tratamentului pentru pacientii expusi la mucegai consta in evitarea expunerii la ciuperci si eliminarea contaminarii cu mucegai acasa si la locul de munca. Orice scurgeri de apa si zonele inundate sau umede trebuie imediat corectate. Suprafetele neporoase precum podelele si peretii, ce prezinta cresteri vizibile de mucegai trebuie curatate. Materialele poroase, pline de apa precum covoarele si mobila trebuie aruncate.

Controlul umiditatii este important pentru a se controla cresterile de mucegai. Folosirea aparatelor de aer conditionat si a dezumidificatoarelor poate reduce semnificativ in timpul verii concentratiile de mucegai de interior raspandit pe calea aerului.[10, 152] Filtrele de aer HEPA pot de asemenea reduce semnificativ concentratiile de ciuperci de interior raspandita pe calea aerului.[141] Pentru eliminarea problemelor severe cauzate de apa si mucegaiul de interior, folosirea unui echipament de protectie precum masti de fata si/sau interventia unei firme de curatare profesionista poate fi esentiala.[50-52] Folosirea unor metode de

imunoterapie (pe cale sublinguala sau injectabila) contra ciupercilor s-a dovedit a fi benefica pentru unii pacienti sensibili la mucegaiurile comune de interior precum *Alternaria* si *Cladosporium herbarium*. [153, 154]

Alte terapii ce s-a descoperit ca sunt eficiente sunt: 1) detoxifierea (sauna, masajul, exercitiile fizice); 2) corectarea deficientelor imunitare ce au fost identificate; 3) folosirea de medicamente topice, nazale sau orale fungicide atunci cand se indica acest lucru. Unele studii efectuate pe animale de laborator sugereaza ca o dieta de calitate cu vitamine antioxidante adecvate, seleniu, substante fitochimice, metionina si proteine pot reduce efectele daunatoare ale micotoxinelor din alimente. [155, 156]

Rezumat

Mucegaiul de interior raspandit pe calea aerului si/sau expunerile la micotoxine cauzeaza o gama larga de efecte adverse asupra sanatatii, asa cum se indica in cele peste 100 de referinte citate. Profesioniștii din sanatate, managerii din constructii, proprietarii de case si publicul trebuie sa fie mult mai constienti de efectele adverse ale mucegaiurilor si micotoxinelor asupra sanatatii, de nevoia de reparare corecta a cladirilor si de necesitatea stabilirii unor diagnostice si tratamente corecte. Exista suficiente date in literatura medicala si un numar mare de rapoarte clinice, pentru a demonstra efectele adverse pe care le are mucegaiul de interior raspandit pe calea aerului, asupra sanatatii. Expunerea la mucegaiul de interior si micotoxine absorbite pe cale respiratorie poate fi o cale majora de lezare a sanatatii prin toate cele trei mecanisme cunoscute: infectie, alergie si toxicitate.

Nota editorului:

Articolul de mai sus a aparut pentru prima data in Journal of the Australasian College of Nutritional & Environmental Medicine, vol. 23, nr. 1, aprilie 2004, pp. 3-8.

Note finale:

(1) Umberger M. The Start that upstaged the economy. Chicago Tribune, January 13, 2002 at 1- available at WL 2612028, database ALLNEWS.

(2) INSURANCE JOURNAL- (No Author) Mold Claims Hit \$4 billion in Texas, Insurance Journal, May 27, 2003, <http://insurancejournal.com>

(3) The Canadian Task Force on the Periodic Health Examination. The Canadian guide to clinical preventative health care. Ottawa, Supply and Services Canada; 1994)

(4) Samson R, Hoekstra E, Frisvad J, Filtenborg O. Introduction to Food and Airborne Fungi. Centraalbureau voor Schimmelcultures, PO Box 85167, 3508 AD UTRECHT, The Netherlands 2000.

(5) Miller JD. Fungi as contaminants of indoor air. Atmospheric Environment 1992 26A (12) :2162-2172.

(6) Presternon DR. Perceived moisture problems in Iowa Homes. Technical Note Forest Products Journal 1991;41(6):47-48.

