MYCOSIS FUNGOIDES PROGNOSIS AND MANAGEMENT.

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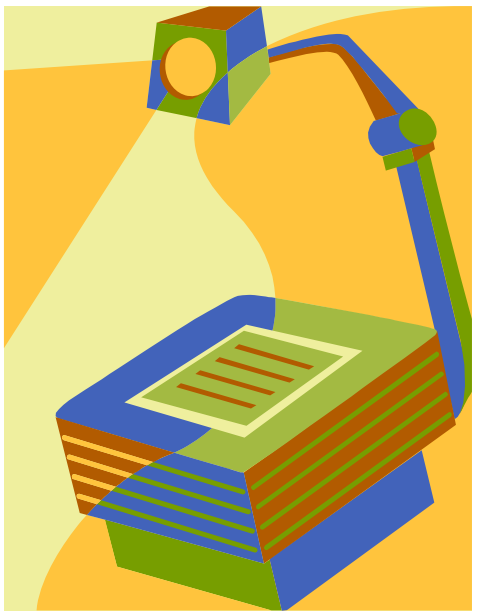
FIGURE 1.—Drawing of first and only case of MF seen by Jean Louis Alibert (180

Introduction

- Case presentation.
- History.
- Staging.
- Prognosis.
- Management
  - Topical HN2
  - PUVA
  - TSEB
    - Rad. Physics
    - Rad. Biology.
- Conclusions.



Case presentation

- 57 year old women
  - blotchy skin over ant. CW with associated itchiness. Bx. + for MF, received topical tx without improvrmrnt. Received 41 treatments of PUVA between 1993 and 1998 with progression of dz. In 8/98 pt. presented to NCI/NIH with c/o generalized pruritis and diffuse skin papules and plaques.
  - No h/o viral infection, exposure to petrochemicals.
  - No family h/o MF.

Case presentation

- On P/E
  - Skin - generalized thickened, dry scally diffuse papules/plaques.
  - LN - no lymphadenopathy.
  - Abd - no organomegaly.

- Lab - no atypical mononuclear cells in PB, HIV neg.
- Skin bx + dense mononucclear atypical lymphoid cell infiltrate in the upper half of the dermis.
- CT chest/abd/pelv neg. for LN/visceral involvement.

⌘ **Dx - MF/CTCL T2N0M0, IB progressive and refractory to PUVA.**

Questions

- What is the prognosis of this pt?
- What is her management?

History

- First MF described in 1806 by Dr. Alibert.
  - Brawny desquamated rash
  - small skin tumors
  - purulent discharg
  - high fever/expired.

FIGURE 1.—Drawing of first and only case of MF seen by Jean Louis Alibert (180

History

Yr	Author(s) and ref No.	Finding
1806	Alibert (1)	Original description
1870	Bazin (3)	3 classic cutaneous stages
1885	Vidal and Brocq (4)	D'emblée variant
1892	Bresnier and Hallopeau (5)	Erythrodermic variant
1938	Sézary et al (6)	Leukemic variant with erythroderma
1968	Lutzner and Jordan (8)	Ultrastructural description of Sézary cell
1970	Crossen et al (15)	Lymphocyte properties of abnormal cell
1973	Brouet et al (16) and Broome et al (17)	T-cell nature of abnormal cell
1970–1973	Crossen et al (15) and Lutzner et al (14)	Abnormal cytogenetics
1972–1973	Epstein et al (32) and Fuks et al (30)	Appreciation of prognostic factors
1974	Long and Mihm (26) and Rappaport and Thomas (27)	Description of extracutaneous MF

Baunn and Lamberg 1979

NCI-VA committee report on CTCL staging.

