



GREA | L'alcoologie au défi du Baclofène – 10.12.2014

Les molécules de la discorde

Socialisation des médicaments et preuve par l'usage

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Unil

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Le Baclofène comme symptôme révélateur

La controverse du Baclofène révèle des tensions au cœur de l'**économie de la preuve** en matière thérapeutique et, plus spécifiquement, pharmacologique.

Ces tensions se situent à plusieurs niveaux: la **connaissance scientifique**, les **pratiques des usagers**, les **intérêts et stratégies économiques** et la **gouvernance** en matière de santé.

Ces tensions sont liées de manière plus générale à des **évolutions socio-sanitaires**.



Une approche de sciences sociales

Les **usages des médicaments** sont profondément marqués par leurs contextes spécifiques: **sociaux, politiques, économiques** et **moraux**.

Ces usages sont orientés par le jeu de positions et d'actions d'**acteurs hétérogènes** (individuel ou collectifs, institutionnel ou non).

Ces acteurs co-élaborent et/ou mobilisent des **normes scientifiques**, des **normes socio-sanitaires** et des **conceptions des sujets malades à traiter**, autant de normes et de conceptions auxquelles s'attachent des **modes d'action**.

Cette dynamique est souvent caractérisée par la **controverse** qui peut avoir lieu sur chacun de ces éléments.



La question qui se pose au sociologue

Comment rendre compte de la diversité des **acteurs**, de leurs **positions** et **actions**, qui participent à la **construction de connaissances crédibles** en matière d'efficacité thérapeutique de substances pharmaceutiques disponibles à la prescription et à la consommation?





Postulat

Toute substance agissant sur la **modulation du sujet** (personnalité, émotions, comportements, désirs, relations sociales, etc.) peut être considéré comme une **substance psychotrope**, quand bien même une telle substance a pu être développée et/ou peut être utilisée à des fins somatiques. L'effet controversé du baclofène portant sur l'assuétude à l'alcool, cet effet relève d'un tropisme psychologique.

Jean Delay (1957): « On appelle psychotrope, une substance chimique d'origine naturelle ou artificielle, qui a un tropisme psychologique, c'est-à-dire qui est susceptible de modifier l'activité mentale, sans préjuger du type de cette modification. »



L'absence de « Témoins fiables »

Philippe Pignarre propose d'appeler « **témoin fiable** » un élément nécessaire et suffisant pour que la cause d'une maladie soit identifiée:

« [Un témoin fiable c'est] quelque chose qui peut être sorti du corps humain et transporté (comme un germe), soit pour faire un diagnostic de laboratoire, loin du face-à-face médecin-patient, soit pour créer des modèles pharmacologiques permettant de tester des candidats-médicaments avant l'entrée dans les essais cliniques. »

Philippe Pignarre, « Qu'est-ce qu'un psychotrope ? Psychothérapeutes et prescripteurs face aux mystères de la dépression », in *Ethnopsy, les mondes contemporains de la guérison*. N°2. Paris. Les empêcheurs de penser en rond : 241-292, p. 242.



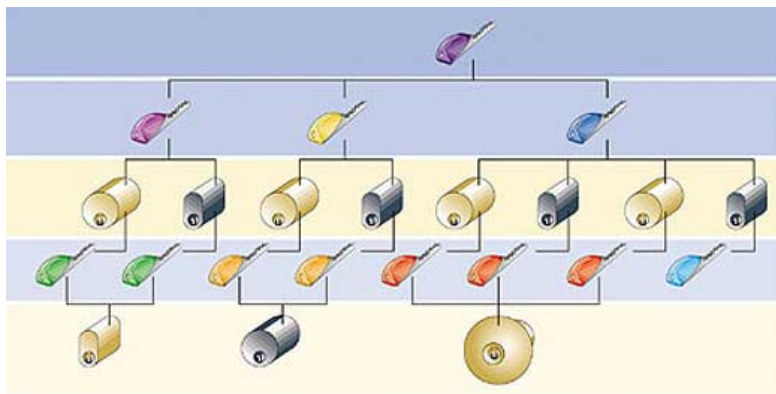
Plasticité pharmacologique

L'absence de témoins fiable, courante dans le cas des psychotropes, remet en question **le paradigme étiologique**, soit le modèle d'une cause déterminée et connue d'un trouble spécifique identifié.

Dans le cas des troubles du comportement, « le médicament joue deux rôles: celui de thérapeutique mais aussi celui du **témoin fiable absent** ».

Pignarre Philippe (2001). Comment la dépression est devenue une épidémie. Paris. La Découverte, pp. 79 et 68.

On observe alors une **plasticité pharmacologique**, la capacité d'une substance à avoir des effets thérapeutiques divers sur les troubles différents dont on ne connaît pas exactement la cause organique.



La **quête d'effets thérapeutiques insoupçonnés** de substances connues va être au cœur de la recherche pharmacologique, surtout dès les années 1950'.

Emerge alors une **nouvelle économie de la recherche** : les critères diagnostiques vont progressivement évoluer au même rythme auquel les laboratoires pharmaceutiques inventent de nouveaux traitements.

Une **stratégie de l'industrie pharmaceutique** va alors consister à « faire varier les caractéristiques du groupe des patients jusqu'à ce que ce groupe "réponde" de manière satisfaisante à la molécule

candidate ». Pignarre Philippe (2001). Comment la dépression est devenue une épidémie. Paris. La Découverte, p. 67.



Plasticité pharmacologique

L'absence de témoins fiables dans la pharmacologie des substances psychotropes modulant les comportements entretient des tensions au niveau des **stratégies thérapeutiques**:

Substances – Psychothérapies

« Le seul point commun entre les psychotropes et les psychothérapies pourrait donc se formuler à partir de cette proposition : "soigner, c'est modifier". L'instabilité et l'artificialité de l'enracinement biologique et psychique des troubles mentaux permettraient alors d'inventer de nouveaux dispositifs de soins, caractérisés par la multiplicité de la clinique, des références, des devenir. »

Philippe Pignarre, Qu'est-ce qu'un psychotrope ? psychothérapeutes et prescripteurs face aux mystères de la dépression, Ethnopsy : les mondes contemporains de la guérison, n°2, 2001.



Plasticité du spectre thérapeutique des substances pharmacologiques

Empirisme et sérendipité

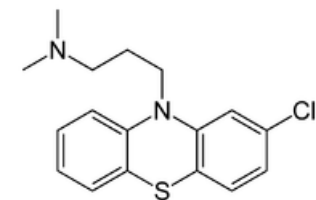
Une exemple célèbre:

Henri Laborit et Pierre Huguenard mélangent différents antihistaminiques dans ce qu'ils appellent des « cocktails lytiques ».

Laborit, chirurgien, remarque que ses patients sont détendus avant l'opération dont ils récupèrent parfaitement. Il constate ainsi **cliniquement** « un effet de désintéressement ».

Il demande à Rhône-Poulenc une molécule qui présenterait cet effet non pas en effet secondaire, mais en qualité centrale. Il s'agit du 4560 RP, écarté par Rhône-Poulenc car trop sédatif et pas assez antihistaminique.

Laborit la fera expérimenter en psychiatrie. On constatera les effet psychotrope de la chlorpromazine (Largactil®), premier médicament antipsychotique, sédatif, calmant, considérée comme un antipsychotique typique.



Chlorpromazine

France: Largactil®

Suisse: Chlorazin®

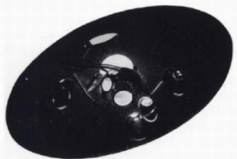
USA: Thorazine®

Les molécules de la discorde

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine

another New use of 'Thorazine'



in Surgery—THORAZINE*

calms the apprehensive and anxious patient
facilitates induction and intubation
potentiates analgesics and anesthetics
controls nausea, vomiting, hiccups and
emergence excitement

a valuable adjuvant in surgical procedures

'Thorazine' Hydrochloride is available in 10 mg., 25 mg.,
50 mg., and 100 mg. tablets; 25 mg. (1 cc.) and 50 mg. (2 cc.)
ampuls; and syrup (10 mg./5 cc.).

For information write:
Smith, Kline & French Laboratories
1530 Spring Garden St., Philadelphia 1

*T.M. Reg. U.S. Pat. Off. for S.K.F.'s brand of chlorpromazine.



in surgery—
THORAZINE*

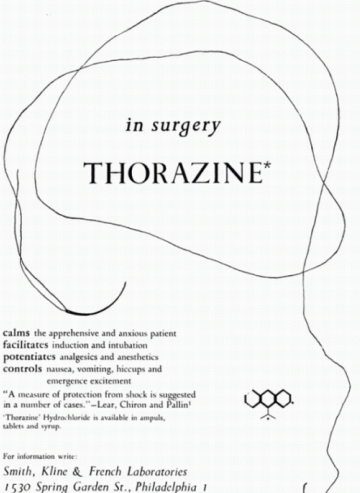
- alleviates anxiety, tension and fear
- stops vomiting, retching and hiccups
- reduces the need for narcotics and sedatives
- lessens the amount of anesthetic required
- controls emergence excitement

provides a smoother course for your surgical patient

'Thorazine' is available in ampuls, tablets and syrup, as the hydrochloride; and
in suppositories, as the base.
'Thorazine' should be administered discriminately; and, before prescribing, the
physician should be fully conversant with the available literature.

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.



in surgery
THORAZINE*

calms the apprehensive and anxious patient
facilitates induction and intubation
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emergence excitement

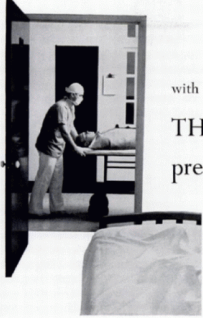
"A measure of protection from shock is suggested
in a number of cases."—Leur, Chiron and Pallas¹

'Thorazine' Hydrochloride is available in ampuls,
tablets and syrup.

