Medical Mycology in India: Past, Present & Future

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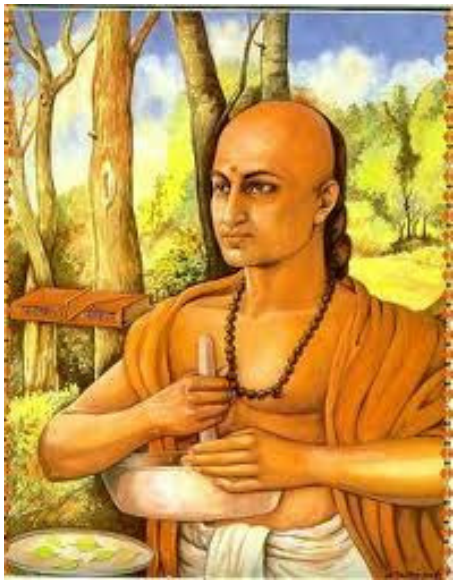
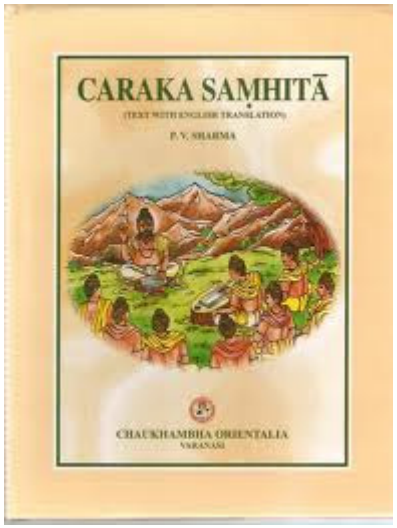
MEDICAL MYCOLOGY

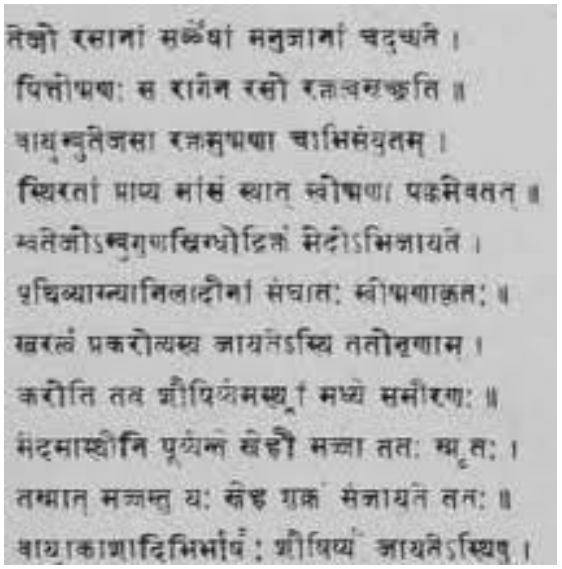
INDIA

Past

3500BC







Mushroom used as food & medicine

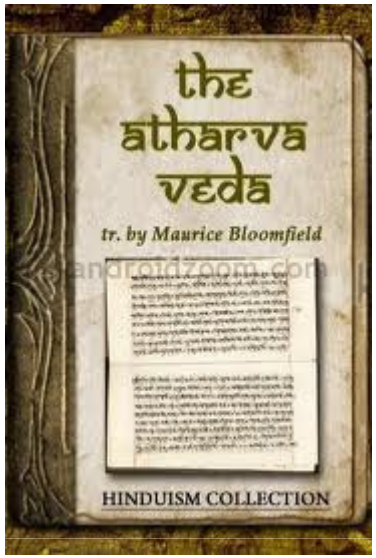
18 - 19th Century

Koenig - got his collection from Tamilnadu

Podaxis pistillaris

Sir J D Hooker – made a collection of fungi from hills of Sikkim-Himalaya

2100 BC



Padavalmika – foot anthill

•Mycetoma was first reported as Madura foot by Dr. John Gill in a dispensary report of Madras Medical Service of British Army in India in 1842

•But, French missionaries described a disease akin to mycetoma in Pondicherry in 1714

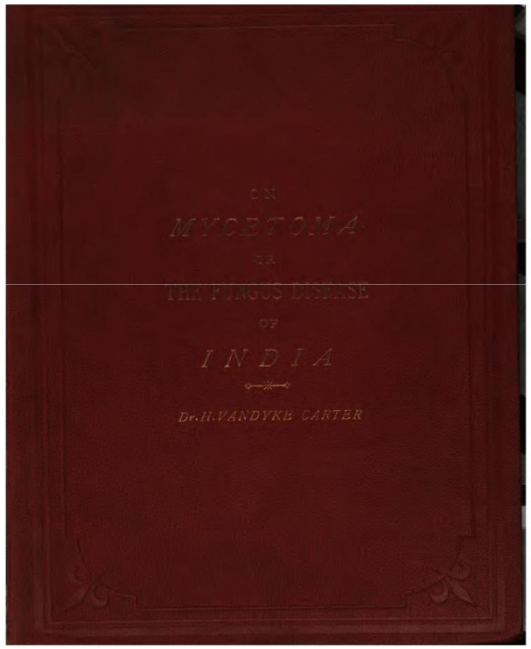
- Godfrey, a surgeon from Bellary in 1846 described mycetoma as ‘morbus tuberculosis pedis’
- **H V Carter** (1874) published the monograph ‘On mycetoma or the fungus disease of India’(J & Churchill) – named mycetoma

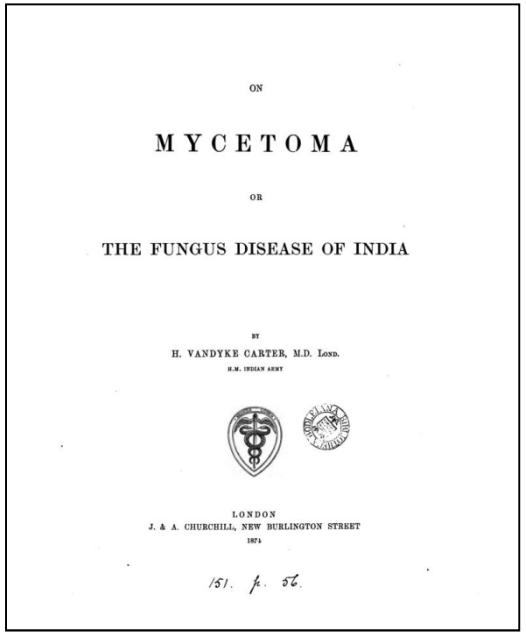
viii PREFACE

acquired. What is made known in the present Memoir, has been elicited at some pains, and by personal effort, under the adverse influences of distant and tropical residence. To those surgeons in India, both European and native, who have aided me with specimens and other help, I hereby tender my best thanks. All published sources of information on practical points, I have carefully acknowledged; and as regards other particulars, such as the structure of ‘Chionyphe C.,’ I should not have hesitated to introduce borrowed illustrations, had it not appeared to me desirable to limit my figures to strictly original views, not hitherto published, and of themselves sufficient to elucidate the text.

Obviously, what has been put forth, can only be very imperfect; and having above referred for solution of certain not irrational doubts, to the [illegible] below displayed and arranged, I should prefer to discussion as to the value of negative or more obscure data, the turning of our attention to such *desiderata* as may be procurable, both in India and elsewhere. For instance:—what are the local conditions, as to soil, water and vegetation, outside the body, under which the two kinds of Mycetoma respectively prevail? Why in one person, the black sort; in another, the pale, shall, in one village, appear side by side? Does this difference depend upon inoculation at a different stage of development of the entophyte? Can botanists tell us under what circumstances fungi and bacteria become interchangeable? And, on the adoption of my views, may not surgeons be able to *prevent* the occurrence of Mycetoma, in much-infected localities?

Then, as concerns the malady itself, it should be well ascertained if it always begins in the same way; precisely, how it spreads in the foot; what its period of incubation; what the conditions of slow or quick growth, within the body. Let the inter- and co-relations of the fungus-particles (entophyta) be elucidated: so let, in all essential details, the correspondence between clinical and natural history of the several varieties of the disease. It is strange, but significant, that these varieties do not co-exist in the foot, and are not, seemingly, connected by intermediate forms: where are the transitional phases that should exist, except upon the view proposed, that even the diverse particles have a common special origin?




ON

MYCETOMA

OR

THE FUNGUS DISEASE OF INDIA

BY

H. VANDYKE CARTER, M.D. Lond.

H.M. INDIAN ARMY

LONDON

J. & A. CHURCHILL, NEW BURLINGTON STREET

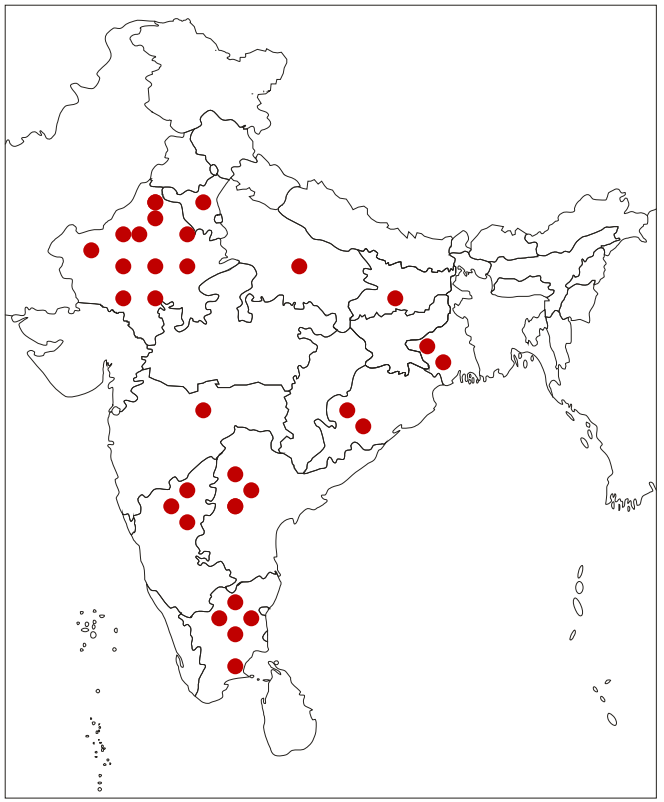
1874

151. f. 56.

elsewhere. For instance:—what are the local conditions, as to soil, water and vegetation, outside the body, under which the two kinds of Mycetoma respectively prevail? Why in one person, the black sort; in another, the pale, shall, in one village, appear side by side? Does this difference depend upon inoculation at a different stage of development of the entophyte? Can botanists tell us under what circumstances fungi and bacteria become

Mycetoma

- Further work on Mycetoma carried by Rustomji (1860), Eyre (1860), H.V. Carter (1874), D. F. Dymock (1881),J. Maitland (1898) in India



Failed study

- With the knowledge of classic study by C. H. Blackley (1873) on hay fever in England - fungus spores/allergens associated with asthma and similar other allergic conditions

- D. D. Cunningham (1873) carried out experiments in the Presidency Jail, Calcutta - correlation between the daily spore content of the air and the incidence of five diseases (plague, dysentery, diarrhoea, dengue and cholera)