- **Stratification of pts according to prognosis/used for selection of primary tx.**

Table 1. TNMB Classification for Mycosis Fungoides

T (Skin)	
T1	Limited patch/plaque (<10% of total skin surface)
T2	Generalized patch/plaque (≥10% of total skin surface)
T3	Tumors
T4	Generalized erythroderma
N (Nodes)	
N0	Lymph nodes clinically uninvolved
N1	Lymph nodes enlarged, histologically uninvolved (includes "reactive" and "dermatopathic" nodes)
N2	Lymph nodes clinically uninvolved, histologically involved
N3	Lymph nodes enlarged and histologically involved
M (Viscera)	
M0	No visceral involvement
M1	Visceral involvement
B (Blood)	
B0	No circulating atypical (Sézary) cells (<5% of total lymphocytes)
B1	Circulating atypical (Sézary) cells (≥5% of total lymphocytes)

Table 2. Clinical Staging System for Mycosis Fungoides

Clinical Stages	TNM Classification*		
	T	N	M
IA	T1	N0	M0
IB	T2	N0	M0
IIA	T1-2	N1	M0
IIB	T3	N0-1	M0
IIIA	T4	N0	M0
IIIB	T4	N1	M0
IVA	T1-4	N2-3	M0
IVB	T1-4	N0-3	M1

**The "B" classification does not alter the clinical stage.*

Baunn and Huberman 1980 Staging

- 1976-1978, 49 MF pts prospectively evaluated for staging.
- Special procedures- cytogenetics/cycology, e microscope. **Reslts**:

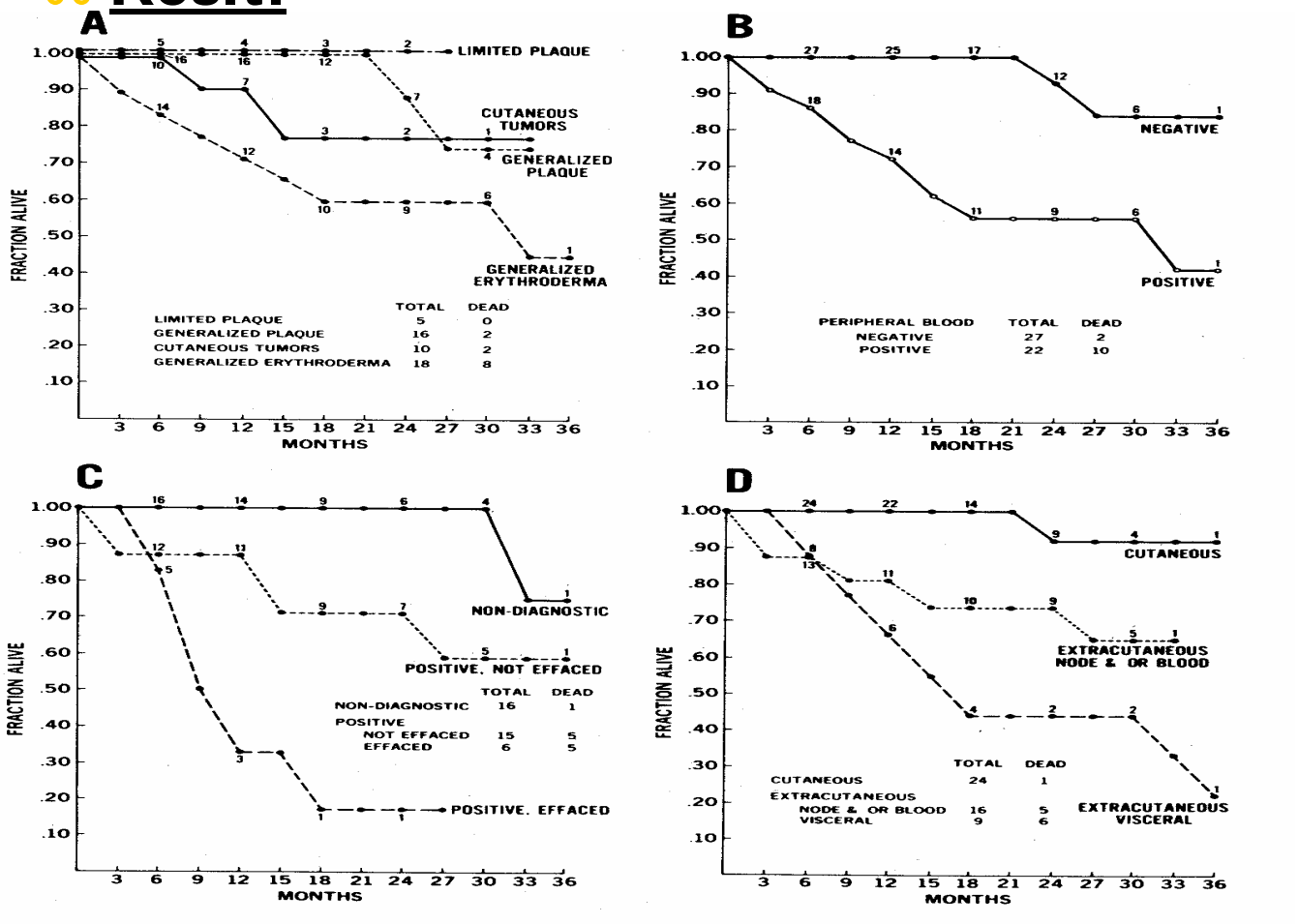
able 4. Association of Skin Type with Frequency of Extracutaneous Disease Determined by Light Microscopy and Special Studies