For information write:
Smith, Kline & French Laboratories
1530 Spring Garden St., Philadelphia 1

¹ Leur, E., Chiron, A.E., and Pallas, A.M. Chlorpromazine—
An Adjunct to Premedication, Clinical Report Based on 1,000
Cases, New York State J. Med. 33:1813 (July 1) 1935.

*T.M. Reg. U.S. Pat. Off. for S.K.F.'s brand of chlorpromazine.



with
THORAZINE*
preoperatively—

"anxiety and apprehension
give way to
relaxation and calmness"¹

When added to premedication, 'THORAZINE':

- "(1) Augments the action of anesthetics so that reduced doses of
these agents can be used to provide satisfactory anesthesia.
- "(2) Decreases reflex irritability.
- "(3) Markedly inhibits postoperative vomiting.
- "(4) Reduces the need for postoperative narcotics and sedatives."¹

¹ Mathews, Morris and Meyer: Am. Pract. & Dig. Treat. 6:380 (Mar.) 1935.

'Thorazine' Hydrochloride is available in ampuls, tablets and syrup.

For information write:
Smith, Kline & French Laboratories
1530 Spring Garden Street, Philadelphia 1

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

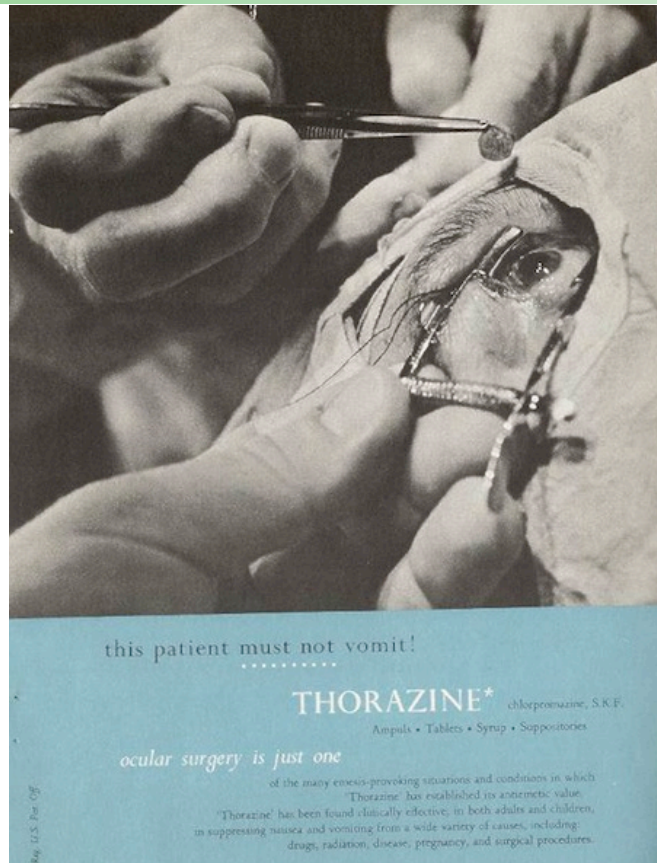
Thorazine pour la chirurgie, 1955 & 1956.

Journal of Bone and Joint Surgery,
Vol. 37-A, No. 5, p. 13; No. 6, p. 21.
Vol. 38-A, No. 2, p. 25; No. 2, p. 25.

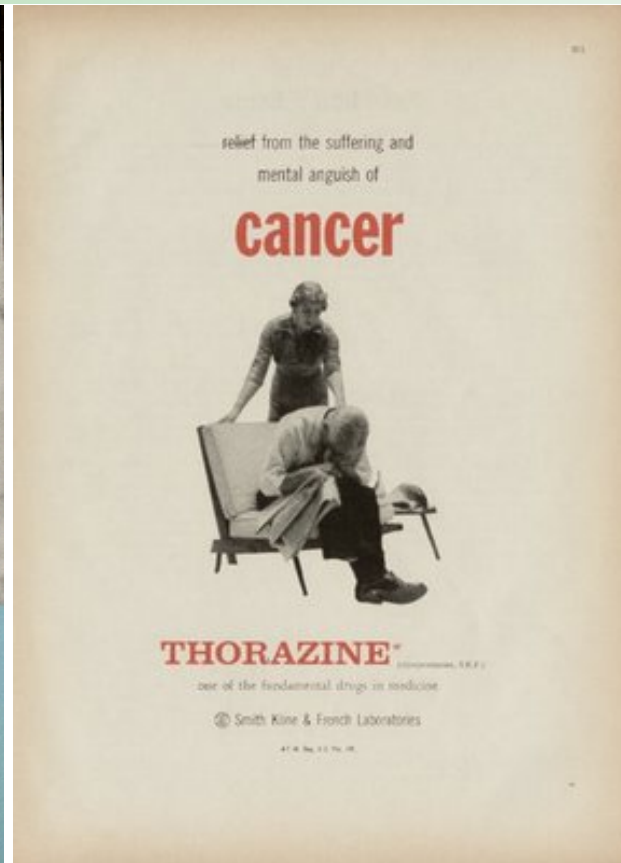
Les molécules de la discorde

Plasticité du spectre thérapeutique des substances pharmacologiques

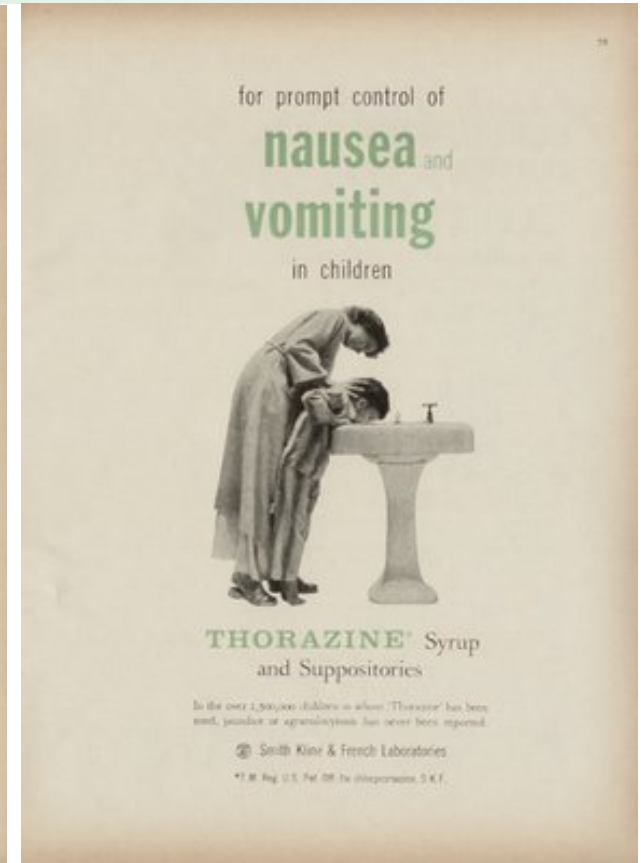
Exemple. Tribulations nosologiques de la chlorpromazine



Thorazine en chirurgie, ca. 1956



Thorazine contre le cancer, 1959.
Journal of the National Medical
Association, Vol. 51, No. 6, p.LV.



Thorazine contre les vomissements,
1959

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine

in many gastrointestinal disorders

THORAZINE*

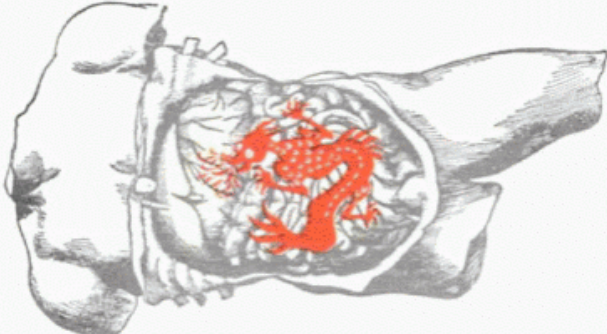
*"would appear to be . . . tranquilizing agent of choice . . ."*¹



in many gastrointestinal disorders

. . . functional as well as secondary to organic disease such as spastic colon, peptic ulcer and a variety of other conditions marked by pain and vomiting, 'Thorazine' has 3 advantages:

1. 'Thorazine' abolishes the emotional turbulence—fear, excitement, anxiety, tension—that adversely affects digestion and the digestive tract.
2. 'Thorazine' effectively controls the nausea and vomiting of gastrointestinal disorders.
3. 'Thorazine' has a mild atropine-like, inhibitory effect on gastric secretion and "would appear to be . . . tranquilizing agent of choice when stimulation of gastric secretion is contraindicated."¹



¹'Thorazine' is available as the hydrochloride in ampuls, tablets and syrup; and as the base in suppositories.

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

1. Haverback, B.J.; Stevenson, T.D.; Sjoerdsma, A., and Terry, L.: The Effects of Reserpine and Chlorpromazine on Gastric Secretion, *Am. J. M. Sc.* 230:601 (Dec.) 1955.

'Thorazine' should be administered discriminately; and, before prescribing, the physician should be fully conversant with the available literature.

Smith, Kline & French Laboratories, Philadelphia

Thorazine contre les désordre gastrointestinaux, 1956.

Psychosomatic Medicine, Vol. 18, No. 2.

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine

in psoriasis—

THORAZINE*

“appears to be indicated . . . particularly
in persons with emotional instability.”¹





psoriasis—

“beneficially influenced” by Thorazine*

The ataractic, tranquilizing effect of ‘Thorazine’ can do much to relieve the emotional stress that is so often a complicating or even a causative factor in many somatic conditions.