‘Ring worm’ & ‘Dhobies itch’

- Powel (1900) described ‘ringworm’ in Assam

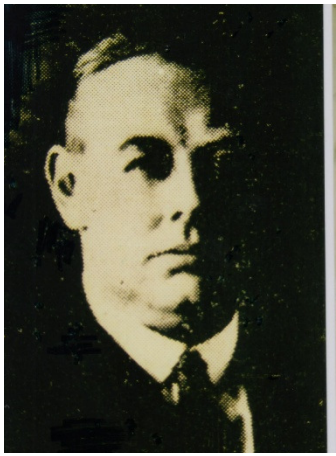
- Castellani in 1905 reported ‘Dhobies itch’, *Epidermophyton being the etiological agent*

Interesting observations

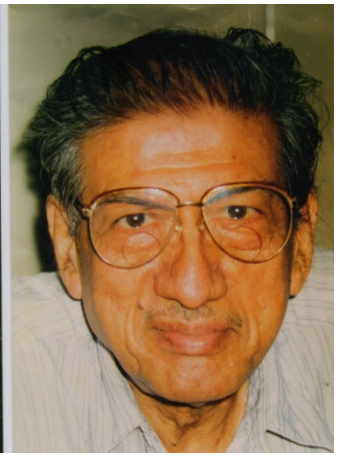
- **Rare** occurrence of ringworm **before puberty**
- Tinea capitis (due to *T. violaceum*) in poor class of men & women (**Coolie itch of purulent folliculitis**)
- **Tinea capitis scarce in the plains of India** (6-7/14,000 cases), mostly imported from hill stations by Anglo-Indians, European & Jewish school children
- **Favus** is common only in **Kashmir & north Punjab**
- Common occurrence of **Tinea imbricata** in India among the **aboriginal tribes in Assam**

School of Tropical Medicine, Calcutta

- Post-first world war, established in 1927
- Separate department of Dermatology & Mycology established in 1931



H W Acton



Niranjan Basu

Maya Sanyal

A Thammayya

School of Tropical Medicine, Calcutta

1926	Acton, McGuire, Panja, Banerjee	-**Red grain mycetoma**, Rx with antimony, Bismuth, X-ray, KI -Culture of *Malassezia ovalis* (Bottle bacillus of Unna) in Petroff's media with 0.005% gentian violet
1928-30	McGuire	-**McGuire stain** -Actinomyces grown on Norri's media -**Growth of *Malassezia* in coconut oil**
1931-33	Maplestone, Dey, Panja, Ghosh	-***Achorion actonii* isolated from favus** -Fungicidal activity of 20 compounds
1942-45	Ghosh	-Antifungal – Nimbeidin -5% glacial acetic acid for prophylaxis of ringworm
1960	Bose	-Perfect stage of dermatophytes -Invasion of human hair
1963-64	Sanyal	-Chorioallantoic membrane for isolation of fungi
1975-95	Sanyal & Thammayya	-***H. capsulatum* from soil** -*C. parvum* from eczematous lesion -White Piedra isolation in India

Important studies

- Rhinosporidiosis – Allen & Dave 1936. The treatment of rhinosporidiosis in man based on the study of 60 cases. Indian Med Gaz. 71: 376-94.
- Tinea capitis – Dey 1953. A review of ringworm of hair in India. Indian Med Gaz 88: 194-6.
- Chromoblastomycosis – Andleigh 1953. Chromoblastomycosis – review with a favourable case. Indian J Med Sci 7: 409-14.
- Pulmonary mycoses – Andleigh 1958. Investigation in the role of fungi in pulmonary diseases in India. Am Rev Tuberculosis 78: 644-6
- Animal to man dermatomycoses - Chakraborty, Ghosh & Banejee 1953. Review on the study of skin disease in animal communicable to man. Indian Med Gaz 88; 152-3.

Stanley Hospital, Madras

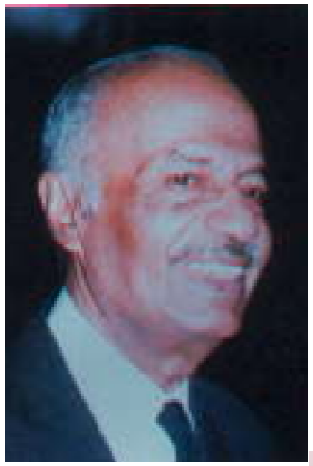
Botany department,
Lucknow University

CDRI, Lucknow

VP Chest Institute, Delhi

CMC, Vellore

PGIMER, Chandigarh



A.S.Thambiah

A.Kamalam

L.N.Mohapatra

Grace Koshi

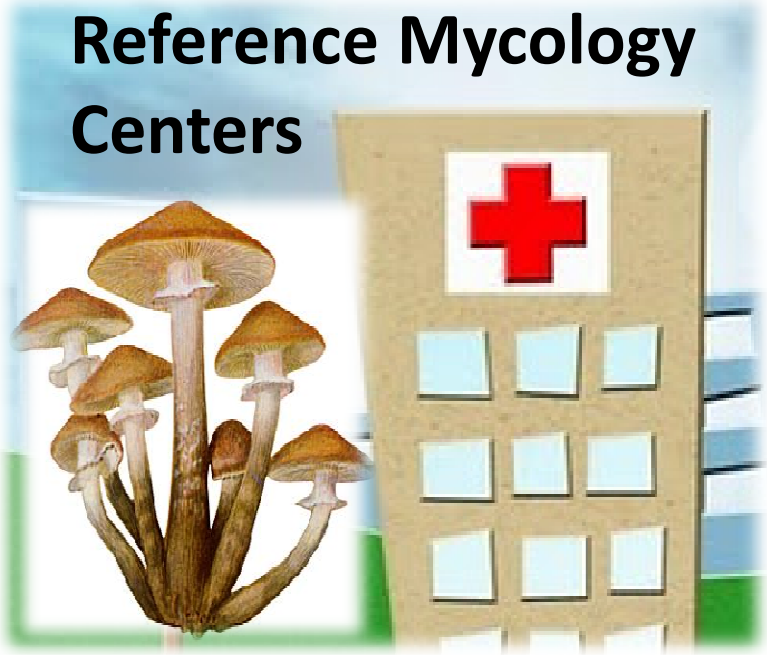
L.R. Dasgupta

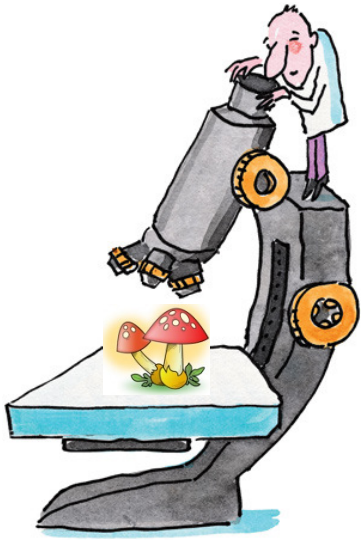
P. Talwar

H.S. Randhawa

Pankaja Laxmi

A.Thammyya





After Retirement
MY-cology Future
DARK…DARK…

The centers crumbled with the retirement of expert

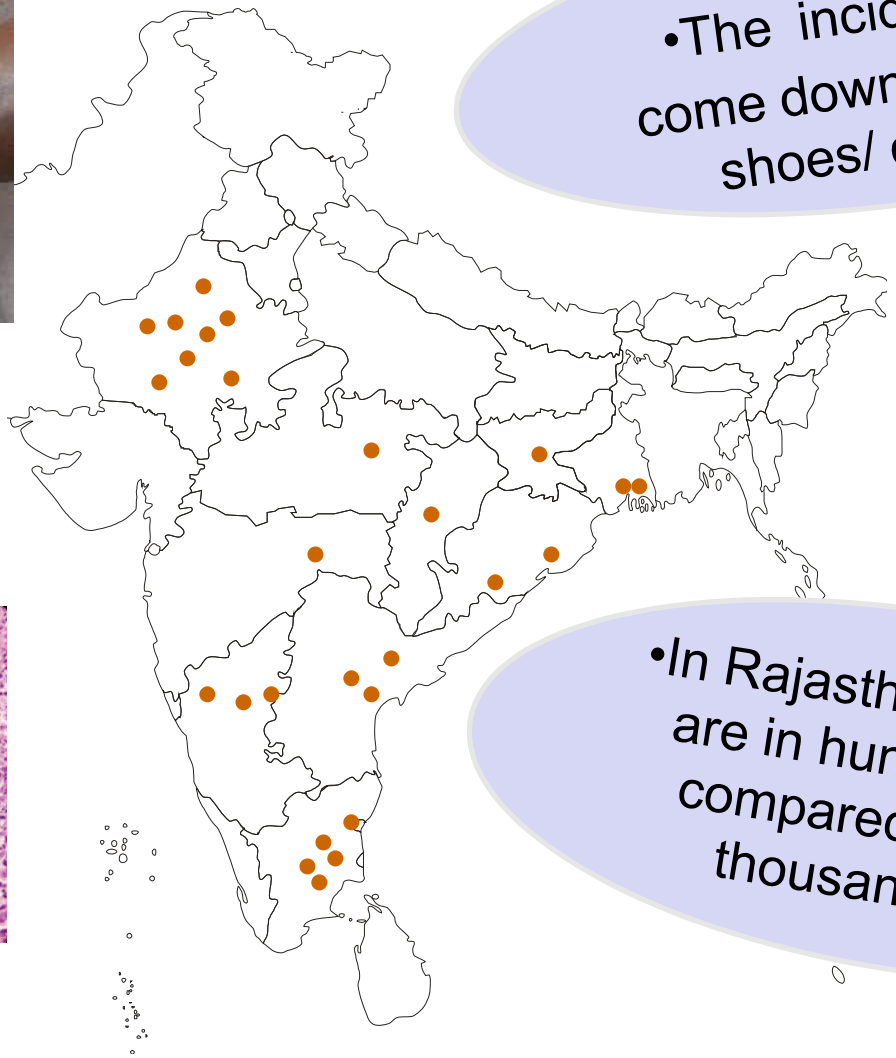
Where is MY
Mycology Lab ?