- (7) Platt S, Martin C, Hunt S, Lewis C. Damp housing, mould growth & symptomatic health state. *British Medical Journal* June 24, 1989; 298:1673-8.
- (8) Brunekreef B, Dockery D, Speizer FE. Home dampness and respiratory morbidity in children, *American Review of Respiratory Disease* 1989;140:1363-1367
- (9) Dales R, Zwanenburg H, Burnett R, Franklin C. Respiratory Health Effects of home dampness and molds among Canadian Children. *American Journal of Epidemiology* 1991a;134(2):196-203.
- (10) Etzel R. Indoor air pollutants in homes and schools. *Pediatric Clinics of North America* October 2001;48(5):1153-65.
- (11) Flannigan B, McCabe E, McGarry F. Allergic and toxigenic microorganisms in houses. *Journal of Applied Bacteriology* 1991;70:615-735.
- (12) Dhillon M. Current status of mold immunotherapy. *Annals of Allergy* 1991;66:385.
- (13) Curtis L, Ross M, Persky V, Scheff P, Wadden R, Ramaskrisnan V, Hryhorczuk D. Bioaerosol concentrations in the Quad Cities 1 year after the 1993 Mississippi River floods. *Indoor and Built Environment* 2000;9:35-43.
- (14) Shelton B, Kirkland K, Flanders WD, Morris G. Profiles of airborne fungi in buildings and outdoor environments in the United States. *Applied and Environmental Microbiology* April 2002;68(4):1743-1753.
- (15) Ren P, Jankun T, Leaderer B. Comparisons of seasonal fungal prevalence in indoor and outdoor air and in house dwellings in one Northeast American county. *Journal of Exposure Analysis and Environmental Epidemiology* 1999;9:560-568.
- (16) Pei-Chih W, Huey-Jen S, Chia-Yin L. Characteristics of indoor and outdoor airborne fungi at suburban and urban homes in two seasons. *Science of the Total Environment* 2000;253:111-8.
- (17) Li CS, Kuo YM. Characteristics of airborne microfungi in subtropical homes. *Science of the total environment*. October 28, 1994;155(3):267-271.
- (18) Ebner E, Hasselwandter K, Frank A. Indoor and outdoor incidence of airborne fungal allergens at low and high alpine environments. *Mycology Research* 1992;97:117-124.
- (19) Solomon WR. A volumetric study of winter fungus prevalence in the air of midwestern homes. *Journal of Allergy and Clinical Immunology* January 1976;57(1):46-55.
- (20) Beaumont F, Kauffman HF, Sluiter HJ, DeVries K. A volumetric-aerobiological study of seasonal fungus prevalence inside and outside dwellings of asthmatic patients living in northeast Netherlands. *Annals of Allergy* December 1984;53(6):486-492.
- (21) Lieberman A. Explosion of mold cases in homes, workplaces and occupational medicine practices. Presented at the 21st Annual Symposium on Man and His Environment in Health and Disease, Dallas, Texas. June 19-22, 2003

- (22) Dennis D. Chronic sinusitis: defective T-cells responding to superantigens, treated by reduction of fungi in the nose and air. *Archives of Environmental Health* July 2003;58(7):433-441.
- (23) Rea WJ, Didriksen N, Simon TR, Pan Y, Fenyves EJ, Griffiths B. Effects of toxic exposure to molds and mycotoxins in building-related illnesses. *Archives of Environmental Health* July 2003;58(7):399-405.
- (24) Kilburn KH. Indoor mold exposure associated with neurobehavioral and pulmonary impairment: a preliminary report. *Archives of Environmental Health* July 2003;58(7):390-8.
- (25) Campbell A, Thrasher J, Madison R, Vojdani A, Gray M, Johnson A. Neural autoantibodies and Neurophysiologic Abnormalities in Patients exposed to molds in water damaged buildings. *Archives of Environmental Health* August 2003 58(8):464-478.
- (26) Kurup V, Shen HD, Vijay H. Immunobiology of fungal allergens. *International Archives of Allergy and Immunology* 2002;129:181-188.
- (27) Gorny RL, Reponen T, Willeke K, Schechel D, Robine E, Bossier M, Grinshpun S. Fungal fragments as indoor air contaminants. *Applied and Environmental Microbiology* 2002;68:3522-3531.
- (28) Institute of Medicine. *Clearing the Air. Asthma and indoor exposures.* Institute of Medicine
- (29) Korpi A, Kasanen JP, Kosma VM, Rylander R, Pasanen AL. Slight respiratory irritation by not inflammation in mice exposed to (1>3)-beta-D-glycan aerosols. *Mediators of Inflammation* June 2003;12(3):139-146.
- (30) Etzel R. Mycotoxins. *Journal of the American Medical Association (JAMA)* January 23/30, 2002,287(4):425-427.
- (31) Nielsen KF. Mycotoxin production by indoor molds. *Fungal Genetics and Biology* 2003;39:103-117.
- (32) Rylander R. Indoor air-related effects and airborne (1>3)-beta-D-glucan. *Environmental Health Perspectives* June 1999;107 Supplement 3:501-3
- (33) Wilkins K, Larsen K, Simkus M. Volatile metabolites from mold growth on building materials and synthetic media. *Chemosphere* August 2000;41(3):437- 446.
- (34) Bennett J, Klich M. Mycotoxins. *Clinical Microbiology Reviews* July 2003;16(3):497-516.
- (35) Hardin B, Kelman B, Saxon A. ACOEM Evidence Base Statement. Adverse Health effects associated with molds in the indoor environment. *Journal of Occupational and Environmental Medicine* May 2003;45(5):470-8.
- (36) Richard J, Plattner R, May J, Liska S. The occurrence of ochratoxin A in dust collected from a problem household. *Mycopathologica* 1999;146(2):99-103.
- (37) Smoragiewicz W, Cossette B, Boutard A, Krystyniak K. Trichothecene mycotoxins

in the dust of ventilation systems in office buildings. *International Archives of Occupational and Environmental Health* 1993;65(2):113-117.

(38) Engelhart S, Loock A, Skutlarek D, Sagunski H, Lommel A, Farbe M, Exner M. Occurrence of toxigenic *Aspergillus versicolor* isolates and sterigmatocystin in carpet dust from damp indoor environments. *Applied Environmental Microbiology* August 2002;68(8):3886-3890.