Reiss¹ observed that 12 out of 15 psoriatic patients “showed a reduction of the number of lesions” after ‘Thorazine’ therapy of 1 to 4 weeks. He concluded that “the psoriatic process can be beneficially influenced” by ‘Thorazine’.

1. Reiss, F. (New York City): Psoriasis and Stress, presented at International Medical Congress, Verona, Italy, Sept. 1, 1955.

‘Thorazine’ should be administered discriminately and, before prescribing, the physician should be fully conversant with the available literature.

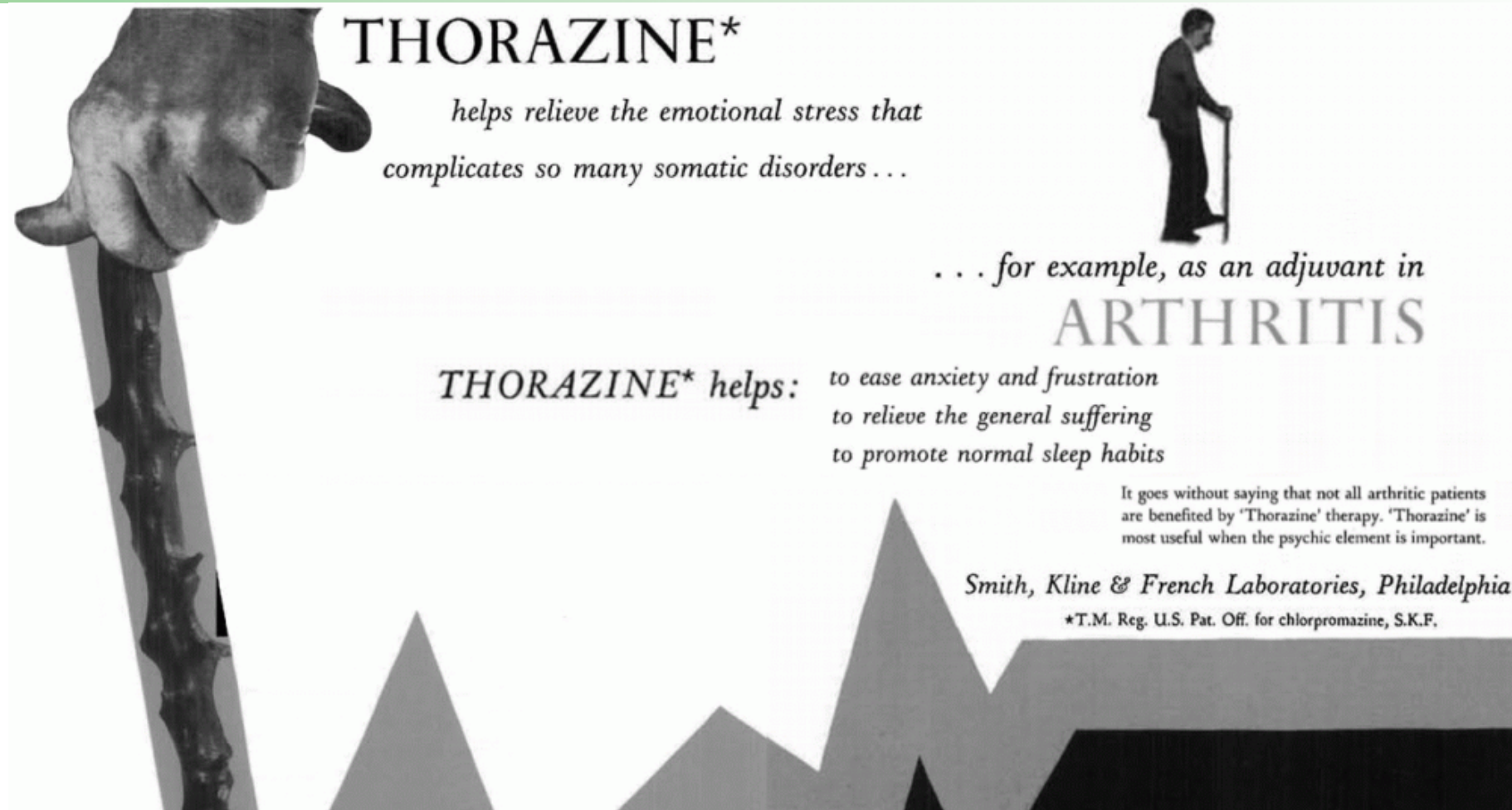
Smith, Kline & French Laboratories, Philadelphia

‘Thorazine’ is available in ampuls, tablets and syrup (as the hydrochloride), and in suppositories (as the base).

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine

A black and white advertisement for Thorazine (chlorpromazine). On the left, a large, detailed illustration of a hand gripping a gnarled, dark, and jagged branch. The background features a stylized mountain range with several peaks of varying heights. In the upper right, a small silhouette of a man in a suit leaning on a cane. The text is arranged in a clean, serif font. The word 'THORAZINE*' is prominently displayed at the top left. Below it, a line of text describes its use for emotional stress. Further down, it mentions its role as an adjuvant in arthritis. A list of benefits follows, and a disclaimer is provided at the bottom right. The manufacturer's name and a trademark notice are at the very bottom.

THORAZINE*

helps relieve the emotional stress that complicates so many somatic disorders . . .

. . . for example, as an adjuvant in
ARTHRITIS

THORAZINE* helps: *to ease anxiety and frustration
to relieve the general suffering
to promote normal sleep habits*

It goes without saying that not all arthritic patients are benefited by 'Thorazine' therapy. 'Thorazine' is most useful when the psychic element is important.

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

Thorazine contre l'arthrite, 1956.

Psychosomatic Medicine, Vol. 18, No. 5.

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine

severe asthma
*is usually aggravated
and prolonged
by a strong emotional overlay*

In one study, 'Thorazine'
relaxed and improved 11 of
12 patients within one hour
after injection . . . in one case
"appeared to be life-saving."¹

'Thorazine' promptly alleviates the emotional
stress which may precipitate, aggravate or
prolong an asthmatic attack. It enables the patient
to sleep, yet does not depress respiration.

Available: Ampuls, Tablets, Syrup (as the
hydrochloride), and Suppositories (as the base).

Smith, Kline & French Laboratories, Philadelphia

1. Ende, M.: Am. Pract. & Dig. Treat. 6:710 (May) 1955.
*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

THORAZINE^{*}
one of the fundamental drugs in medicine



'Thorazine' is available, as the hydrochloride, in 10 mg., 25 mg., 50 mg., 100 mg.
and 200 mg. tablets; 25 mg. (1 cc.) and 50 mg. (2 cc.) ampuls; and syrup
(10 mg./5 cc.); and, as the base, in 25 mg. and 100 mg. suppositories.

in asthma
when emotional stress is a complicating factor



'Thorazine' by injection (ampuls or multiple dose vials) often
provides immediate relief from severe attacks.

'Thorazine' Spansule[†] capsules q12h provide sustained,
24-hour protection against emotional stress that can precipitate attacks.

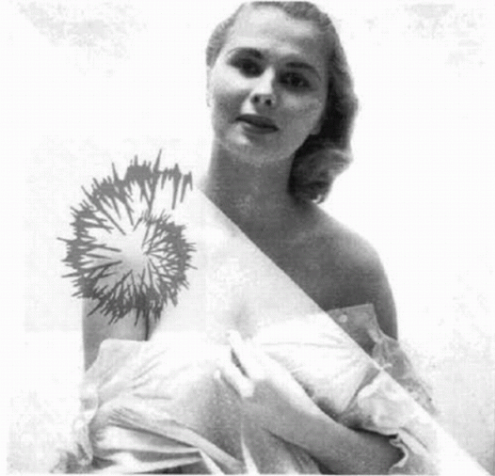
'Thorazine', in any dosage form, promotes sound sleep
without respiratory depression.

THORAZINE^{*} one of the fundamental drugs in medicine
chlorpromazine, S.K.F.

Tablets, 10 mg., 25 mg., 50 mg., 100 mg. and 200 mg.; Ampuls, 25 mg. (1 cc.) and 50 mg. (2 cc.); Multiple
Dose Vials, 10 cc. (25 mg./cc.); Spansule[†] sustained release capsules, 50 mg., 75 mg., 150 mg. and 200 mg.;
Suppositories, 25 mg. and 100 mg.; and Syrup: 10 mg. per 5 cc. teaspoonful.

Smith Kline & French Laboratories, Philadelphia 1

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F. †T.M. Reg. U.S. Pat. Off. for sustained release capsules, S.K.F.



THORAZINE^{*} *can allay the suffering
caused by the pain of SEVERE BURSITIS*

The ataractic, tranquilizing action of 'Thorazine' can reduce the
anguish and suffering associated with bursitis. 'Thorazine' acts not
by eliminating the pain, but by altering the patient's reaction—
enabling her to view her pain with a "serene detachment" . . . Howell
and his associates¹ reported: "Several of [our patients] expressed the
feeling that ['Thorazine'] put a curtain between them and their pain,
so that whilst they were aware that the pain existed, they were not
upset by it."

Smith, Kline & French Laboratories, Philadelphia

1. Howell, T.H.; Harth, J.A.P., and Dietrich, M.: Practitioner 173:172.
*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

Thorazine contre l'ashme, 1957 & 1958.

California Medicine, Vol. 86, No.1; Vol. 88, No. 4.