	Cutaneous Stage				Total
	Limited Plaque	Generalized Plaque	Tumors	Generalized Erythroderma	
Light microscopy					
Peripheral blood involvement	0/5*	1/16	3/10	18/18	22/49
Lymph node involvement	0/5	3/16	4/10	14/18	21/49
Visceral involvement	0/5	1/16	2/10	6/18	9/49
Total	0/5	3/16	4/10	18/18	25/49
Special studies†					
Peripheral blood involvement	3/5	11/15	6/9	18/18	38/47
Lymph node involvement	0/2	8/8	7/9	14/14	29/33
Total	3/5	14/16	8/10	18/18	43/49

* Number positive/number tested.
† Cytogenetic analysis, electron microscopy, and T-cell cytology.

Baunn and Huberman 1980 Staging

⌘ Reslt:



Cocnl:

- survival was directly related to the type of skin involvement, and the presence or absence of extracutaneou s dz.
- Recent TNM staging system is useful.

Kim and Lourdes 1976/MSKCC TSEB/Rad. Biology

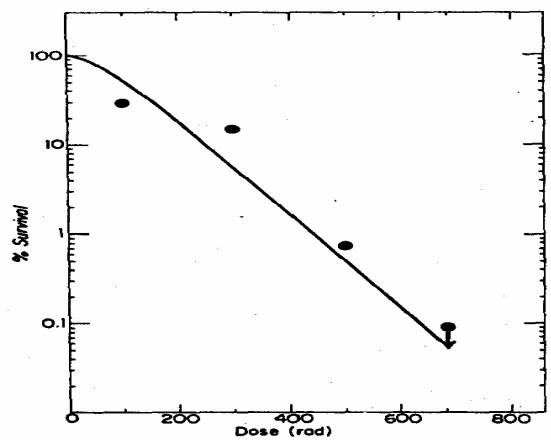
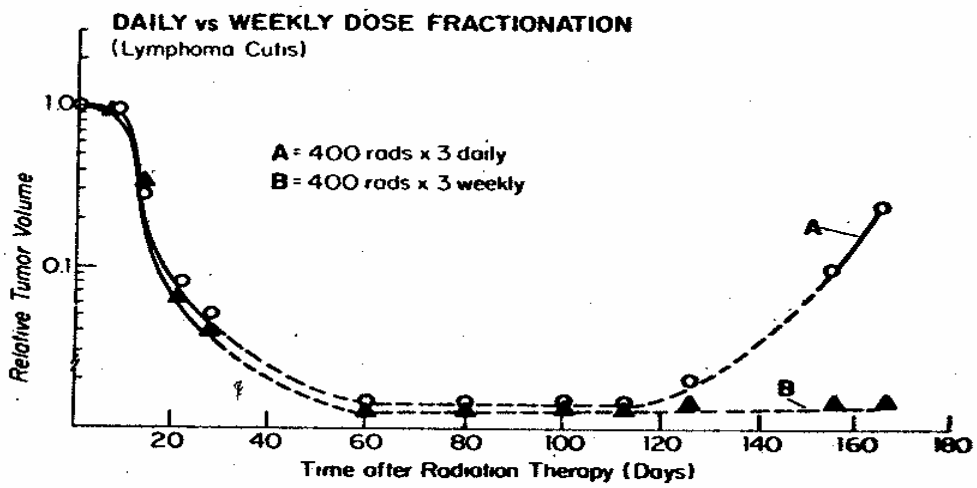