(39) Iavicoli I, Brera C, Carelli G, Caputi R, Marinaccio A, Miraglia M. External and internal dose in subjects occupationally exposed to ochratoxin A. *International Archives of Occupational and Environmental Health* August 2002;75(6):381-6.

(40) Fischer G, Dott W. Relevance of airborne fungi and their secondary metabolites for environmental, occupational and indoor hygiene. *Archives of Microbiology* 2003;179:75-82.

(41) Sorenson WG. Fungal Spores: Hazardous to Health? *Environmental Health Perspectives* June 1999;107(Supplement 3):469-472.

(42) Van Emon J, Reed A, Yike I, Vesper S. ELISA measurement of Stachylysin in serum to quantify human exposures to the indoor mold *Stachybotrys charatarum*. *Journal of Occupational and Environmental Medicine* June 2003;45:582-591.

(43) Croft W, Jastromski BM, Croft AL, Peters HA. Clinical confirmation of trichothecene mycotoxicosis in patient urine. *Journal of Environmental Biology* 002;23(3):301-320.

(44) Johnson P, Sarosi G. Community Acquired Fungal Pneumonias. *Seminar in Respiratory Infections* March 1989;4(1):56-63.

(45) Tierney L, McPhee S, Papadakis M. *Current Medical Diagnosis and Treatment*. 2003 Lange Medical Books, New York City.

(46) Nicod L, Pache J, Howarth N. Fungal infections in transplant recipients. *European Respiratory Journal* January 2001;17(1):133-140.

(47) Garber G. An Overview of fungal infections. *Drugs* 2001;61 Supplement 1:1-12.

(48) Groll AH, Shah PM, Mentzel C, Schneider M, Just-Nuebling G, Huebner K. Trends in the postmortem epidemiology of invasive fungi at a university hospital. *Journal of Infection* 1996;33:23-32.

(49) Husain S, Alexander BD, Munoz P, Avery RK, Houston S, Pruett L, Jacobs R, Dominguez EA, Tollemar JG, Baumgarten JK, Yu CM, Wagener MM, Kusne S, Singh N. Opportunistic mycelial fungal infections in organ transplant recipients: emerging importance of non-*Aspergillus* fungi. *Clinical and Infectious Diseases* July 15, 2003;37(2):221-229.

(50) Denning D. Report on a European Science Foundation Workshop on invasive Aspergillosis. October 21-2, 1998, U of Manchester, Manchester, United Kingdom.

(51) Kontoyiannis D, Bodey G. Invasive Aspergillosis in 2002: An Update. *European Journal of Clinical Microbiology and Infectious Disease* 2002;21:161-172.

(52) Denning D. Therapeutic outcome in invasive aspergillosis. *Clinical and Infectious*

- (53) Lin S, Schranz J, Teutsch S. Aspergillosis case-fatality rate: systemic review of the literature. *Clinical and Infectious Diseases* February 1, 2001;32(3):358-366.
- (54) Pasanen AL. A review: Fungal Exposure Assessment in Indoor Environments. *Indoor Air* 2001;11:87-98.
- (55) Dillon HK, Miller JD, Sorenson WG, Douwes J, Jacobs R. Review of methods applicable to the assessment of mold exposure in children. *Environmental Health Perspectives* June 1999; 107(Supplement 3):473-480.
- (56) Tiffany J, Bader H. Detection of *Stachybotrys charatarum*: the effectiveness of culturable-air sampling and other methods. *Environmental Health* May 2000, 9-11.
- (57) Gent J, Ren P, Belanger K, Triche E, Bracken M, Holfand T, Leaderer B. Levels of household mold associated with respiratory symptoms in the first year of life in a cohort at risk for asthma. *Environmental Health Perspectives* December 2002;110(12):A781-A786.
- (58) Dales R, Burnett R, Zwanenburg H. Adverse health effects among adults exposures to home dampness and molds. *American Review of Respiratory Disease* 1991b;143:505-509.
- (59) Ostro B, Lipsett M, Mann J, Braxton-Owens H, White M. Air pollution and exacerbation of asthma in African-American children in Los Angeles. *Epidemiology* December 2001;12:200-208.
- (60) Zock J, Jarvis D, Lucynska G, Sunyer J, Burney P. Housing characteristics, reported mold exposure, and asthma in the European Community Respiratory Health Survey. *Journal of Allergy and Clinical Immunology* August 2002;110(2):285-292.
- (61) Williamson I, Martin C, McGill G. Damp housing and asthma: a case control study. *Thorax* 1997;52:229-234.
- (62) Verhoeff AP, Van Strien RT, Van Wijnen JH, Brunekreef B. Damp housing and household respiratory symptoms: the role of sensitization to dust mites and molds. *American Journal of Epidemiology* 1995;141:103-110.
- (63) Strachan DP, Flannigan B, McCabe E, McGarry F. Quantification of airborne moulds in the homes of children with and without wheeze. *Thorax* 1990;45:382-387.
- (64) Brunekreef, B. Damp housing and adult respiratory symptoms. *Allergy* 1992;47: 498-502
- (65) Waegemaekers M, Van Wageningen N, Brunekreef B, Boleij JS. Respiratory symptoms in damp homes. A pilot study. *Allergy* 1989;44:192-198.
- (66) Jedrychowski W, Flak E. Separate and combined effects of the indoor and outdoor air quality on chronic respiratory symptoms adjusted for allergy among preadolescent children. *International Journal of Occupational Medicine and Environmental Health* 1998; 11:19-35
- (67) Hu FB, Persky V, Flay BR, Richardson J. An epidemiological study of asthma

prevalence and related factors among young adults. *Journal of Asthma* 1997;34(1):67-76.