Les molécules de la discorde

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine



“disturbed wards have virtually disappeared”¹

Many hospitals have found that

THORAZINE^{*}

- makes patients accessible and receptive to psychotherapy
- reduces or eliminates the need for restraint and seclusion
- improves ward morale
- speeds release of hospitalized patients
- reduces destruction of personal and hospital property
- reduces need for shock therapy and lobotomy
- increases capacity of hospital to serve more patients than ever before

¹ ‘Thorazine’ is available in ampuls, tablets and syrup (as the hydrochloride), and in suppositories (as the base).

Smith, Kline & French Laboratories, Philadelphia

¹ Overholser, W.: in Chlorpromazine and Mental Health, Philadelphia, Lea & Febiger, 1955.
^{*} T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.



THORAZINE^{*}

helps to keep more patients out of mental hospitals

With ‘Thorazine’ “more patients will be released after shorter periods of hospitalization and fewer patients will require re-hospitalization. More patients can be treated in the community, at clinics or in the psychiatrist’s office without being hospitalized at all.”¹

‘Thorazine’ is available as the hydrochloride in ampuls, tablets and syrup; and as the base in suppositories.

For information write: Smith, Kline & French Laboratories, 1530 Spring Garden Street, Phila. 1

¹ Hoffman, J.L.: in Chlorpromazine and Mental Health, Philadelphia, Lea & Febiger, 1955.

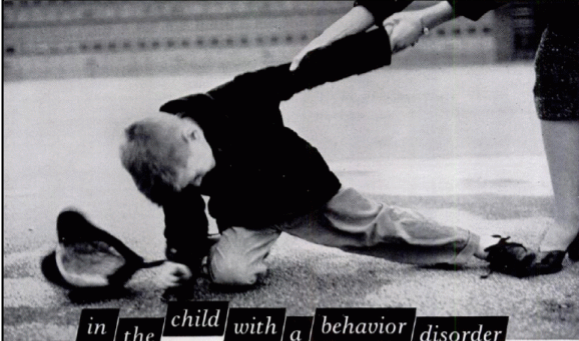
^{*} T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

Thorazine en psychiatrie, 1956.
Mental Hospitals, Vol. 7, No. 8., p. 2.

Thorazine en psychiatrie, 1956.
Mental Hospitals, Vol. 7, No. 4.

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine



in the child with a behavior disorder

THORAZINE*

reduces hyperactivity and aggressiveness
decreases anxiety and hostility
improves mood, behavior and sleeping habits
establishes accessibility to guidance or psychotherapy
increases amenability to supervision

facts to bear in mind— Even though the dramatic calming effect of 'Thorazine' on belligerent, overactive children may give the impression of a cure, simultaneous supportive counseling and guidance are necessary if lasting benefits are to be assured.

Adequate 'Thorazine' dosage for certain seriously disturbed youngsters will sometimes exceed 50-100 mg. t.i.d.

'Thorazine' should be administered discriminately and, before prescribing, the physician should be fully conversant with the available literature.

'Thorazine' is available in ampuls, tablets and syrup (as the hydrochloride), and in suppositories (as the base).

C1=CC=C2C(=C1)C(=C(C=C2)N)C3=CC=CC=C3

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

Thorazine contre agitation, 1956.
Ment. Hospitals, Vol. 7, No. 7. page 2.

to help you relieve
the severe emotional upset
of the menopausal patient



THORAZINE*

'Thorazine' can facilitate the over-all management of your menopausal patient. Its unique, non-hypnotic tranquilizing effect relieves anxiety, tension, agitated depression and helps you to restore to the patient a feeling of well-being and a sense of belonging.

'Thorazine' is available in ampuls, tablets and syrup (as the hydrochloride), and in suppositories (as the base).

For information write:
Smith, Kline & French
Laboratories, Philadelphia 1

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

Thorazine contre ménopause, 1956.
Psychosomatic Medicine, Vol. 18, No. 6.

To control agitation—a symptom that
cuts across diagnostic categories



Thorazine®, a fundamental drug in brand of chlorpromazine psychiatry

—Because of its sedative effect, 'Thorazine' is especially useful in controlling hyperactivity, irritability and hostility. And because 'Thorazine' calms without clouding consciousness, the patient on 'Thorazine' usually becomes more sociable and more receptive to psychotherapy.

leaders in psychopharmaceutical research

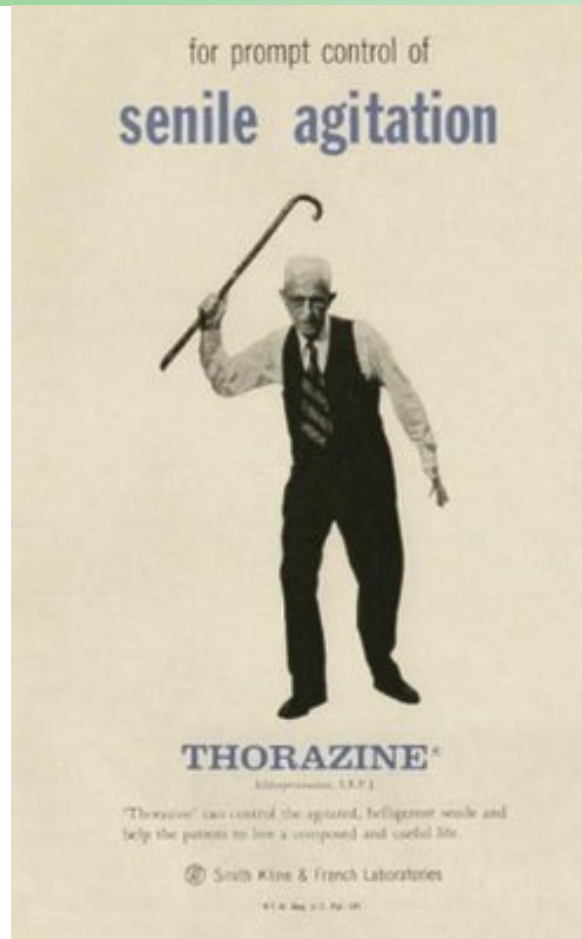
SMITH
KLINE &
FRENCH

Thorazine contre agitation, 1960.
Mental Hospitals, Vol. 11, No. 5.

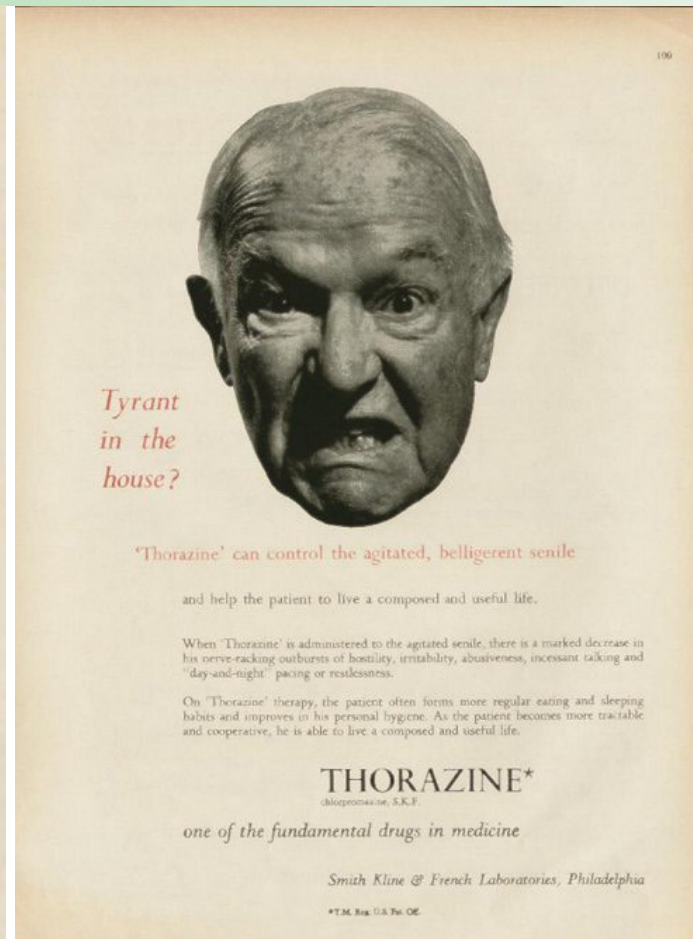
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Plasticité du spectre thérapeutique des substances pharmacologiques

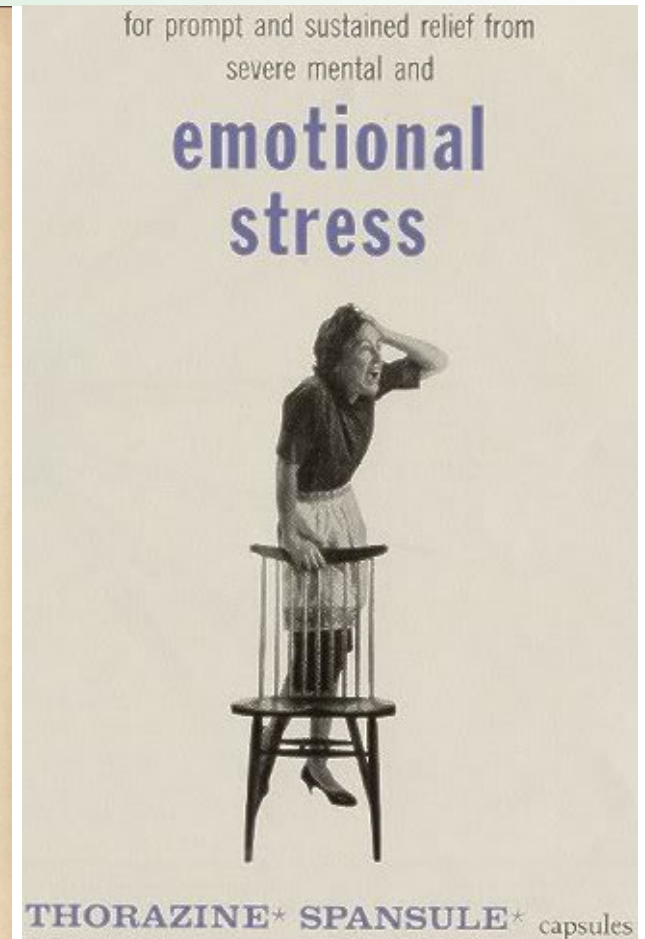
Exemple. Tribulations nosologiques de la chlorpromazine