Fig. 4. The cell survival curve of lym-



- D0 = 90 cGy, N < 2.
- Large component of alpha.
- a/b ratio high.

- **Concl:**
  - Disease free interval is dose depended, similar remmission with same dose.
  - Weekly dose fractionation regimen is superior.

Hoppa and Cox 1979/Stanford TSEB

- 1966 - 1977, 141 MF pts txed with TSEB 20 - 40 Gy.
- Adjuvant HN2 in adverse prognostic group.
- **Reslts:**

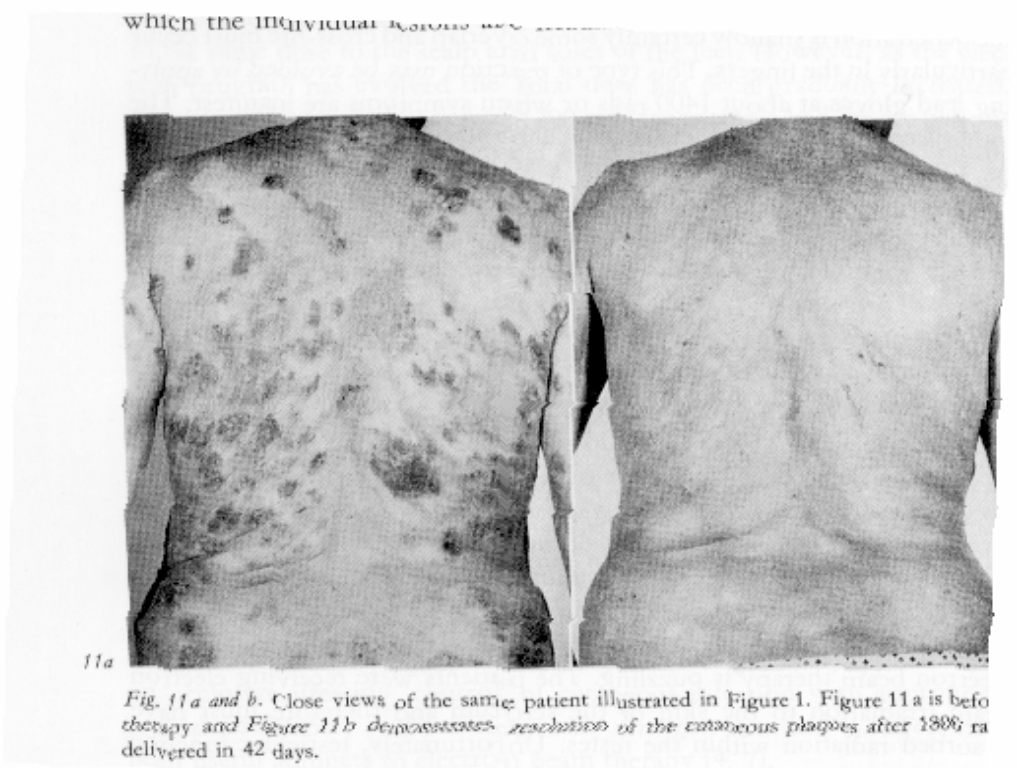
Extent of skin dz	CR (%)	FFR (%) 9 yr	OS (%) 9 yr
limited	96	42	96
generalize	87	10	50
tumor	72	0	28
erythemat	71	20	55

Stanford stage	FFR (%) 9 yr	OS (%) 9 yr
Ia	45	95
Ib	25	55
II	10	40
III/IV	0	0

- Most relapsed after 1 yr - 3 yrs.