(68) Jaakkola J, Jaakkola N, Ruotsalainen R. Home dampness and molds as determinants of respiratory symptoms and asthma in pre-school children. *Journal of Exposure Analysis and Environmental Epidemiology* 1993;3(supplement 1):126-142

(69) Slezak J, Persky V, Kviz F, Ramakrishnan V, Byers C. Asthma prevalence and risk factors in selected Head Start sites in Chicago. *Journal of Asthma* 1998; 35(2): 203-212.

(70) Lee YL, Lin YC, Hsiue TR, Hwang BF, Guo YL. Indoor and outdoor environmental exposures, parental atopy and physician diagnosed asthma in Taiwanese schoolchildren. *Pediatrics*, November 2003;112(5):e389=e395.

(71) Sly RM. Changing prevalence of allergic rhinitis and asthma. *Annals of Allergy, Asthma and Immunology* March 1999;82(3):233-248.

(72) Belanger K, Beckett W, Triche E, Bracken M, Holford T, Ren P, McSharry JE, Gold D, Platt-Mills T, Leaderer B. Symptoms of wheeze and persistent cough in the first year of life: associations with indoor allergens, air contaminants, and maternal history of asthma. *American Journal of Epidemiology* August 1, 2003;158:195-202.

(73) Stark PC, Burge HA, Ryan LM, Milton DK, Gold DR. Fungal levels in the home and lower respiratory tract illness in the first year of life. *American Journal of Respiratory and Critical Care Medicine* July 15, 2003;168(2):232-237.

(74) Thorn J, Rylander R. Airways inflammation and glucan in a rowhouse area. *American Journal of Respiratory and Critical Care Medicine* 1998;157:1798-803.

(75) Chao HJ, Schwartz J, Milton DK, Burge HA. The work environment and workers' health in 4 large office buildings. *Environmental Health Perspectives* July 2003;111(9):1242-8.

(76) Pirhonen I, Nevalainen A, Husman T. Home dampness, moulds and their influence on respiratory infections in Finland. *European Respiratory Journal* 1996;9:2618-2622.

(77) Koskinen OM, Husman TM, Meklin TM. The relationship between mould and moisture observations in houses and state of health of their occupants. *European Respiratory Journal* 1999;14:1363-7.

(78) Ruotsalainen R, Jaakola N, Jaakola J. Dampness and molds in day-care centers as an occupational health care problem. *International Archives of Occupational and Environmental Health* 1995;66:369-374.

(79) Wan GH, Li CS. Dampness and airway inflammation and systemic conditions in office building workers. *Archives of Environmental Health* 1999;54:58-63.

(80) Targonski P, Persky V, Ramakrishnan V. Effect of environmental molds on risk of death from asthma during the pollen season. *Journal of Allergy and Clinical Immunology* May 1995;95(5 Part 1):955-961.

(81) Neas LM, Dockery DW, Burge H, Koutrakis P, Speizer FE. Fungus spores, air pollutants, and other determinants of peak expiratory flow rates in children. *American*

Journal of Epidemiology 1996;143(8):797-807.

(82) Delfino RJ, Zeiger RS, Seltzer JM, Street DH, Matteucci RM, Anderson PR, Koutrakis P. The effect of outdoor fungal spores concentrations on daily asthma severity. Environmental Health Perspectives 1997;105(6):622-635.

(83) Dales RE, Cakmak S, Judek S, Dann T, Coates F, Brook JR, Burnett RT. Influence of outdoor aeroallergens on hospitalization for asthma in Canada. Journal of Allergy and Clinical Immunology February 2004;113:303-6.

(84) Liccorish K, Novey H, Kozak P, Fairshter R, Wilson A. Role of Alternaria and Penicillium spores in the pathogenesis of asthma. Journal of Allergy and Clinical Immunology December 1985 76(6):819-825.

(85) O'Halloren M, Yungiger J, Offord K, Somers M, O'Connell E, Ballard D, Sachs M. Exposure to an aeroallergen as a possible precipitating factor in respiratory arrest in young patients with asthma. New England Journal of Medicine February 1991;324(6):359-363.

(86) Zureik M, Neukirch C, Leynaert B, Laird R, Bousquet J. Sensitization to airborne moulds and severity of asthma: cross sectional study from European Community Respiratory Health Survey. British Medical Journal (BMJ) August 24, 2002;325(7361): 411-4.

(87) Gergen PJ, Turkeltaub PC. The association of individual allergen reactivity with respiratory disease in a national sample: data from the second National Health and Nutrition Examination Survey, 1976-1980 (NHANES II). Journal of Allergy and Clinical Immunology 1992;90(4 Pt 1):579-588.