Thorazine contre l'agitation sénile, ca. 1957



Thorazine contre l'agitation sénile, ca 1957



Thorazine contre le stress émotionnel, ca. 1959

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine

Patients with pain often have anxiety



Thorazine ® brand of chlorpromazine
helps reduce reaction to pain, relieves anxiety

Before prescribing, the physician should be familiar with the complete prescribing information for SM-AT (teriparatide) or PGE. The following is a brief pre-auditory statement. Contraindications, Concomitant therapy or the presence of large amounts of C.N.S. depressants. Precautions: Administration of C.N.S. depressants may result in a further decrease of C.N.S. depressants when used concomitantly. Anesthetic effect may be more pronounced. Possibility of increased risk if he/she is used for patients who have a history of, or are pregnant, use only when necessary to the extent of the patient. Side Effects: Dizziness, headache, drowsiness, loss of consciousness, loss of consciousness, anorexia, nausea, vomiting, hypotension, tachycardia, arrhythmias, etc.

Patients with anxiety often have pain



Thorazine® brand of chlorpromazine
helps relieve anxiety, reduces reaction to pain

with LM administration, expected side effects may be reversed: dermatologic reactions, paronychia-like symptoms in high doses; in rare instances, myopathy, weight gain, muscle wasting and moderate breast engorgement in females on high doses; and low frequency of cholestatic jaundice. Side effects occurring rarely include: myopathy, arthralgias, and pyelonephritis, teratogenic and congenital defects (see associated *Adverse Reactions*).

For a comprehensive presentation of 'Thucydides' and using information and software reported with previous methodologies, please refer to STAD structure of POP.

 Smith Kline & French Laboratories

Thorazine contre l'anxiété, 1967.

JAMA: The Journal of the American Medical Association, Vol. 199, No. 8, pp. 50-51.

Les molécules de la discorde

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine



Remember these?
About 13 years ago,
Thorazine®
brand of chlorpromazine
helped make them
obsolete.

Even more important, it helped to eliminate or modify delusions and hallucinations, lessen confusion, and make the patient more amenable to other forms of therapy.

In psychiatry, 'Thorazine' remains today's most widely prescribed ataractic.

Before prescribing, please see the complete prescribing information, including side effects reported with phenothiazine derivatives and symptoms and treatment of overdosage, in SK&F literature or PDR. The following is a brief precautionary statement.

Contraindications: Comatose states or the presence of large amounts of C.N.S. depressants. **Precautions:** Potentiation of C.N.S. depressants may occur (reduce dosage of such agents when used concomitantly). Antiemetic effect may mask signs of overdosage of toxic drugs or obscure diagnosis of other conditions. Administer in pregnancy only when necessary for patient's welfare. Possibility of drowsiness should be kept in mind for patients who drive cars, etc. **Side Effects:** Drowsiness; dry mouth; nasal congestion; constipation; amenorrhea; miosis; mild fever; weight gain; hypotensive effects, sometimes severe with I.M. administration; epinephrine effects may be reversed; dermatological reactions; parkinsonism-like symptoms on high dosages (in rare instances, may persist); lactation and moderate breast engorgement (in females on high dosages); and less frequently, cholestatic jaundice (use cautiously in patients with liver disease). Side effects occurring rarely include: mydriasis; agranulocytosis; skin pigmentation; lenticular and corneal deposits (after prolonged substantial doses). Available: Tablets—10 mg., 25 mg., 50 mg., 100 mg. and 200 mg. Ampuls—1 cc. and 2 cc. (25 mg./cc.). Multiple-dose Vials—10 cc. (25 mg./cc.). Spansule® capsules—30 mg., 75 mg., 150 mg., 200 mg. and 300 mg. Concentrate—30 mg./cc.

Smith Kline & French Laboratories, Philadelphia 

BEFORE THE REVOLUTION

Tortured minds and shackled limbs—common conditions from an era past. The era before the introduction of Thorazine®, an event that was to revolutionize psychiatric care.

Back in 1954, Thorazine was notable for its effective control of the manifestations of psychosis, for increasing patient accessibility to psychotherapy, for helping restore large numbers of patients to productive lives in the community. Today, 28 years later, it still is.

THORAZINE®
brand of
CHLORPROMAZINE

Tablets: 50 and 100 mg. of the HCl

THORAZINE®
brand of
CHLORPROMAZINE
The original chlorpromazine.

From SK&F, pioneers in psychopharmacology.

Please see next page for a brief summary of prescribing information.

SK&F
a Subsidiary Company

THORAZINE® brand of **CHLORPROMAZINE**

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

Indications: For the management of manifestations of psychotic disorders. To control the manifestations of the manic type of manic-depressive illness. For the treatment of severe behavioral problems in children marked by combativeness and/or explosive hyperexcitable behavior (out of proportion to immediate provocations), and in the short-term treatment of hyperactive children who show excessive motor activity with accompanying conduct disorders consisting of some or all of the following symptoms: impulsivity, difficulty sustaining attention, aggressivity, mood lability and poor frustration tolerance.

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the other indication as follows:
Possibly effective: For control of excessive anxiety, tension and agitation as seen in neuroses.
Final classification of the less-than-effective indication requires further investigation.

Contraindications: Comatose states, presence of large amounts of C.N.S. depressants, or bone marrow depression.

Warnings: The possibility of extrapyramidal reactions from chlorpromazine may confuse the diagnosis of Reye's syndrome or other encephalopathy. Therefore, avoid use in children or adolescents with suspected Reye's syndrome.

Avoid using in patients hypersensitive (e.g., blood dyscrasias, jaundice) to any phenothiazine. Caution patients about activities requiring alertness (e.g., operating vehicles or machinery) especially during the first few days' therapy. Avoid concomitant use with alcohol. May counteract antihypertensive effect of guanethidine and related compounds.

Use in pregnancy only when essential. There are reported instances of jaundice, prolonged extrapyramidal signs or hyperreflexia in newborns whose mothers had received chlorpromazine. Chlorpromazine is excreted in the breast milk of nursing mothers.

Precautions: Use cautiously in persons with cardiovascular, liver or chronic respiratory disease, or with acute respiratory infections. Patients with a history of hepatic encephalopathy due to cirrhosis have increased sensitivity to the C.N.S. effects of chlorpromazine. Due to cough reflex suppression, aspiration of vomitus is possible. May prolong or intensify the action of C.N.S. depressants, organophosphorus insecticides, heat, atropine and related drugs. (Reduce dosage of concomitant C.N.S. depressants.) Anticonvulsant action of barbiturates is not intensified. Antiemetic effect may mask signs of overdosage of other drugs or obscure diagnosis and treatment of conditions such as intestinal obstruction, brain tumor and Reye's syndrome (see Warnings). When used concomitantly, may obscure vomiting as a sign of toxicity of a cancer chemotherapeutic agent. Discontinue high-dose, long-term therapy gradually. Patients with a history of long-term therapy with Thorazine and/or other neuroleptics should be evaluated periodically for possible adjustment or discontinuance of drug therapy. Use cautiously in patients with glaucoma. Neuroleptic drugs cause elevated prolactin levels that persist during chronic administration. Since approximately one-third of human breast cancers are prolactin-dependent in vitro, this elevation is of potential importance if neuroleptic drug administration is contemplated in a patient with a previously detected breast cancer. Neither clinical nor epidemiologic studies to date, however, have shown an association between the chronic administration of neuroleptic drugs and mammary tumorigenesis. Chlorpromazine diminishes the effect of oral anticoagulants. It may lower the convulsive threshold. Dosage adjustments of anticonvulsants may be necessary. Concomitant administration with propranolol results in increased plasma levels of both drugs. Patients should not receive Thorazine 48 hours before or 24 hours after myelography with the contrast medium metrizamide.

Thorazine tablets have recently been reformulated to remove FD&C Yellow #5 (tartrazine). Reformulated lots can be identified by the wording "Modified Formula" on the immediate container labels. However, until the transition process is complete, some lots of Thorazine tablets containing FD&C Yellow #5 (tartrazine) will still be in stock. FD&C Yellow #5 (tartrazine) may cause allergic-type reactions (including bronchial asthma) in certain susceptible individuals. Although the overall incidence of FD&C Yellow #5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin sensitivity. For specific information, contact: Smith Kline & French Laboratories (outside Pa., call toll-free 1-800-523-4835, ext. 4262; in Pa., call collect 215-751-4262).

Adverse Reactions: Drowsiness, cholestatic jaundice, agranulocytosis, eosinophilia, leukopenia, hemolytic anemia, aplastic anemia, thrombocytopenic purpura and pancytopenia, postural hypotension, tachycardia, fainting, dizziness and occasionally a shock-like condition, reversal of epinephrine effects. EKG changes have been reported, but relationship to myocardial damage is not confirmed. neuromuscular (extrapyramidal) reactions: pseudo-parkinsonism, motor restlessness, dystonias, persistent tardive dyskinesia, dyscholic symptoms, catatonik-like states, cerebral edema, convulsive seizures, abnormality of the cerebrospinal fluid proteins, urticarial reactions and photosensitivity, exfoliative dermatitis, contact dermatitis, lactation and breast engorgement (in females on large doses), false positive pregnancy tests, amenorrhea, gynecocystitis, hyperglycemia, hypoglycemia, glycosuria, dry mouth, nasal congestion, constipation, adynamic ileus, urinary retention, miosis, mydriasis, after prolonged substantial doses, skin pigmentation, epithelial keratopathy, lenticular and corneal deposits and pigmentary retinopathy, visual impairment, mild fever (after large I.M. dosage), hyperpyrexia, increased appetite and weight, a systemic lupus erythematosus-like syndrome, peripheral edema.