TSEB

- 80 yom with generalized plagues treated with RT.



which the individual lesions are

11a

Fig. 11a and b. Close views of the same patient illustrated in Figure 1. Figure 11a is befo therapy and Figure 11b demonstrates resolution of the cutaneous plaques after 1806 ra delivered in 42 days.

Kaye and Bunn 1989
NCI - Navy

- 1979 - 1987, 103 pts prospectively randomized between

  - **conservative** - initial topical HN2 with sequential PUVA, TSEB.
  - **combined** - TSEB 30 - 32 Gy over 8 -12 wks followed by boost RT. concurrent systemic cyclo/doxo/etopo/vincristine.

- **Reslts:** median F/U 75 months.

	OR(%)	**CR(%)**	**median surv.**
Conservative	65	18	76 months
combination	90	40	91 months
p values	0.003	0.032	NS

Kaye and Bunn 1989

NCI - Navy

- **Rslts:**

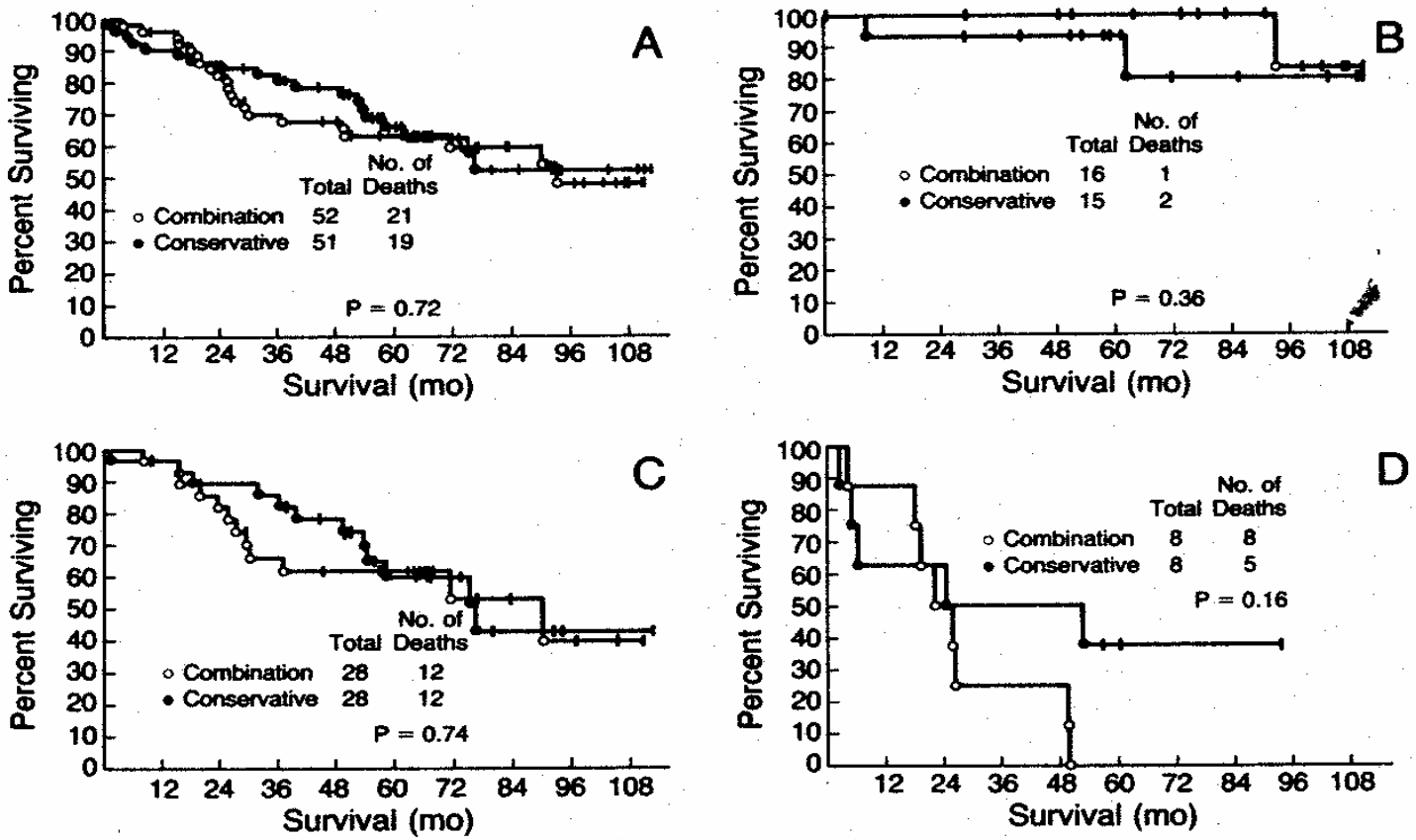


Figure 2. Survival among Patients Receiving Either Combined Therapy or Conservative Therapy.

Panel A shows overall survival; Panel B, survival among low-risk patients (Stage IA, IB, or IIA); Panel C, survival among intermediate-risk patients (Stage IIB, III, or IVA); and Panel D, survival among high-risk patients (Stage IVB).

Kaye and Bunn 1989