(88) Tariq SM, Matthews SM, Stevens M, Hakim EM. Sensitization to Alternaria and Cladosporium by the age of 4 years. Clinical and Experimental Allergy 1996;26(7):794-798.

(89) Perzanowski MS, Sporik R, Squillance SP, Gelber LF, Call R, Carter M, Platt-Mills T. Association of sensitization to Alternaria allergens with asthma among school aged children. Journal of Allergy and Clinical Immunology 1998;101(5):626-632.

(90) Nelson RP, DiNiccolo R, Fernandez-Caldas E, Seleznick MJ, Lockey R, Good RA. Allergen specific IgE levels and mite allergen exposure in children with acute asthma first seen in an emergency department and in nonasthmatic control subjects. Journal of Allergy and Clinical Immunology 1996; 98(2):382-388.

(91) Lander F, Meyer HW, Norn S. Serum IgE specific to indoor moulds, measured by basophil histamine release, is associated with building-related symptoms in damp buildings. Inflammation Research 2001;50:227-231.

(92) Schubert M. Medical treatment of allergic fungal sinusitis. Annals of Allergy, Asthma and Immunology. August 2000;85(2):90-101.

(93) Greenberger P. Allergic bronchopulmonary aspergillosis, allergic fungal sinusitis and hypersensitivity pneumonitis. Clinical Allergy and Immunology 2002;16:449-468.

(94) Ponikau JU, Sherris R, Kern EB. The diagnosis and incidence of allergic fungal sinusitis. Mayo Clinic Proceedings 1999;74:877-884.

- (95) Lebowitz R, Waltzman M, Jacobs J, Pearlman A, Tierno P. Isolation of fungi by standard laboratory methods in patients with chronic rhinosinusitis. *The Laryngoscope* 2002; 112(12):2189-2191.
- (96) Rains BM, Mineck CW. Treatment of allergic fungal sinusitis with high-dose itraconazole. *American Journal of Rhinology* January-February 2003;17(1):1-8.
- (97) Apostolakos M, Rossmore H, Beckett W. Hypersensitivity pneumonitis from ordinary residential exposures. *Environmental Health Perspectives* September 2001;109(9):979-981.
- (98) Kita T, Nishi K, Fujimura M, Abo M, Ohka T, Yasul M, Ogawa H, Minato H, Kurumaya H, Nakao S. A case of hypersensitivity pneumonitis caused by *Humicola fuscoatra*. *Respirology* 2003;8:95-98.
- (99) Ando M, Yoshida K, Soda K, Araki S. Specific bronchoalveolar lavage IgA antibody in patients with summer type hypersensitivity pneumonitis induced by *Trichosporon cutaneum*. *Annual Review of Respiratory Disease* 1986;134:177-9.
- (100) Centers for Disease Control (CDC): Pulmonary Hemorrhage/ Hemosiderosis Among Infants- Cleveland, Ohio, 1993-6. *MMWR* 1997;46:33-35
- (101) Montana E, Etzel R, Allan T, Horgan T, Dearborn D. Environmental Risk factors associated with pediatric idiopathic pulmonary hemorrhage and hemosiderosis in a Cleveland community. *Pediatrics* 1997;99:117-124.
- (102) Etzel R, Montana E, Sorenson W, Kullman G, Allen T, Dearborn D, Olson D, Jarvis B, Miller J. Acute pulmonary hemorrhage in infants associated with exposure to *Stachybotrys atra* and other fungi. *Archives of Pediatric and Adolescent Medicine* 1998;152:757-762.
- (103) Vesper S, Dearborn D, Yike I, Sorenson W, Haugland R. Hemolysis, toxicity and randomly amplified polymorphic DNA analysis of *Stachybotrys chartarum* strains. *Applied and Environmental Microbiology* July 1999;65(7):3175-3181.
- (104) Dearborn D, Smith P, Dahms B, Allan T, Sorenson W, Montana E, Etzel R. Clinical profile of 30 infants with acute pulmonary hemorrhage in Cleveland. *Pediatrics* September 2002;110(3):627-637.
- (105) Center for Disease Control and Prevention CDC. Update: pulmonary hemorrhage/ hemosiderosis among infants-Cleveland, Ohio 1993-6. *MMWR* 2000;49:18-184.
- (106) Etzel T. *Stachybotrys*. *Current Opinion in Pediatrics* February 2003;15(1):103-6.
- (107) Vesper S, Magnuson M, Dearborn D, Yike I, Haugland R. Initial characterization of the hemolysin stachylysin from *Stachybotrys chartarum*. *Infection and Immunity* February 2001;69(2):912-6.
- (108) Vesper S, Vesper MJ. Stachylysin may be a cause of hemorrhaging in humans exposed to *Stachybotrys chartarum*. *Infection and Immunity* April 2002; 70(4): 2065-2069.