NOTE: Sudden death in patients taking phenothiazines (apparently due to cardiac arrest or asphyxia due to failure of cough reflex) has been reported, but no causal relationship has been established.

Supplied: Tablets, 10 mg., 25 mg., 50 mg., 100 mg. and 200 mg., in bottles of 100; Single Unit Packages of 100 (intended for institutional use only). Spansule® capsules, 30 mg., 75 mg., 150 mg., 200 mg. and 300 mg., in bottles of 50; in Single Unit Packages of 100 (intended for institutional use only). Injection, 25 mg./ml.; Syrup, 10 mg./5 ml.; Suppositories, 25 mg. and 100 mg.; Concentrate (intended for institutional use only), 30 mg./ml. and 100 mg./ml.

Smith Kline & French Laboratories
Philadelphia, Pa.

© SmithKline Corporation, 1982

Thorazine en psychiatrie, 1967.
Hospital & Community Psych., 18, 9.

Thorazine en psychiatrie, 1982.
Hospital & Community Psychiatry, Vol. 33, No. 6.

Les molécules de la discorde

Plasticité du spectre thérapeutique des substances pharmacologiques

Exemple. Tribulations nosologiques de la chlorpromazine

FOR IMMEDIATE EFFECT!

in acute alcoholism

THORAZINE* Ampuls

"Thorazine" should be used discriminately and, before prescribing, the physician should be fully conversant with the available literature.

always carry 'Thorazine' Ampuls in your bag

Smith, Kline & French Laboratories, Philadelphia

**T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.*

prompt control of

acute alcoholism

THORAZINE* Injection

Ampuls and Multiple dose vials

Smith Kline & French Laboratories

**T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.*

Thorazine contre l'alcoolisme, 1956 & 1959

Les acteurs de la sérendipité légitime?

Dans le domaine des psychotropes en particulier, les molécules sont souvent identifiées par **l'observation clinique de « sides effects »** qui sont investis pour redéfinir et souvent élargir leur spectre d'action. Il s'agit là d'un mélange de hasard et de sagacité qui a pris pour nom la **serendipité**.

La question qui se pose aujourd'hui est donc précisément celle du **périmètre des acteurs** reconnus et légitimes à participer de l'expertise de ces observations et à la détermination des modes d'actions qui en découlent.





Les molécules de la discorde

Une cas princeps

La mobilisation des activistes contre le SIDA

30 A The Dallas Morning News Wednesday, May 17, 1989 H

Club offers latest drugs for AIDS

Continued from Page 27A.

age the process individually. About 60 experimental treatments are available through the network.

But the arrangements are not profit-making ventures, those involved emphasize. "We are not trying to make money on these drugs," said Mr. Woodroof. "We have a 17 percent gross markup or less. It covers the basic product cost and shipping."

While some local doctors are concerned about potential health problems from treatments that have not met U.S. standards, increasingly they are accepting their patients' decision to look beyond accepted therapies for a disease that has no cure.

"It's a reality of my practice and I'd be a fool not to expect it," said Dr. Stephen Nightingale, director of the AIDS clinic at Parkland Memorial Hospital. "But in the past year I have not seen any patient who was physically damaged by any remedy they were taking."

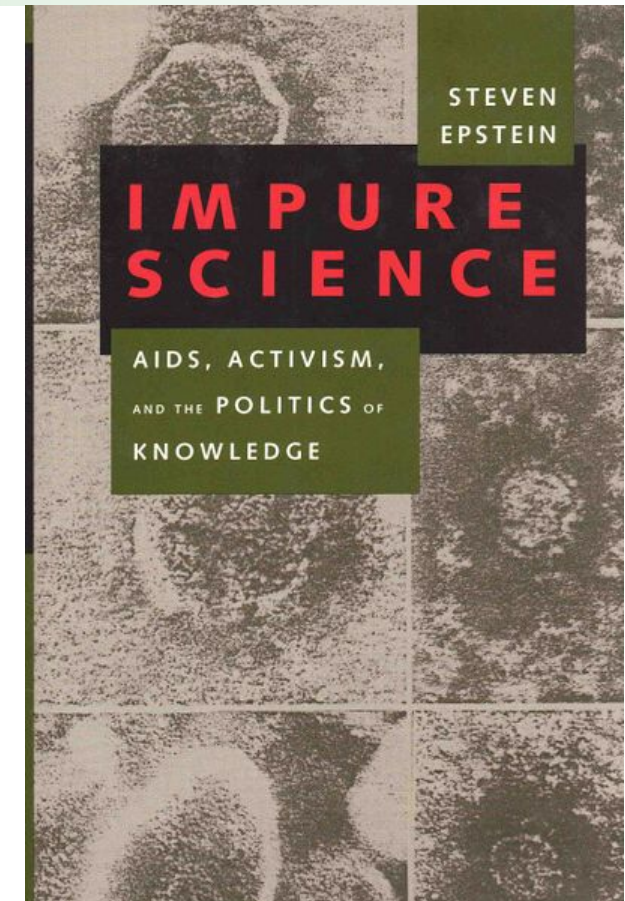
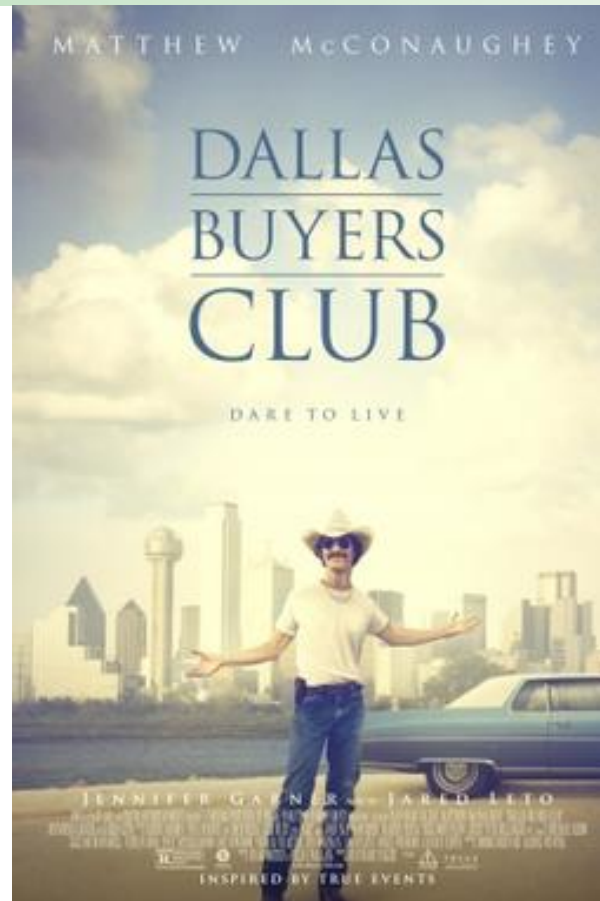
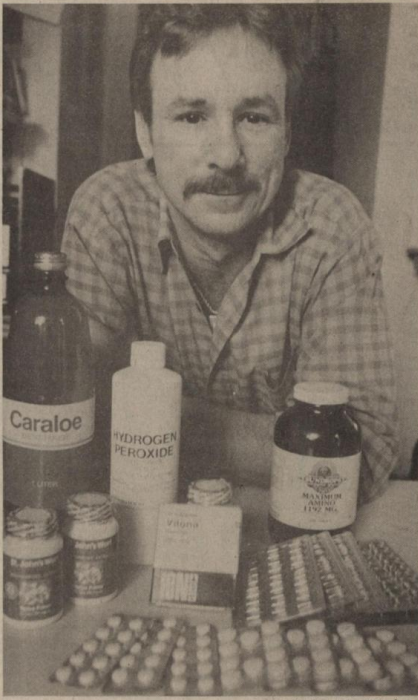
Last month, however, the FDA issued a warning to AIDS patients who were drinking a diluted solution of hydrogen peroxide in the belief that it would somehow stop the spread of the human immunodeficiency virus, or HIV, which causes AIDS. In the past year, a Conroe child died and several others were severely injured when they were mistakenly served high concentrations of the liquid. A mother of one child had mistaken the drink for chilled water stored in the refrigerator.

The FDA warning has not deterred Mr. Woodroof from continuing to offer the drug. He said he knows of 17 patients locally who are using the potion and seeing positive results.

point of this is to give people options. If they see results, then that's all that matters."

Ron Woodroof, president of the Dallas Buyers Club, operates a distribution centers for experimental AIDS treatments. The non-profit organization imports treatments from other countries, none of which has FDA approval.

The Dallas Morning News: William Snyder



Dallas Buyers Club: premier des clubs qui permettront aux séropositifs américains de se fournir en médicaments antirétroviraux étrangers en provenance du Mexique ou du Japon.