MEDICAL MYCOLOGY

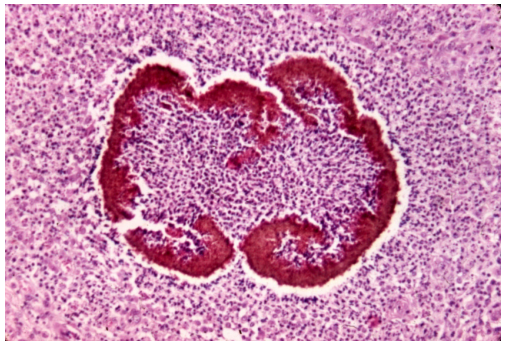
INDIA

Present

Mycetoma in India

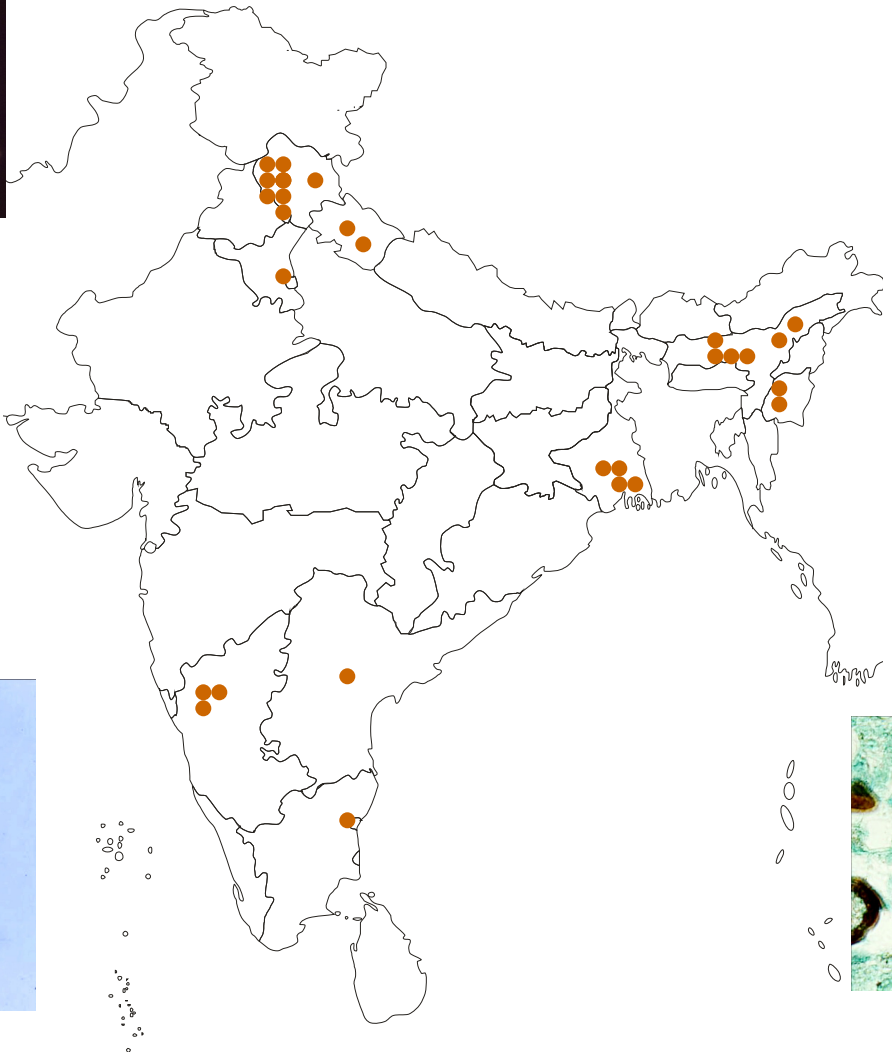


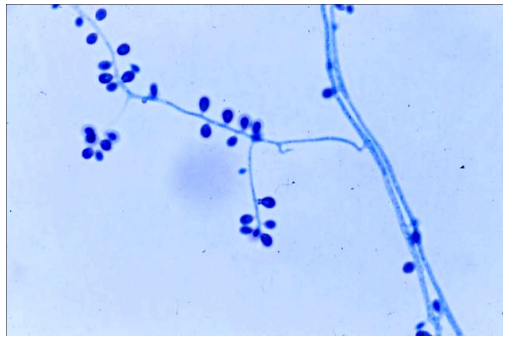
- The incidence has come down after using shoes/ chappals

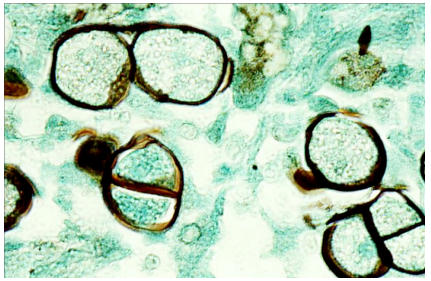


- In Rajasthan the cases are in hundreds/year compared to earlier thousands/year

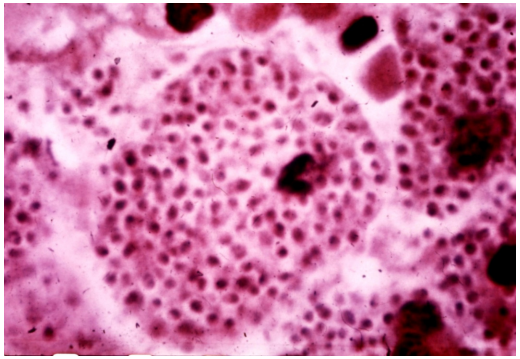
Sporotrichosis in India



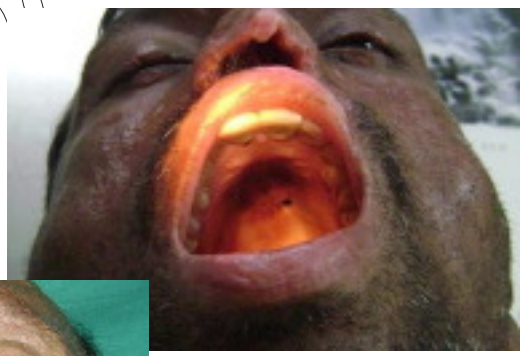




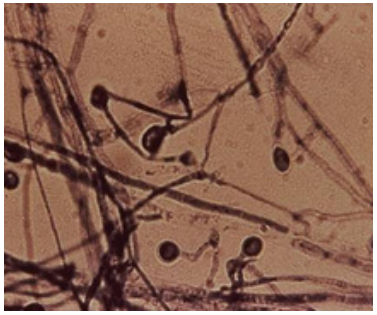
Histoplasmosis in India

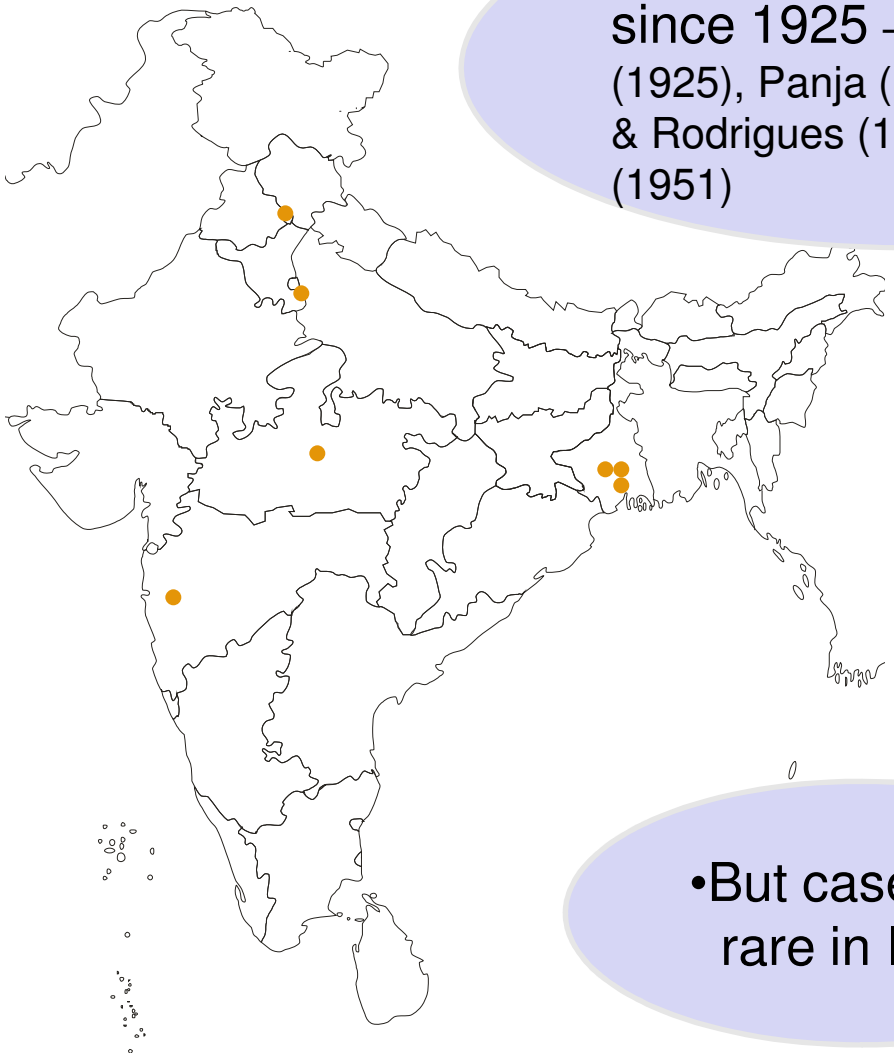


•Case numbers increased only after the advent of HIV infection



Blastomycosis in India





•Cases were detected since 1925 – Ganguli (1925), Panja (1925), de Mello & Rodrigues (1929), Andleigh (1951)

•But cases are rare in India

Penicilliosis in India

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 1999, p. 2699–2702 Vol. 37, No. 8
0095-1137/99/$04.00+0

Indigenous Disseminated *Penicillium marneffei* Infection in the State of Manipur, India: Report of Four Autochthonous Cases

P. NARENDRA SINGH,[1] K. RANJANA,[2] Y. INDIVER SINGH,[1] K. PRIYOKUMAR SINGH,[1] S. SURCHANDRA SHARMA,[3] M. KULACHANDRA,[2] Y. NABAKUMAR,[3] A. CHAKRABARTI,[4] A. A. PADHYE,[5]* L. KAUFMAN,[5] AND L. AJELLO[6]

J Infect. 2002 Nov;45(4):268-71.

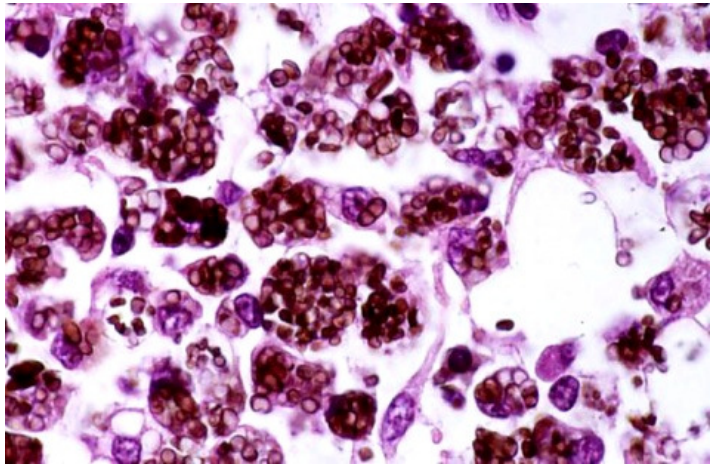
Disseminated Penicillium marneffei infection among HIV-infected patients in Manipur state, India.

Ranjana KH, Priyokumar K, Singh TJ, Gupta ChC, Sharmila L, Singh PN, Chakrabarti A.
Department of Microbiology, J. N. Medical Hospital, Imphal 795001, Manipur, India.

JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 2004, p. 5070–5075 Vol. 42, No. 11
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.11.5070–5075.2004

Role of *Cannomys badius* as a Natural Animal Host of *Penicillium marneffei* in India

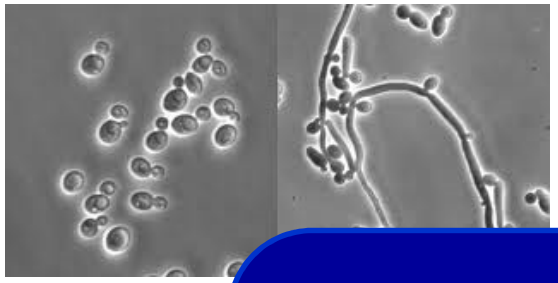
Harish Gugnani,[1] Matthew C. Fisher,[2]* Anubha Paliwal-Johsi,[1] Nongnuch Vanittanakom,[3] Irabanta Singh,[4] and Pratap Singh Yadav[4]

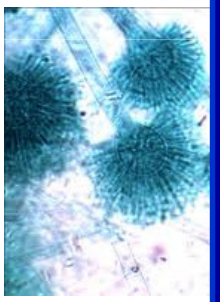


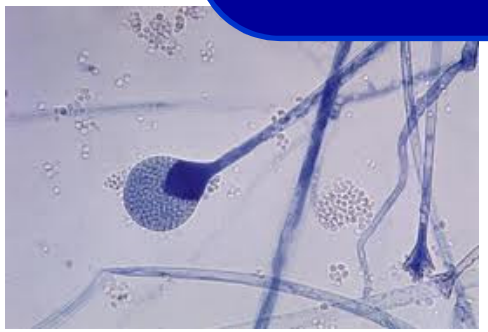
Other endemic mycoses

- Coccidioidomycosis, paracoccidioidomycosis, histoplasmosis duboisii are not endemic in India
- Only imported cases of coccidioidomycois reported

Opportunistic fungal infections







Opportunistic fungi
Include all species from

A (Aspergillus)
To
Z (Zygomycetes)

- **Candidiasis**
- **Aspergillosis**
- **Mucormycosis**

>80%

- Cryptococcosis
- Scedosporiosis, fusariosis
- Trichosporonosis
- **Unusual fungal infections**

Indian subcontinent

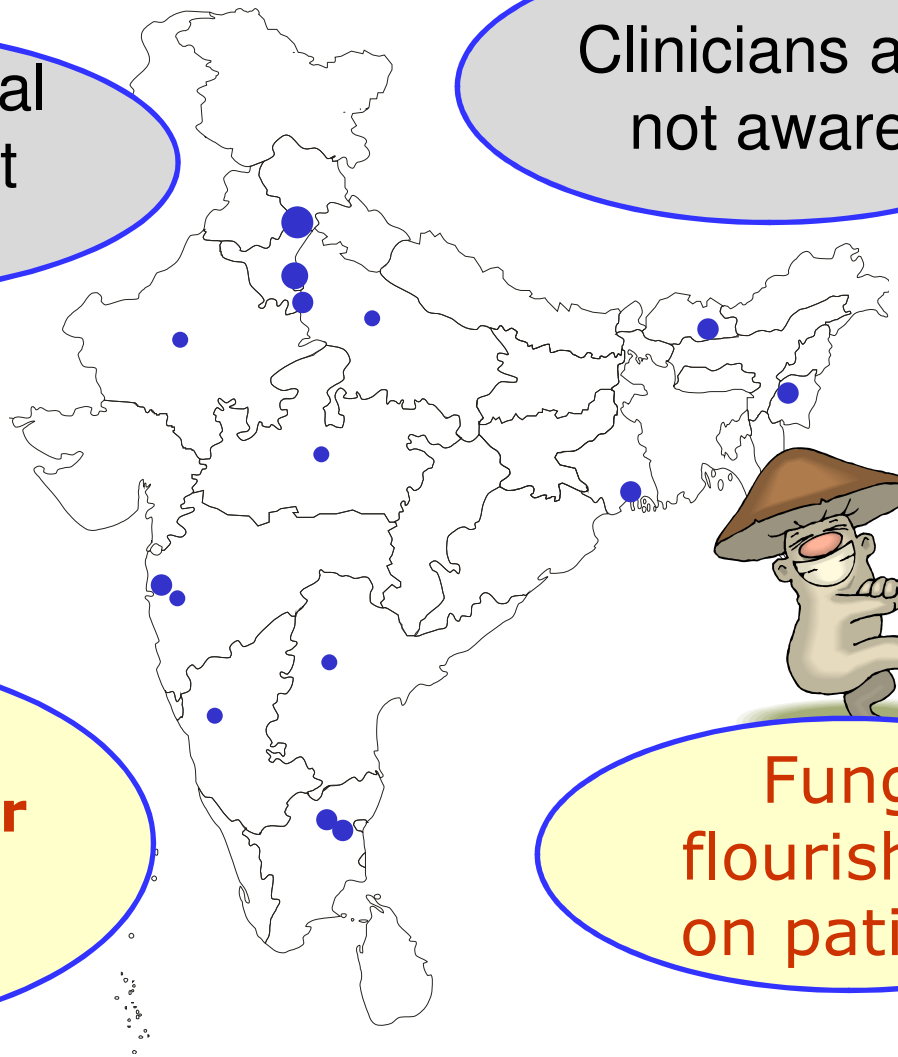
Let's have a party

- Located in tropics, heavy annual monsoon
- HIV infected population – 3-6 million
- Diabetic patients >30 million
- Solid organ & bone-marrow transplant centers are increasing
- Systemic steroids/broad-spectrum antibiotics
  available over the counters, misused by the quacks
- Infection control practices are less than optimal
  - **Fertile ground for fungi to flourish on human**

Few mycology laboratories

Burden of fungal Infection is not known

Clinicians are not aware



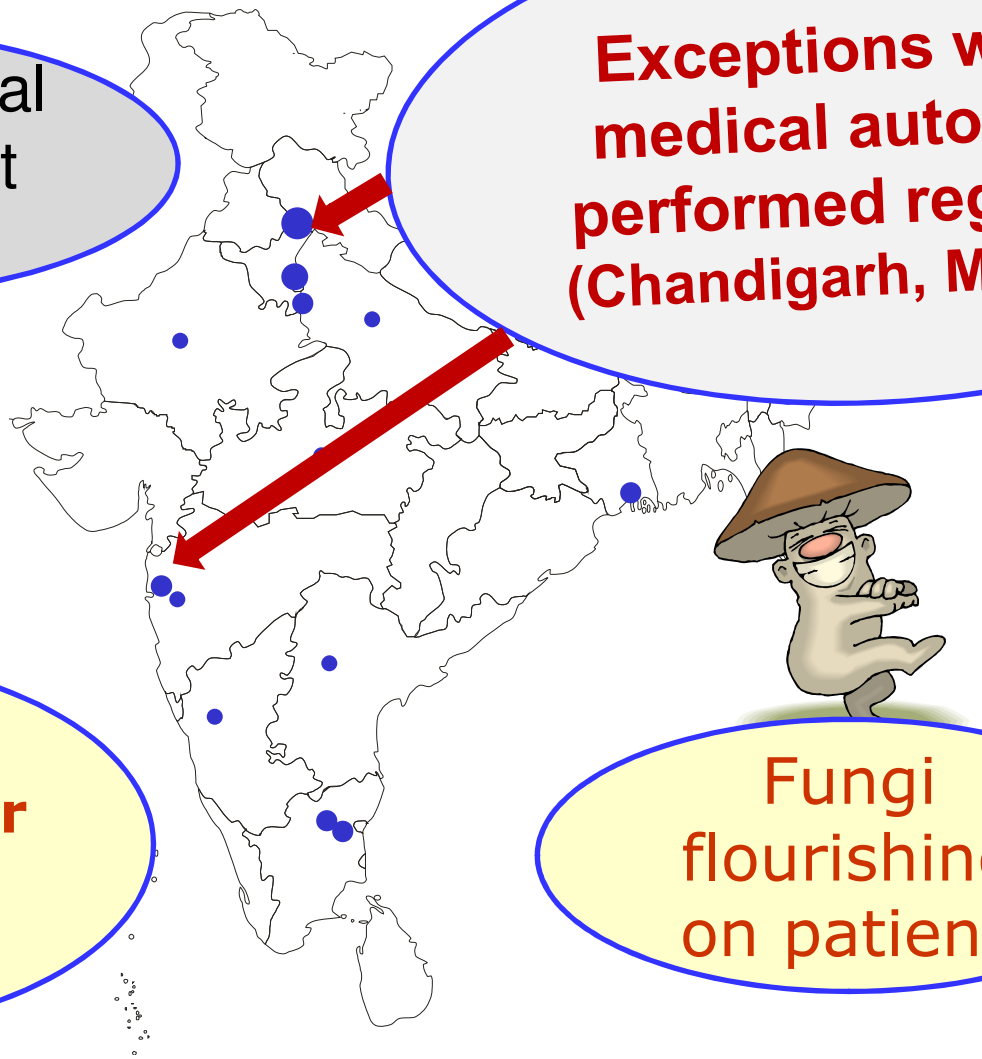
Climate is well suited for fungal infections

Fungi flourishing on patients

Few mycology laboratories

Burden of fungal Infection is not known

Exceptions where medical autopsies performed regularly (Chandigarh, Mumbai)



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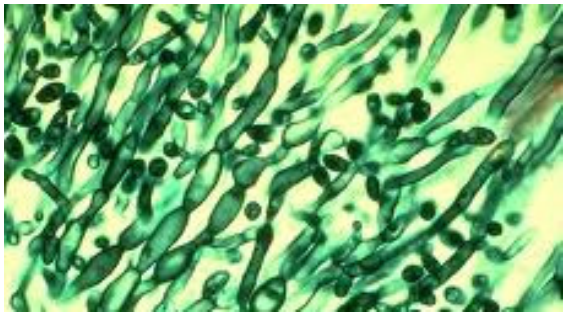
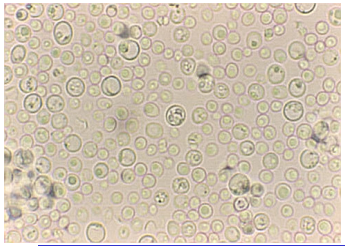


Invasive candidiasis

- Incidence very high - ~400 cases/year in 1600 bedded tertiary care center in India (compared to candidemia in Australia ~300 cases/year)
- Incidence – 1-12/1,000 admissions (compared to 0.09-0.36/1000 admissions)
- Non-*albicans Candida* spp. – (46-95%)
- *C. tropicalis* commonest among NAC spp
- Many outbreaks due to unusual *Candida* spp.