- (109) Yike I, Allan T, Sorenson W, Dearborn D. Highly sensitive protein translation assay for trichothecene toxicity in airborne particulates: comparison with cytotoxicity assays. *Applied and Environmental Microbiology* January 1999;65(1):88-94.
- (110) Johanning E, Biagini R, Hull D, Morey P, Jarvis B, Landsbergis P. Health and immunology study following exposure to toxigenic fungi (*Stachybotrys chartarum*) in a water-damaged office environment. *International Archives of Environmental Health* 1996;68:207-218.
- (111) Elidemir O, Colasurdo G, Rossmann S, Fan L. Isolation of *Stachybotrys* from the lung of a child with pulmonary hemosiderosis. *Pediatrics* October 1999;104(4Part1):964-966.
- (112) Hooper D. Molecular evaluation for autopsy and clinical tissue in patients. Presented at the 22th Annual Symposium on Man and His Environment in Health and Disease, Dallas, Texas. June 27, 2004.
- (113) Vojdani A, Campbell A, Kashanian A, Vojdani E. 2003. Antibodies against molds and mycotoxins following exposure to toxigenic fungi in water-damaged building. *Archives of Environmental Health* June 2003;58(6):324-336.
- (114) Vojdani A, Thrasher J, Madison R, Gray M, Heuser G, Campbell A. 2003. Antibodies to molds and satratoxin individuals in a water-damaged building. *Archives of Environmental Health* July 58(7):421-432.
- (115) Savilahti R, Uitti J, Laippala P, Hussman T, Reiman M. Immunoglobulin G antibodies of children exposed to microorganisms in a water-damaged school. *Pediatric Allergy and Immunology* December 2002;13(6):438-442.
- (116) Patovirta RL, Reiman M, Husman T, Haverinen U, Toivola M, Nevalainen A. Mould specific IgG antibodies connected with sinusitis in teachers of a mould damaged school: A 2 year follow up study. *International Journal of Occupational Medicine and Environmental Health* 2003;16(3):221-230.
- (117) Taskinen TM, Laitinen S, Nevalainen A, Vepsalainen A, Meklin T, Reiman M, Korppi M, Hussman T. Immunoglobulin G antibodies to moulds in schoolchildren from moisture problem schools. *Allergy* January 2002;57(1):9-16.
- (118) Malkin R, Martinez K, Marinovich V, Wilcox T, Wall D, Biagini R. The relationship between symptoms and IgG and IgE antibodies in an office environment. *Environmental Research* February 1998;76(2):85-93.
- (119) Dales R, Miller D, White J, Dulberg C, Lazarovitis A. Incidence of residential fungal contamination on peripheral blood lymphocyte populations in children. *Archives of Environmental Health* May/June 1998;53(3):190-195.
- (120) Vojdani A. 2003 Health effects and immunotoxicology of toxigenic molds and mycotoxins. Presented June 20, 2003 at the 21st international symposium of man and his environment in health and disease. Dallas, Texas.
- (121) Beijer L, Thorn J, Rylander R. Mould exposure at home relates to inflammatory markers in blood. *European Respiratory Journal*. February 2003;21(2):317-322.
- (122) Bondy G, Pestka J. Immunomodulation by fungal toxins. *Journal of Toxicology*

and Environmental Health, Part B. 2000;3(2):109-143.

- (123) Berek L, Petri IB, Msterhazy A, Teren J, Molnar J. Effects of mycotoxins on human immune functions in vitro. *Toxicology In Vitro* February 2001;15(1):25-30.
- (124) Singer R. *Neurotoxicity Guidebook*, Van Nostrand Reinold, New York City, 1990.
- (125) Gray M, Kilburn K, Crago R. Molds, Mycotoxins and Public Health: Summary of 195 patients treated collaboratively. Presented 11/11/2002 at the American Public Health Association (APHA) meeting in Philadelphia, PA.
- (126) Crago BR, Gray M, Nelson L, Davis M, Arnold L, Thrasher J. Psychological, Neuropsychological and Electrocortical effects of Mixed Mold Exposure. *Archives of Environmental Health* August 2003;58(8):452-463.
- (127) Simon T. Neurotoxicity- Mold Exposure Versus All Causes. Presented at the 21st Annual Symposium on Man and His Environment in Health and Disease, Dallas, Texas. June 19-22, 2003
- (128) Gordon W, Johanning E, Haddad L. Cognitive impairment associated with exposure to toxigenic fungi. Presented at the 3rd International Conference on Fungi, Mycotoxins and Bioaerosols- September 23-5, 1998, Saratoga Springs, New York. In *Bioaerosols, Fungi and Mycotoxins: Health Effects. Assessments, Prevention and Control*, Eastern New York Center for Environmental and Occupational Health, Albany, New York 1999.
- (129) Didricksen N- Neurocognitive Deficits in Individuals Exposed to Toxigenic Molds. Presented at the 21st Annual Symposium on Man and His Environment in Health and Disease, Dallas, Texas. June 19-22, 2003
- (130) Baldo JV, Ahmad L, Ruff R. Neuropsychological performance of patients following mold exposure. *Applied Neuropsychology* 2002;9(4):193-202.
- (131) Anyanwu E, Campbell A, Vojdani A. Neurophysiological effects of chronic indoor environmental toxic mold exposure on children. *ScientificWorldJournal* April 28, 2003;3(4):281-290.
- (132) Boysen SR, Rozanski EA, Chan DL, Grobe TL, Fallon MJ, Rush J. Tremorgenic mycotoxicosis in four dogs from a single household. *Journal of the American Veterinary Medical Association* Nov 15, 2002;221(10):1441-4.
- (133) Young DL, Villar D, Carson TL, Ierman PM, Moore RA, Bottoff MR. Tremorgenic mycotoxin intoxication with penitrem A and roquefortine in two dogs. *Journal of the American Veterinary Medical Association* Jan 1, 2002;222(1):52-3.
- (134) Naude TW, O'Brien OM, Rundberget T, McGregor AD, Roux C, Flaoyen A. Tremorogenic neuromycotoxicosis in 2 dogs ascribed to ingestion of penitrem A and possibly roquefortine in rice contaminated with *Penicillium crustosum*. *Journal of the South African Veterinary Association* Dec 2002;73(4):211-5.
- (135) Chen JW, Luo YL, Hwang MJ, Peng FC, Ling KH. Territrem B, a tremorgenic mycotoxin that inhibits acetylcholinesterase with a noncovalent yet irreversible binding mechanism. *Journal of Biological Chemistry* 1999;274(49):34916-34923.