La mobilisation des activistes contre le SIDA

« Inside of a large and often floodlit arena with a diffuse and porous perimeter, an eclectic assortment of actors have all sought to assert and assess claims. **The arena of fact making encompasses not just immunologists, virologists, molecular biologists, epidemiologists, physicians, and federal health authorities-but various credentialed experts plus the mass media and the pharmaceutical and biotechnology companies;** it also encompasses a strong and internally differentiated activist movement along with various organs of alternative media, including activist publications and the gay press. »

Steven Epstein (1995). The Construction of Lay Expertise: AIDS Activism and the Forging of Credibility in the Reform of Clinical Trials. Science, Technology, & Human Values, Vol. 20, No. 4, pp. 408-437, pp. 408-409.



La mobilisation des activistes contre le SIDA

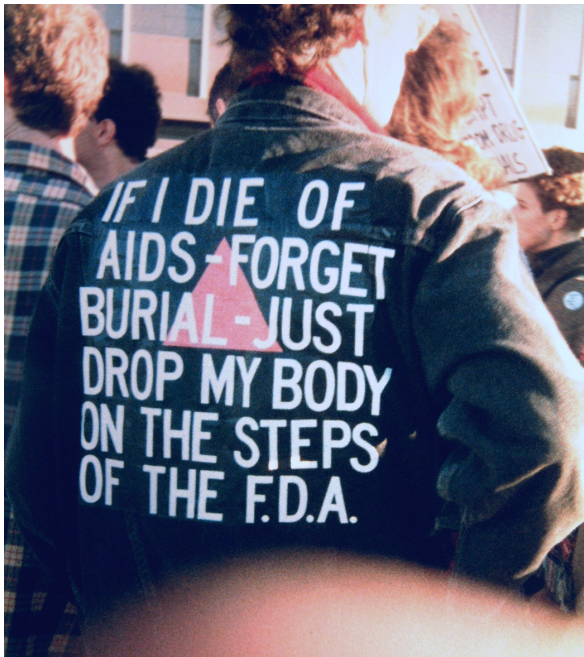
« This case demonstrates that activist movements, through amassing different **forms of credibility**, can in certain circumstances become genuine participants in the construction of scientific knowledge that they can (within definite limits) effect changes both in the epistemic practices of biomedical research and in the therapeutic techniques of medical care.»

Steven Epstein (1995). The Construction of Lay Expertise: AIDS Activism and the Forging of Credibility in the Reform of Clinical Trials. Science, Technology, & Human Values, Vol. 20, No. 4, pp. 408-437, pp. 408-409.



La mobilisation des activistes contre le SIDA

Ce type de situation témoigne de l'émergence d'une nouvelle figure: les « **Activistes des traitements** » (*Treatment activists*) qui peuvent intervenir dans certains cas de manière prépondérante dans la conception, la conduite et l'interprétation des essais cliniques utilisés pour tester la sécurité et l'efficacité des médicaments.



David Wojnarowicz, Artiste et militant, 1988.



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Le « potentiel d'action des patients »

Empowerment | Capacitation

- ❖ Capacité à développer des compétences en ce qui concerne son état de santé.
- ❖ Capacité d'obtenir des informations médicales.
- ❖ Capacité de faire valoir ses compétences et son point de vue face à des professionnels.
- ❖ Capacité de disposer de droits vis-à-vis de la communauté médicale.
- ❖ Capacité à se faire reconnaître dans un/des communautés sociales.

Le potentiel d'action des patients est ce qui concourt à promouvoir leur participation dans leur prise en charge.



Nouvelles figures du patient (individuel et collectif)

Le patient politique: la montée en puissance des associations

Triple revendication du mouvement « self-help »:

- ❖ **Connaissances** : les expériences échangées entre les malades doivent être considérées comme des connaissances à part entière sur leurs maladies. Capacité de s'approprier les connaissances académiques.
- ❖ **Politique** : demande de prise en compte des problèmes par les autorités et les professionnels de santé.
- ❖ **Identitaire** : être reconnus comme des partenaires à part entière.



EURORDIS
Rare Diseases Europe

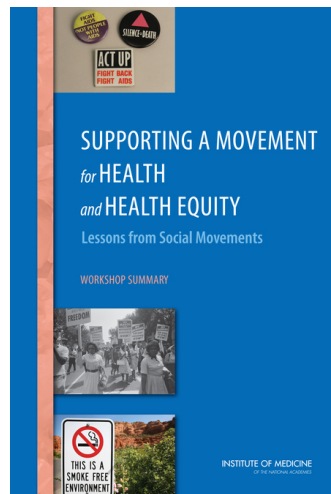
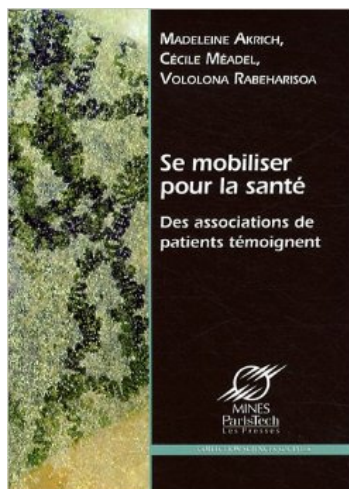
Exemple: Objectifs de l'Enquête Européenne EURORDIS.

« Encourager la collaboration entre les malades et les chercheurs et influencer les politiques publiques et les priorités de la recherche. »

Le patient politique: la montée en puissance des associations

« La constitution d'une **expertise profane** a joué un rôle moteur dans le développement de la **démocratie sanitaire**: c'est en partie parce que certains mouvements ont su se faire reconnaître comme des **interlocuteurs compétents**, informés et porteurs d'un savoir propre que l'intégration des associations dans la gouvernance de la santé a progressé, dans un contexte marqué par des incertitudes et des controverses face auxquelles l'expertise médicale a montré ses limites. »

Akrich, M. and V. Rabearisoa (2012). L'expertise profane dans les associations de patients, un outil de démocratie sanitaire. *Santé Publique* 24(1): 69-74.





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Albumin
Total B
Direct I
Alanine
Alkaline
Gamma g

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Based
Medicine**

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à partir de 6 ans

30 comprimés

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Limites de l'Evidence based medicine

On assiste dès les années 1980-90 à un renouvellement de la médecine comme science sous la forme de l'EBM. Son but est d'**articuler les données produites par la recherche, l'expertise du praticien-clinicien et la vie – et l'avis – du patient.** Cette méthode est parfois difficile à mettre en œuvre et parfois controversée.



<http://www.hsl.unc.edu>

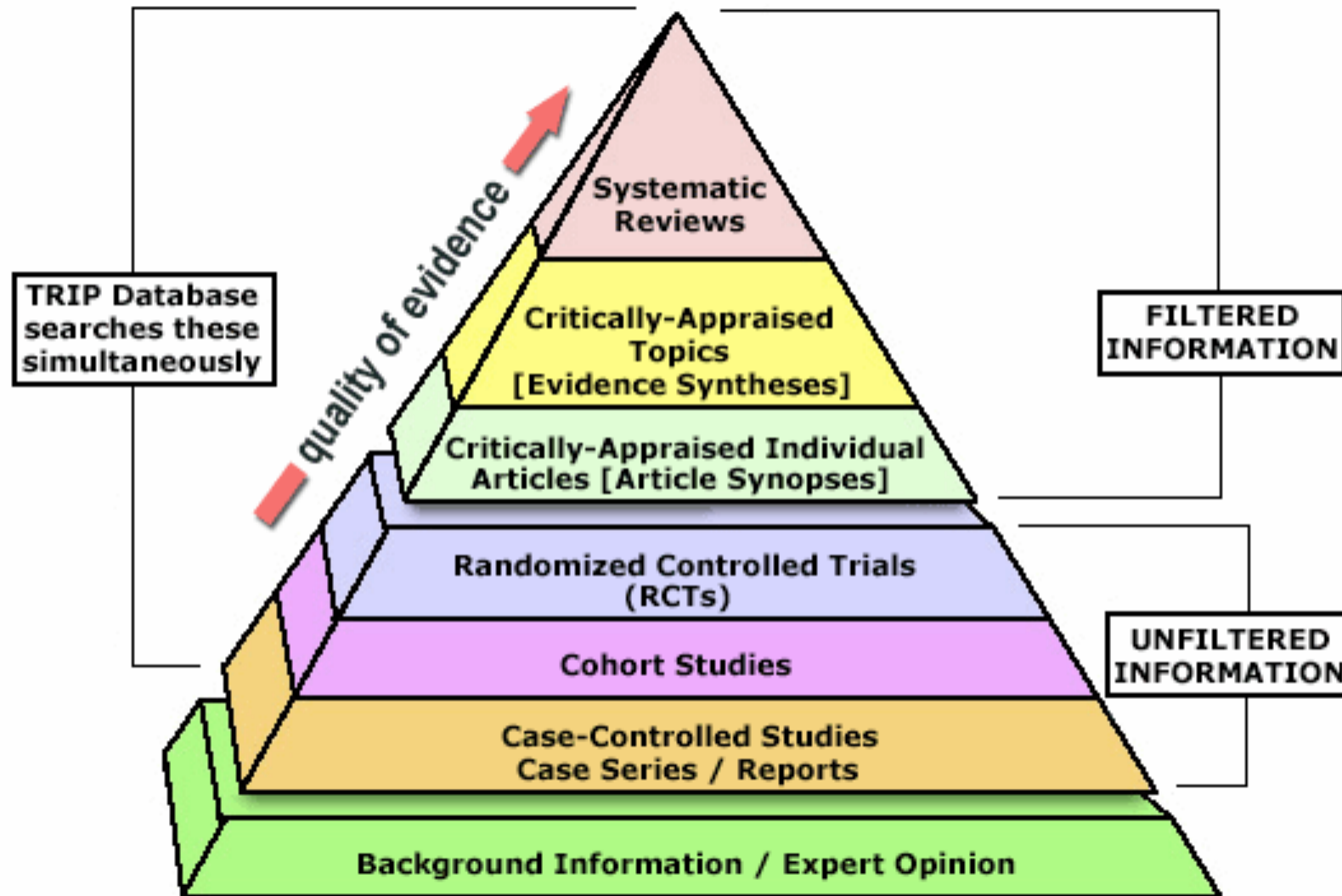
Limites de l'Evidence based medicine

« Supporters of EBM say that it has many benefits. It...