NCI - Navy

- adverse effets

	leukopenia	acute skin	leukemia
conservative	n/a	29%	1/51 pt
combination	70%	26%	2/50 pts

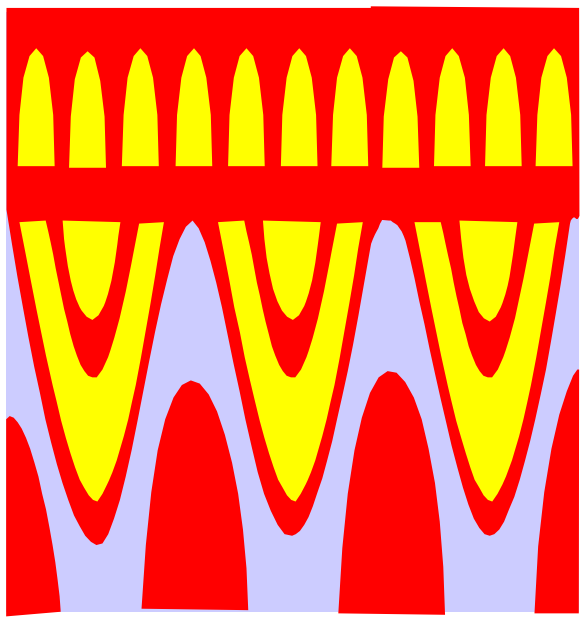
  - **hospitalization** - 12 pts for fever/neutropenia - combined arm.
  - **CHF** - 5 pts - combined arm.

- **Concl:**
  - Initial combination therapy produced higher rate CR.
  - Early aggressive therapy with TSEB and chemotherapy did not improve DFS or OS in MF pts.
  - Combined therapy produced considerable toxicity.

Conclusions

- In early stage MF pts initial primary therapy of topical HN2 vs PUVA vs TSEB does not alter long term survival of.

Conclusions



- Topical HN2/PUVA may be considered as initial therapy in stage I/II pts.

Conclusions

- TSEB is efficacious in treating MF and tolerated well.

- MF pts txed with TSEB has a dose response with better survival above 30 Gy.

Conclusions

- Our pt. MF IB progressive/refractory PUVA.

- She was txed with Stanford TSEB to 36 Gy and boosted based on TLD measurements. COT 10/98 with CR.
- Relapsed 8 months later with four lesions under axilla/inner thigh. Currently receiving radiation 200 cGy/fx to 2000 cGy.

Conclusions

⌘**THE END.**