- (136) Krogh P, Hald B, Pedersen J. Occurrence of ochratoxin A and citrinin in cereals associated with mycotoxic porcine nephropathy. *Acta Path Micro Scand* 1973;81 Sect B: 689-695.
- (137) Castegnaro M, Plestina R, Dirheimer O, Chernosemsky IN, Barsch H (eds), *Mycotoxins, Endemic Nephropathy and Urinary Tract Tumors*. IARC Sci Publication 1991;115:1-340.
- (138) Kristensen P, Irgens L, Andersen A, Bye AS, Sundheim L. Gestational age, birth weight, and perinatal death among births to Norwegian farmers, 1967-1991. *American Journal of Epidemiology* 1997;146:329-338.
- (139) Kristensen P, Andersen A, Irgens L. Hormone-dependent cancer and adverse reproductive outcomes in farmers families- effects of climatic conditons favoring fungal growth in grain. *Scandinavian Journal of Work and Health* 2000;26(4):331-337.
- (140) Diekman M, Green M. Mycotoxins and reproduction in domestic livestock. *Journal of Animal Science* 1992;70:1615-1627.
- (141) Cotran, RS. *Robbins Pathologic Basis of Disease*. 5th edition, 1994, page 914. WB Saunders, New York City.
- (142) Cheta D. Animal models of type 1 (insulin-dependent) diabetes mellitus. *Journal of Pediatric Endocrinology and Metabolism* Jan-Feb 1998;11(1):11-19.
- (143) Hoffmeister PA, Storer BE, Sanders JE. Diabetes mellitus in long-term survivors of pediatric hematopoietic cell transplantation. *Journal of Pediatric Hematology and Oncology* Feb 2004;26(2):81-90.
- (144) Eggleston PA. Environmental Control for fungal allergen exposure. *Current Allergy and Asthma Reports* September 2003;3(5):424-9.
- (145) Heuser G, Axelrod P, Heuser S. *Defining Chemical Injury: A Diagnostic Protocol and Profile of Chemically Injured Civilians, Industrial Workers and Gulf War Veterans*. *International Perspectives in Public Health* 2000;13:1-16.
- (146) Marshall L, Weir E, Abelsohn A, Sanborn MD. Identifying and managing adverse environmental effects: 1) taking an exposure history. *CMAJ Canadian Medical Association Journal* April 16, 2002;166(8):1049-1055.
- (147) Dales RE, Miller D, McMullen E. Indoor air quality and health: validity and determinants of reported home dampness and molds. *International Journal of Epidemiology* 1997;26:120-124.
- (148) Macher J editor. *Bioaerosols: Assessment and Control*. American Conference of Governmental and Industrial Hygienists (ACGIH) Cincinnati, Ohio 1999.
- (149) Portnoy JM, Barnes CS, Kennedy K. Sampling for indoor fungi. *Journal of Allergy and Clinical Immunology* February 2004;113:189-198.
- (150) Institute of Medicine Committee on the Health Effects of Indoor Allergens: *Engineering Control Strategies*. *Allergens: Assessing and Controlling Adverse Health Effects*. Engineering Control Strategies 1993;206-232 Published by National Academy Press, Washington DC.