Whatever happens in India – happens in large number

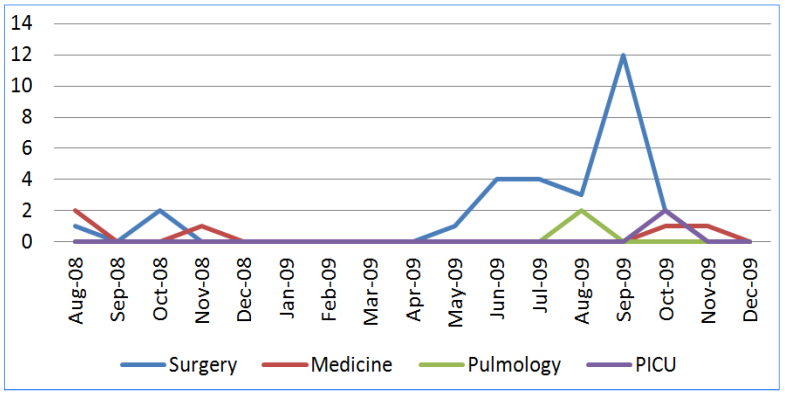


Pichia anomala outbreaks

Series	Place of outbreak	No. of patients	Type of patients
Murphy *et al.*, 1986	Liverpool, UK	8	Pediatric
Yamada *et al.*, 1995	Japan	4	Pediatric
Thuler *et al.*, 1997	**Rio de Janeiro, Brazil**	**24**	**Pediatric**
Chakrabarti *et al.*, 2001	**Chandigarh, India**	**379**	**Pediatric**
Aragao *et al.*, 2001	**Sao Paulo, Brazil**	**8**	**Pediatric**
Kalenic *et al.*, 2001	Croatia	8	Adult
Mestroni *et al.*, 2003	**La Plata, Argentina**	**4**	**Adult**
Pasqualotto *et al.*, 2003	**Brazil**	**17**	**Pediatric**
Kalkanci *et al.*, 2010	**Ankara, Turkey**	**4**	**Pediatric**

Outbreaks of unusual fungemia in India

- ***Pichia anomala***
- ***Kodamaea ohmeri***
- ***Candida haemulonii***
- ***Pichia fabianii***



- *C. guilliermondii*
- *C. lusitaniae*
- *C. dubliniensis*
- *C. inconspicua*
- *C. famata*
- *C. rugosa*
- *C. norvegensis*

Candida haemulonii

- From Sir Ganga Ram Hospital – *C. haemulonii* (15.5%) of all candidemia cases (Dr. Wattal – personal communication)
  - Sensitivity – AMB – 28%, FLU – 0%, ITR – 0%, VOR – 64%
  - Extremes of age, central line, mechanical ventilation, malignancy are significantly associated
- Then from Max hospital – 14 cases of *C. haemulonii* fungemia reported (Dr. Omender & Bansidhar – p. communication)
- Now PGIMER, Chandigarh – multiple cases; MIC_{50} – AMB – 16µg/ml, FLU – 64, ITR – 4, VOR – 8
- We need to study the molecular epidemiology of *C. haemulonii* fungemia in India

Drug resistance in Candida strains

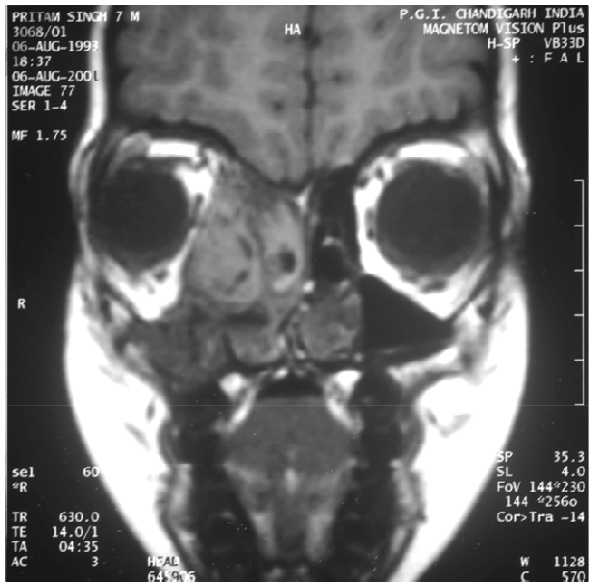
species	Fluconazole			Voriconazole			Itraconazole			Caspofungin		
	S	SDD	R (%)	S	SDD	R (%)	S	SDD	R (%)	MIC <0.125 mg/L	MIC 0.125-1mg/L	MIC >0.1 mg/L
C. albicans	**13**	**1**	**2(13)**	**13**	**0**	**3(19)**	**13**	**1**	**2(13)**	**16**	**0**	**0**
C. tropicalis	**51**	**2**	**6(10)**	**52**	**1**	**6(10)**	**51**	**0**	**8(14)**	**56**	**1**	**2**
C. glabrata	3	0	1(25)	3	0	1(25)	3	0	1(25)	4	0	0
C. guilliermondii	32	1	1(3)	32	1	1(3)	32	1	1(3)	34	0	0
C. pelliculosa	17	3	0	20	0	0	19	0	1(5)	20	0	0
C. parapsilosis	1	0	0	1	0	0	1	0	0	1	0	0
C. krusei	2	0	0	2	0	0	2	0	0	2	0	0
C. ustus	1	0	0	1	0	0	1	0	0	1	0	0
T. asahii	3	0	0	3	0	0	3	0	0	1	1	1
Total	123	7	10 (7)	127	1	12 (9)	126	1	13 (9)	135	2 (1)	3 (2)

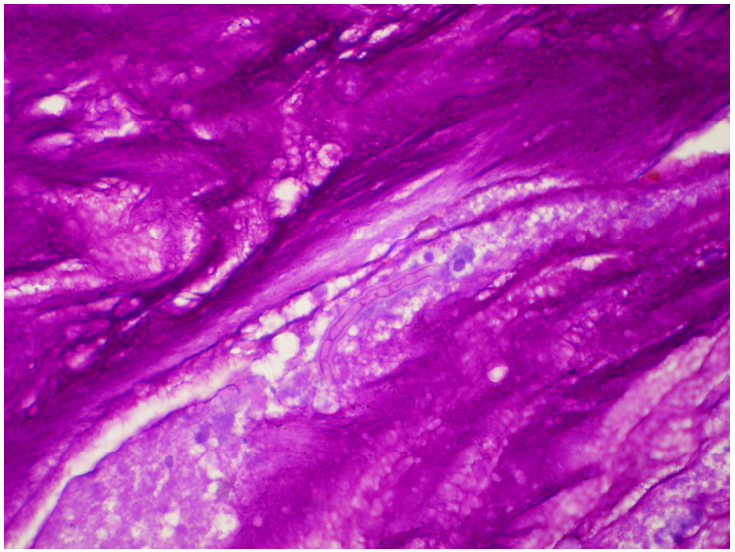
Scand J Infect Dis 2009; 41: 275-284

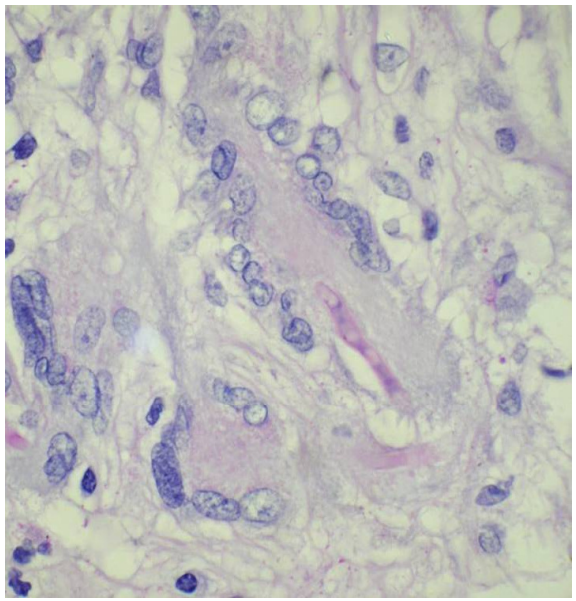
Invasive aspergillosis in India -certain peculiarities

- The incidence is expected to be high
  - Below optimal hospital care practice, **continuous hospital renovation work**, overuse/misuse of steroids, contaminated infusion set/fluid
- The disease also occurs in so called **immuno-competent host (6-14%)**
  - ↑*Aspergillus* spore count (>12X10^6/m^3)
- ***A. flavus*** more prevalent in eye & fungal sinusitis

Fungal rhinosinusitis

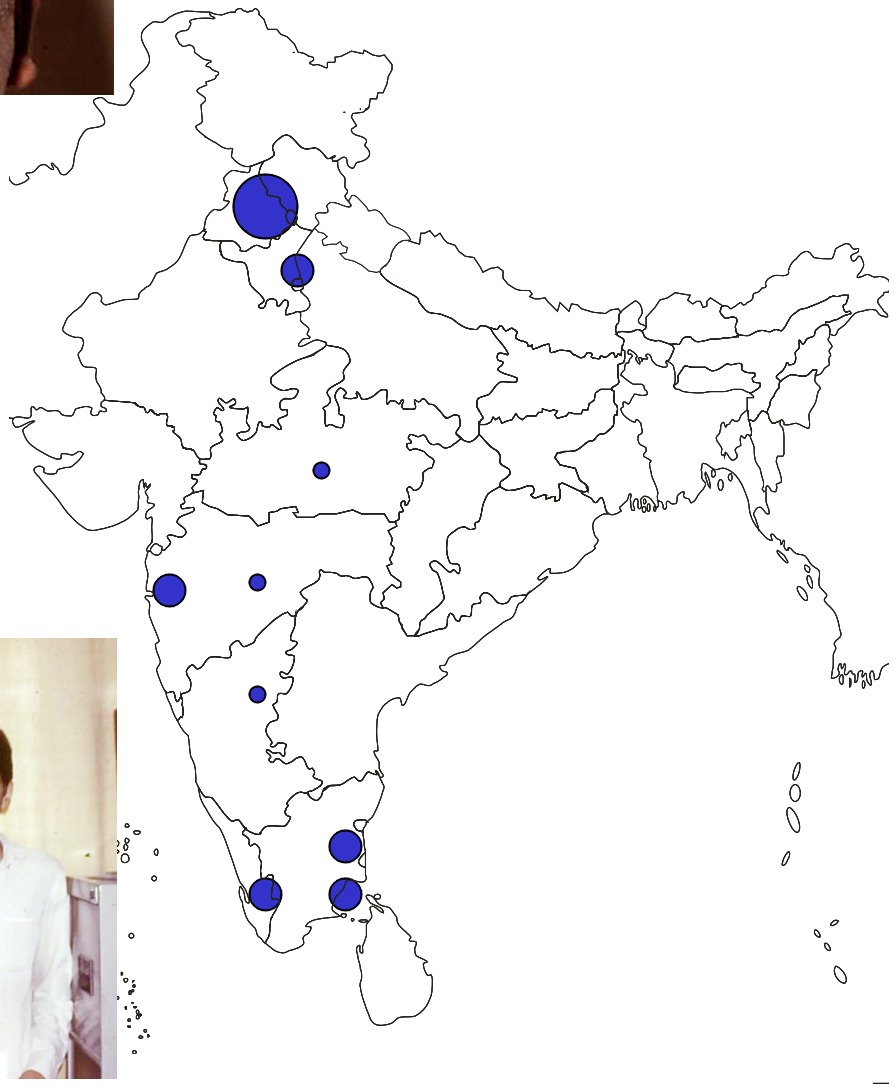




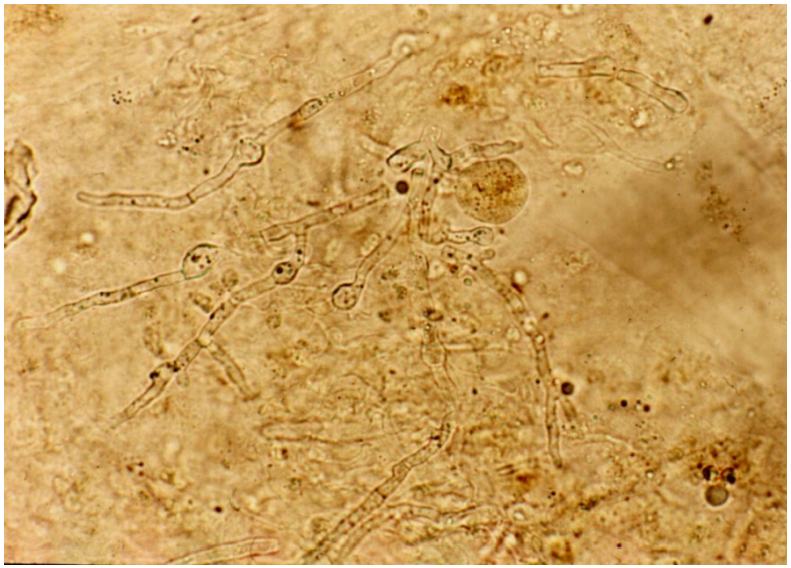


- Common disease in India
- Immunocompetent patient with proptosis
- *Aspergillus flavus* is the commonest isolate (~90%)

Fungal rhinosinusitis in India

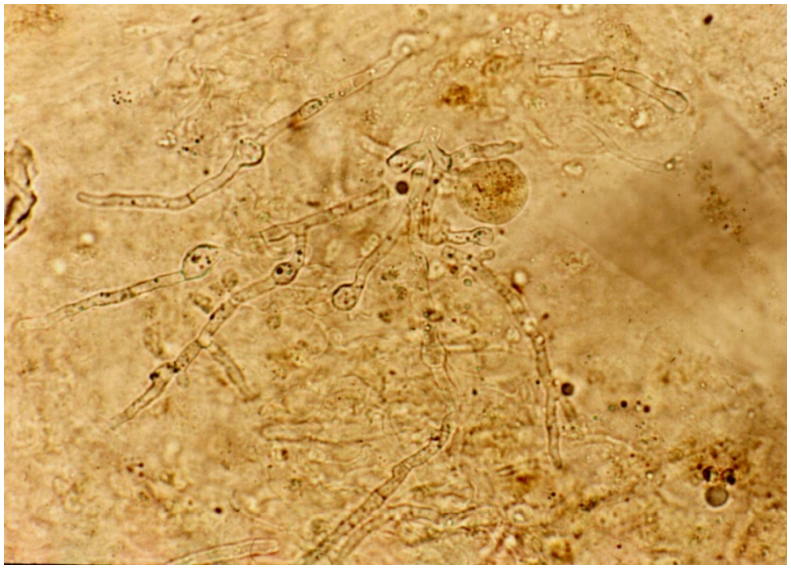


Fungal eye infections (keratitis & endophthalmitis)



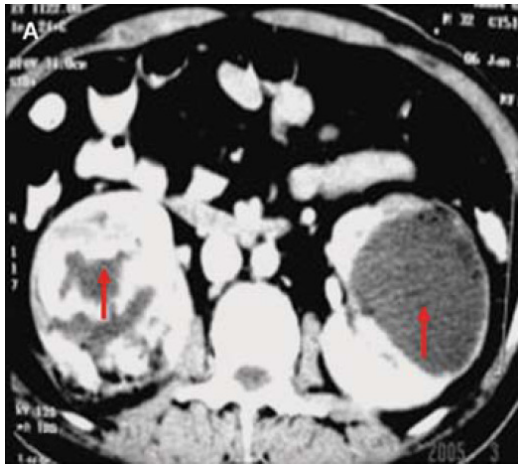
- 139 mycotic keratitis in 3-months in Madurai (Br J Ophthalmol, 1997)
- In contrast, 125 patients in 10-year in south Florida (Cornea, 2000)
- 24 patients in 9-year in Philadelphia (Ophthalmology, 1994)
- Keratitis – *Aspergillus flavus* & *Fusarium* spp. equally found
- Endophthalmitis – *Aspergillus flavus* commonest

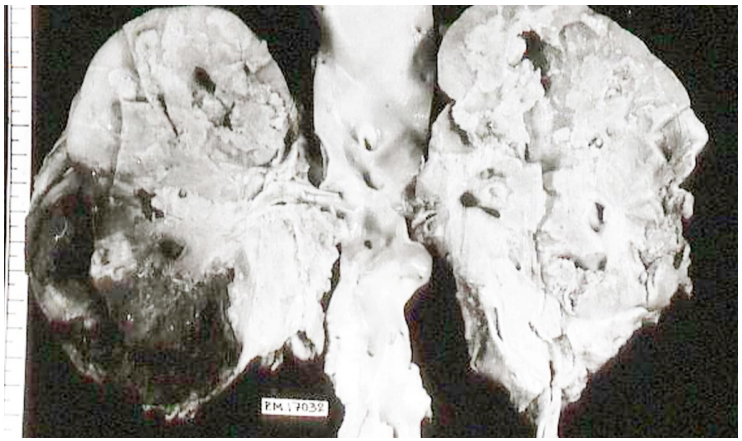
Fungal eye infections



Fungal endophthalmitis after a single intravenous administration of presumably contaminated dextrose infusion fluid Retina 2000; 20: 262-268

Mucormycosis in India





- 1990-1999 - 129 – 13/y
- 2000-2004 - 178 – 36/y
- 2006-2007 - 75 – 50/y

J Infect 2001; 42: 261
Med Mycol 2006; 44: 335
Postgrad Med J 2009; 85: 573

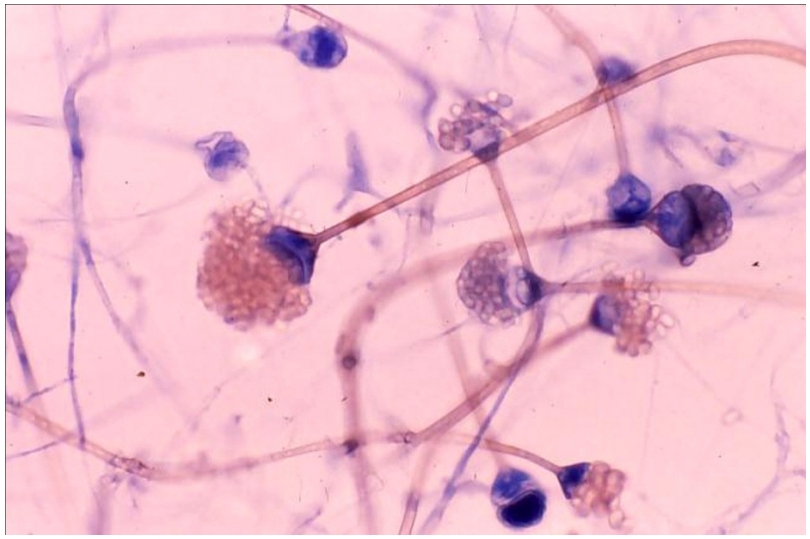
- Very high incidence
- Rising trend in association with uncontrolled diabetes mellitus
- Emergence of isolated renal zygomycosis
- Emergence of *Apophysomyces elegans, Saksenaea vasiformis, Rhizopus homothallicus*

Indians are fond of sweets

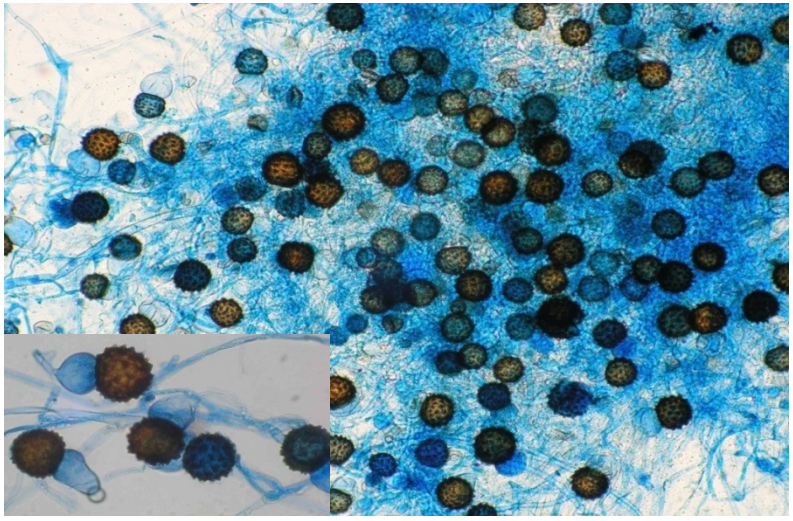
- >30 million diabetics live in India
- Compliance to anti-diabetic therapy is also poor
- 23% patients in our study were ignorant of underlying diabetes before reporting with zygomycosis in our hospital