- (151) Institute for Inspection, Cleaning and Restoration. IICRC S520 Standard and reference guide for professional mold remediation. December 2003. IICRC Press, 2715 E Mill Plain Blvd, Vancouver, Washington 98611 (360) 693-5675.
- (152) Higgins BG, Francis HC, Yates G, Warburton CJ, Fletcher AM, Pickering CA, Woodcock AA. Environmental exposure to air pollution and allergens and peak flow changes. *European Respiratory Journal* July 2000;16(1):61-66.
- (153) Thorn J, Brisman J, Toren K. Adult-onset asthma is associated with self-reported mold or environmental tobacco smoke in the home. *Allergy* 2001;56:287-292.
- (154) Chen WY, Tseng HI, Wu MT, Hung HC, Wu WT, Chen HL, Lu CC. Synergistic effect of multiple indoor allergen sources on atopic symptoms in primary school children. *Environmental Research* September 2003;93(1):1-8.
- (155) Skoner DP. Viral infection and allergy: lower airway. *Allergy and Asthma Proceedings* July-August 2002;23(4):229-232.
- (156) Fireman P. Virus-provoked rhinitis in patients who have allergies. *Allergy and Asthma Proceedings* March-April 2002;23(2):99-102.
- (157) Hirsch D, Hirsch R, Kalbfleish S. Effect of central air-conditioning and meteorological factors on indoor spore counts. *Journal of Allergy and Clinical Immunology* July 1978;62(1):22-26.
- (158) Sheretz RJ, Belani A, Kramer BS, Efenbein GJ, Weiner RS, Sullivan ML, Thomas RG, Samsa GP. Impact of air filtration on nosocomial *Aspergillus* infections. *American Journal of Medicine* October 1987;83(4):709-718.
- (159) Dearborn D. Clinical findings and clinical research on indoor mold exposure: children. Presented at the Society for Environmental Health Conference on Mold Related Health Effects, Washington, DC, June 28-29, 2004.
- (160) Panackal A, Dahlman A, Keil K, Peterson C, Mascola L, Mirza S, Phelan M, Lasker B, Brandt M, Carpenter J, Bell M, Warnoci D, Hajjeh R, Morgan J. Outbreak of invasive aspergillosis among renal transplant patients. *Transplantation* April 15, 2003;75(7):1050-3.
- (161) Oren I, Haddad N, Finkelstein R, Rowe J. Invasive pulmonary aspergillosis in neutropenic patients during hospital construction: before and after chemoprophylaxis and institution of HEPA filters. *American Journal of Hematology* April 2001;66(4):257-262.
- (162) Loo V, Bertrand C, Dixon C, Vitye D, DeSalis B, McLean A, Brod A, Robson H. Control of construction-associated nosocomial aspergillosis in an antiquated hematology unit. *Infection Control and Hospital Epidemiology* June 1996;17(6):360-4.
- (163) Iwen P, Davis J, Reed EC, Winfield BA, Hinrichs SH. Airborne fungal spore monitoring in a protective environment during hospital construction, and correlation with outbreak of invasive aspergillosis. *Infection Control and Hospital Epidemiology* May 1994;15(5):303-6.
- (164) Hahn T, Cummings K, Michalek AM, Lipman B, Segel B, McCarthy P. Efficacy of

high-efficiency particulate air filtration in preventing aspergillosis in immunocompromised patients with hematologic malignancies. *Infection Control and Hospital Epidemiology* September 2002;23(9):525-531.

(165) Cornet M, Levy V, Fleury L, Lortholary J, Barquins S, Coureul M, Deliere E, Zittoun R, Brucker G, Bouvet A. Efficacy of prevention by high-efficiency articulate air filtration or laminar airflow against *Aspergillus* airborne contamination during hospital renovation. *Infection Control and Hospital Epidemiology* July 1999;20(7):508-513.

(166) Withington S, Chambers ST, Beard ME, Inder A, Allen J, Ikram RB, Schousboe MI, Heaton DC, Spearing RI, Hart DN. Invasive aspergillosis in severely eutropeic patients over 18 years: impact of intranasal amphotericin B and HEPA filtration. *Journal of Hospital Infection* January 1998;38(1):11-8.

(167) Annaisie EJ, Stratton SL, Dignani MC, Summerbell RC, Rex JH, Monson TP, Spencer T, Kasai M, Francesconi A, Walsh TJ. Pathogenic *Aspergillus* species recovered from a hospital water system: a 3 year prospective study. *Clinical and Infectious Diseases* March 15 2002;34(6):780-789.

(168) Annaisie EJ, Stratton SL, Dignani MC, Lee CK, Mahfouz TH, Rex JH, Summerbell RC, Walsh TJ. Cleaning patient shower facilities: a novel approach to reducing patient exposure to aerosolized *Aspergillus* species and other opportunistic molds. *Clinical and Infectious Diseases* October 15, 2002;35(8):E86-8.

(169) Bernardis P, Agnoletto M, Puccinelli P, Parmiani S, Pozzan M. Injective versus sublingual immunotherapy in *Alternaria tenuis* allergic patients. *Journal of Investigative Allergology and Clinical Immunology* January-February 1996; 6(1):55-62.

(170) Helbling A, Reimers A. Immunotherapy in fungal allergy. *Current Allergy and Asthma Reports* September 2003;3(5):447-453.

(171) Galvano F, Piva A, Ritieni A, Galvano G. Dietary strategies to counteract the effects of mycotoxins: a review. *Journal of Food Protection* January 2001;64(1):120-131.

(172) Atroshi F, Rizzo A, Westermarck, Ali-Vehmas T. Antioxidant nutrients and mycotoxins. *Toxicology* November 15, 2002;180(2):151-167.

Despre autori:

Luke Curtis, Master in Stiinta, CIH, Scoala de Sanatate Publica, Universitatea din Illinois, Chicago, Illinois, SUA;

Allan Lieberman, Medic, Centrul pentru Sanatate Profesionala si de Mediu, North Charleston, Carolina de Sud, SUA;

Martha Stark, Medic, Universitatea Harvard, Newton Center, Massachusetts, SUA;

William Rea, Centrul de Sanatate a Mediului, Dallas, Texas, SUA;

Marsha Vetter, Medic, Dr., Centrul de Sanatate a Mediului, Hoffman Estates, Illinois, SUA.