Saksenaea vasiformis

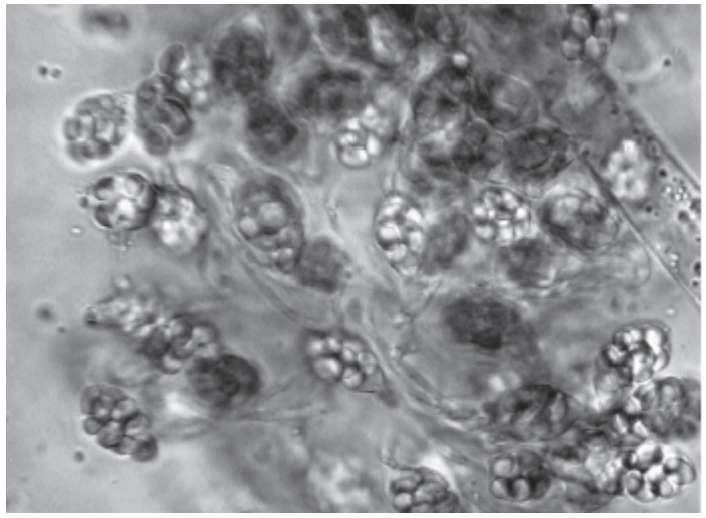
Apophysomyces elegans



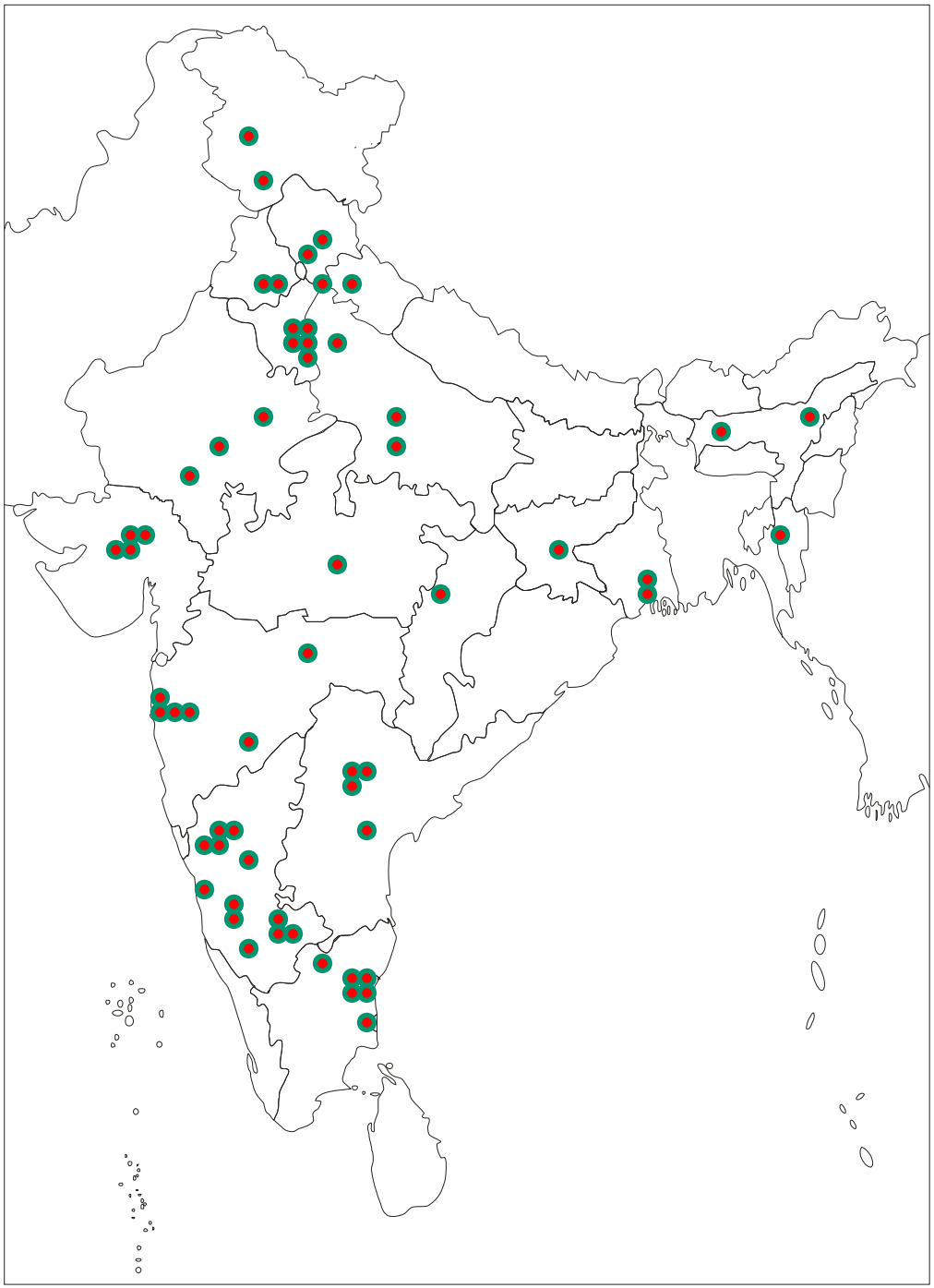
Rhizopus homothallicus



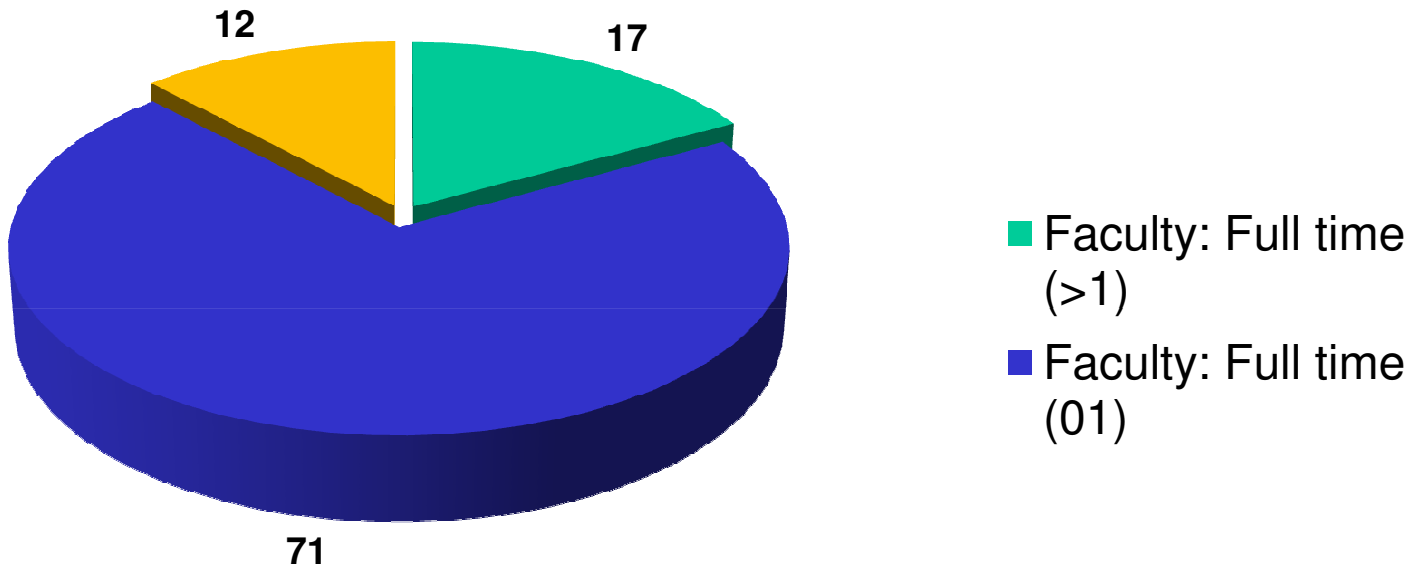
Thamnostylum lucknowense



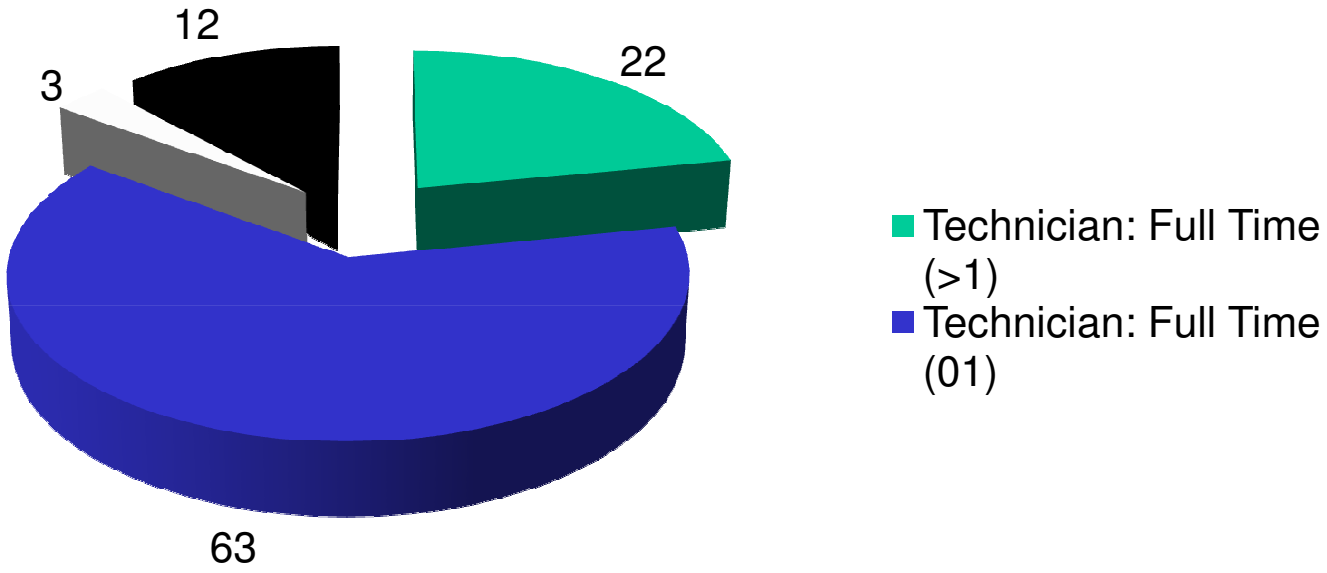
Diagnostic Mycology Setup in 71 Institutes across India



Faculty Posted in Mycology Laboratory (%)



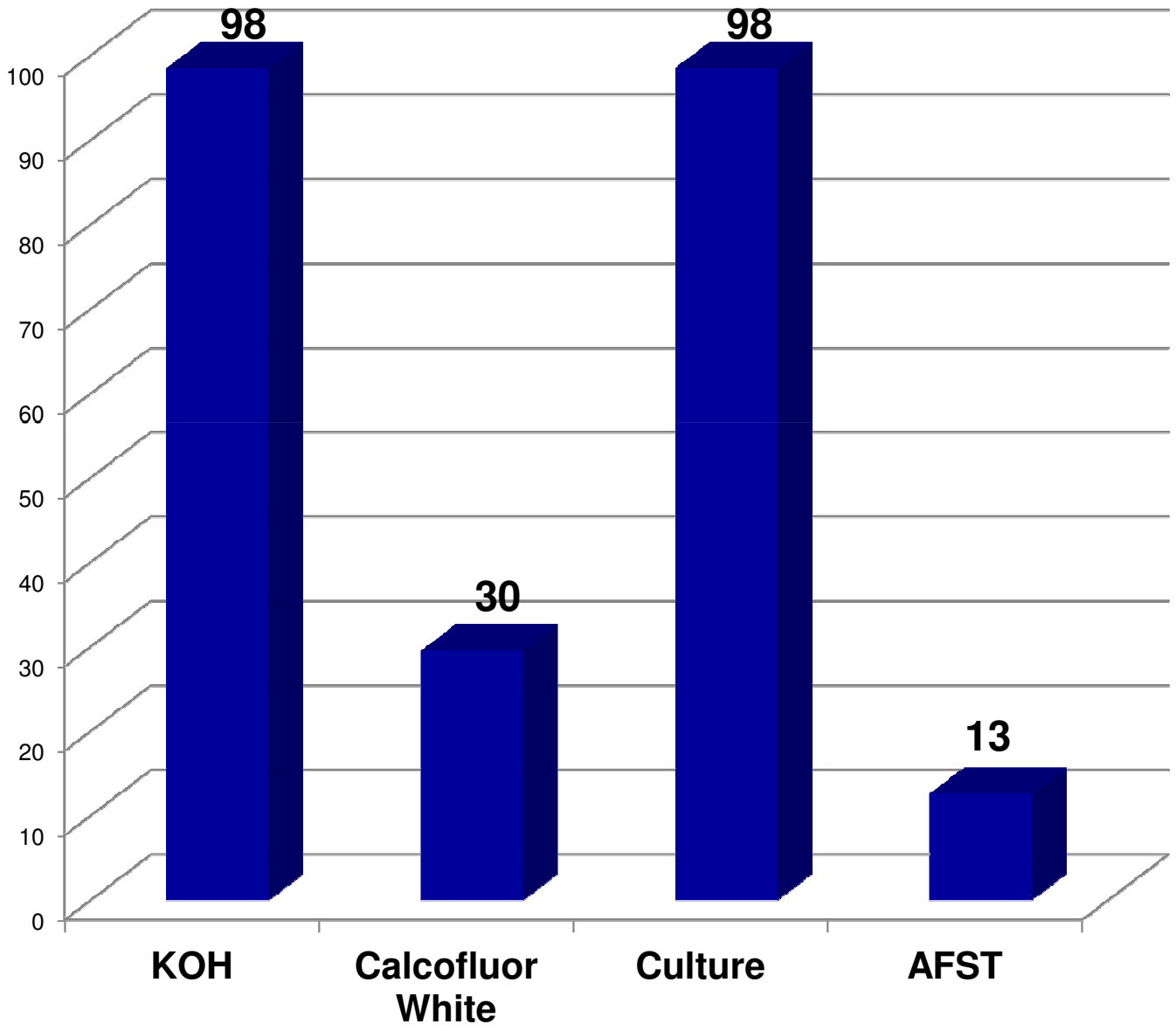
Technicians Posted in Mycology Laboratory (%)



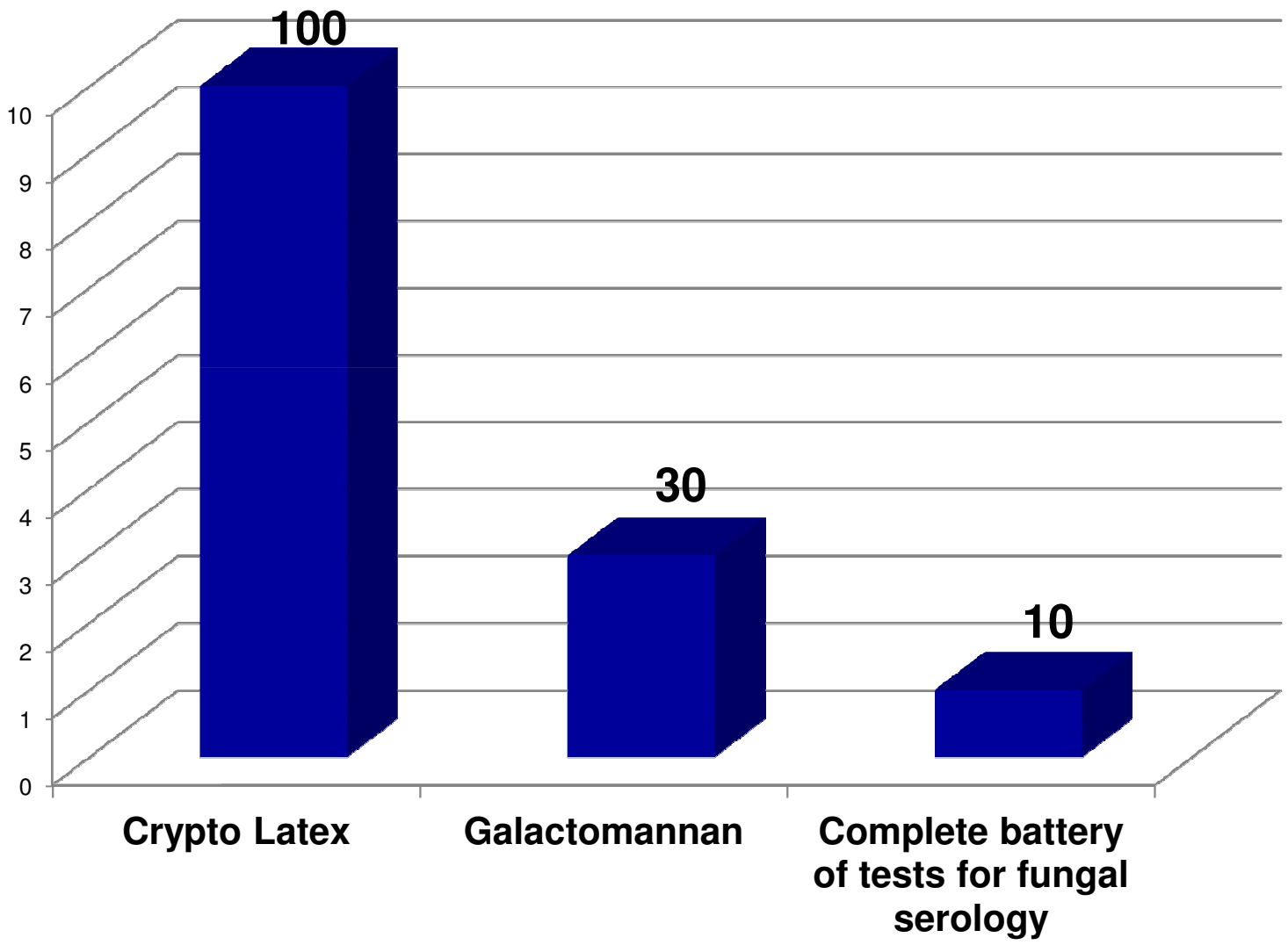

Doctor what is the diagnosis ? Any fungal infection ?
Sorry Dear ! We don't have any mycologist.

Very few people are concerned !

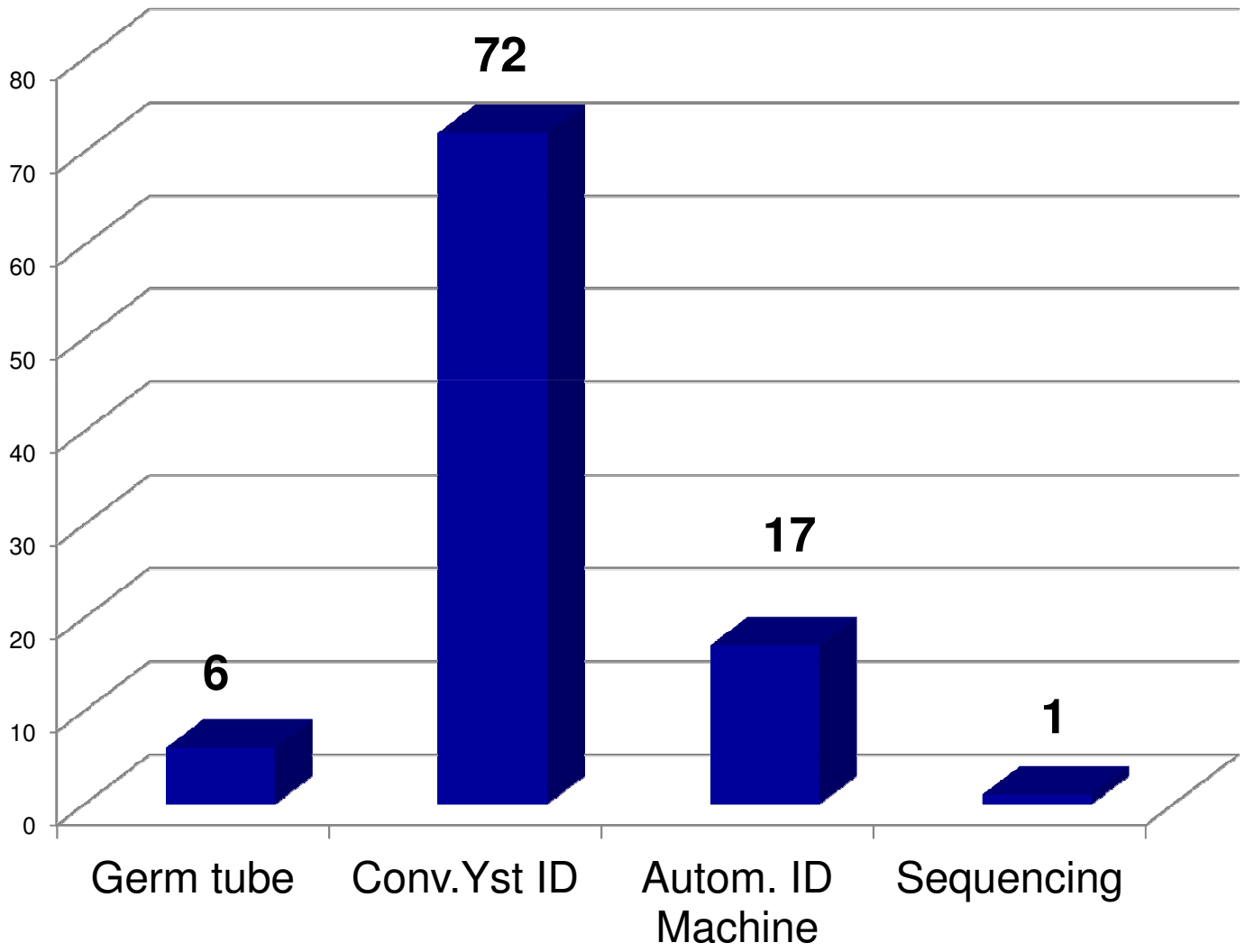
Conventional Diagnostic Tests (%)



Fungal Serology (%)



Level of Yeast Identification(%)



MEDICAL MYCOLOGY

INDIA

FUTURE

Silver lining

- **Society for Indian Human & Animal Mycologists**
- **SIHAM candidemia and zygomycosis network**
- **DBT initiated consortium research plan**
- **Center of Advance Research in Medical Mycology (ICMR)**
- **Culture Collection for Pathogenic Fungi (ICMR)**
- **Working groups – ‘fungal sinusitis’, ‘ABPA in asthmatics’**
- **Fungal Working Group of India**

Society for Indian Human & Animal Mycologists (SIHAM)

- Established in 1995 with great efforts from Dr. S M Singh & 16 founder members
- Affiliated to ISHAM
- Organizes National Conferences every two years
- Continuously trying to improve - discipline ‘Medical Mycology’

Candidemia network

Centre of Advanced Research (CAR) in Medical Mycology (ICMR)

Postgraduate Institute of Medical Education & Research
Chandigarh – 160012, India

National Culture Collection of Pathogenic Fungi (ICMR)

Postgraduate Institute of Medical Education & Research
Chandigarh – 160012, India

Training courses

- Twice a year at PGIMER, Chandigarh – summer for faculty, winter for technician
- Once a year – Sri Ramchandra University (Chennai)
- Many more small training course round the year

Future need

- Diagnostic mycology lab. In every tertiary center
- Modification of mycology course in medical graduation curriculum
- Awareness program through CME/workshop/conferences
- Training program in the other two corners of the country
- Mycology research
  - Systematic epidemiology study
  - Consortium research (including basic scientists, medical mycologists, clinicians to develop bridge) especially on unique fungi prevalent in India (*C. tropicalis, A. flavus, zygomycetes*)
  - Rapid & early diagnosis of fungal infections
  - Development of specific management guidelines for our country