- ① ... allows clinicians to draw upon the **objective experience** of many researchers working with **accepted scientific standards**;
- ② ... improves **efficacy** and **efficiency** of providers;
- ③ ... decreases the use of **ineffective clinical practices**;
- ④ ... promises to better inform patients and clinicians about clinical practices by offering **collectively agreed upon and publicly available information** about treatment options;
- ⑤ ... provides a **scientific basis for the construction of health care policy**. »

Hasnain-Wynia R. « Is Evidence-Based Medicine Patient-Centered and Is Patient-Centered Care Evidence-Based ? », Health Services Research. 2006 February; 41(1): 1–8.

Limites de l'Evidence based medicine



Limites de l'Evidence based medicine

- ❖ Tension entre **logiques d'efficacité de la prise en charge** et **logiques de justification des choix thérapeutiques**.

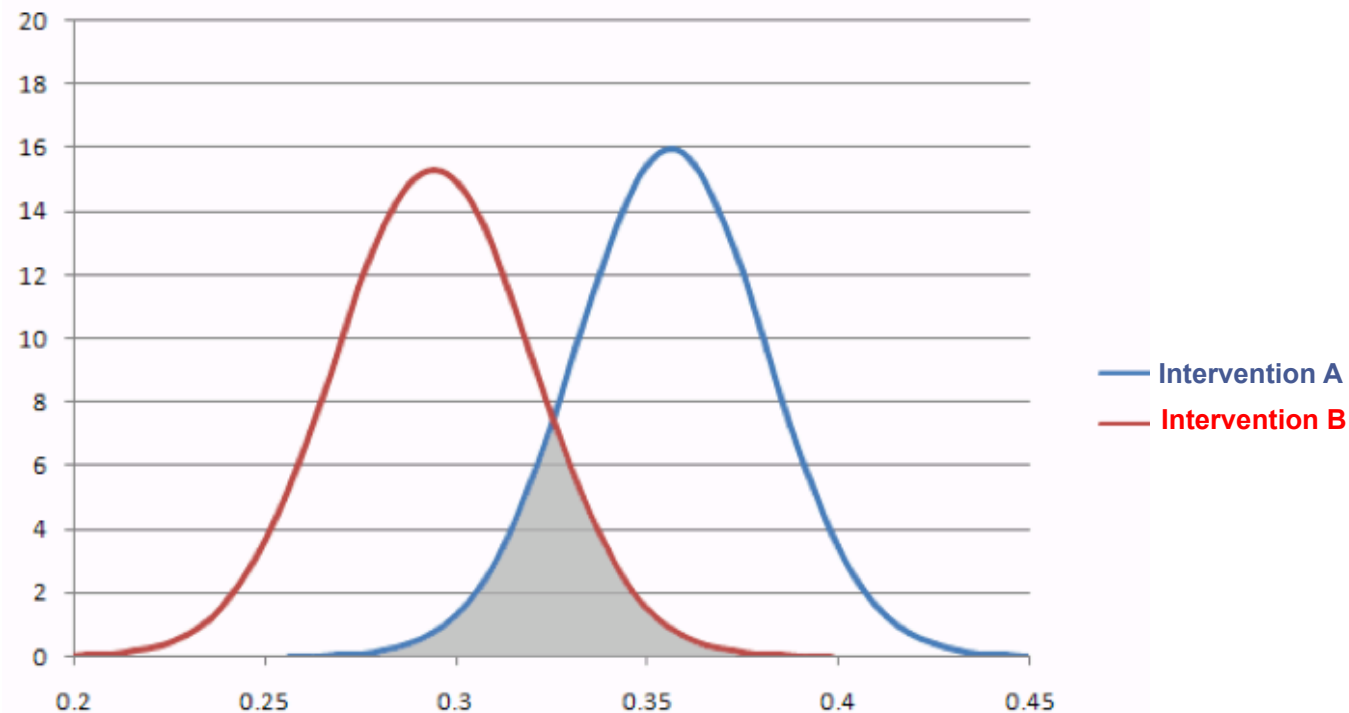
« EBM en viendrait à **contraindre l'idiosyncrasie des cliniciens** et, pour employer des termes statistiques, la variabilité autour de la moyenne de pratique dans l'espoir que cela améliore la qualité des traitements et les résultats pour la majorité des patients. »

Alain D Lesage, Emmanuel Stip, Frédéric Grunberg, « "What's up, doc?" Le contexte, les limites et les enjeux de la médecine fondée sur des données probantes pour les cliniciens (Evidence-Based Medicine) », *Rev Can psychiatrie* 2001; 46:396–402.

Limites de l'Evidence based medicine

- ❖ « At worst, a mean used in EBM might come from a bimodal distribution rather than a normal distribution (**making it generally inapplicable to most patients**), but even within a normal distribution some patients will lie at the far ends ».

Hasnain-Wynia R. « Is Evidence-Based Medicine Patient-Centered and Is Patient-Centered Care Evidence-Based ? », *Health Services Research*. 2006 February; 41(1): 1–8.



Limites de l'Evidence based medicine

- ❖ Le problème de l'intégration de l'**expérience singulière des patients** dans la validation de la **pertinence générale d'un traitement**.

L'expérience singulière est toujours corrélée à des formes de subjectivité, c'est-à-dire « la manière dont le sujet fait l'expérience de lui-même dans un **jeu de vérité** où il a rapport à soi. »

Michel Foucault, Dits et écrits IV, Paris, Gallimard, 1994 (1984), p. 633.



Limites de l'Evidence based medicine

❖ **Le problème de la standardisation.** Les opérations statistiques relatives aux essais cliniques portent sur des variables à la fois fines, ciblées et testées sur des grands nombres. Mais elles peinent à rendre compte de variables impliquées dans la production de différences biologiques. Pour rendre compte de ce genre de phénomènes, le sociologue Steven Epstein a proposé la notion utile de « **niche de normalisation** »:

« [The binary focus between universalism and particularism] diverts attention from **niche normalisation**: the biopolitical management (and redefinition) of population subgroups via a specification of standards at the 'intermediate' level of the categorical group. »

Steven Epstein, Inclusion: The Politics of Difference in Medical Research. Chicago: University of Chicago Press, 2007, p. 136.



Ancrages multiples du Pharmakon

Les effets spécifiques attribués aux psychotropes ne relèvent pas uniquement des qualités intrinsèques aux médicaments. Ces effets sont bien plus le résultat d'une **interaction complexe** entre **substance chimique, expertise médicale, expériences d'usagers et mode d'administration de la santé.**

A partir de: Andrew Lakoff, La raison pharmaceutique, Paris, Le Empêcheurs/Seuil, 2008, p. 11.





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30 comprimés

Merci de votre patiente attention



**Markus Raetz, Métamorphose
II (Beuys-Lapin) 1991-1992.**

Le « potentiel d'action des patients »

Rappel – La relation entre thérapeute et malade est aussi ancienne que l'humanité. Mais les modèles de relation thérapeutique entre celui qui soigne et celui qui est soigné varient beaucoup au fil du temps et à travers les sociétés.

Le **potentiel d'action des patients** est l'un des facteurs socioculturels et historiques de cette variation, laquelle caractérise les modèles de relation médecin-malade.



Le patient expert | partenaire | contradicteur

Accessibilité accrue aux sources d'informations médicales (laïcisation).

Développement de l'*empowerment* des patients (en part. mal. chroniques).

Réappropriation active du souci thérapeutique.

Meilleure gestion de leur condition/capital de santé.

Partenariat thérapeutique accru ET émancipation du patient par rapport au médecin.

Versus

Prolifération et fiabilité très inégale des sources d'informations médicales.

Rapport de forces dans la relation de soin et la prescription.

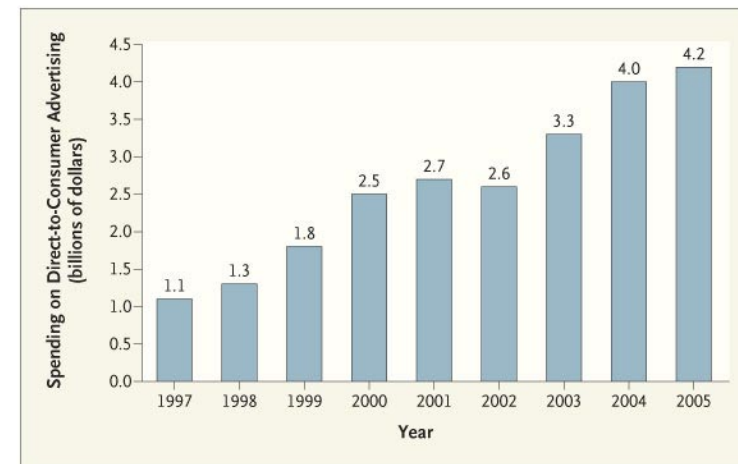
« Bricolage » de paradigmes corporels et thérapeutique.

Hybridation des itinéraires thérapeutiques.

Revendication de singularité

Le patient expert | partenaire. DTC: Direct-To-Consumer-Advertising

- ❖ +/- Relation de concurrence dans l'indication thérapeutique.
- ❖ + Meilleure connaissance des traitements et meilleure information des patients.
- ❖ - « Idées fausses »; demandes de traitements inutiles; pression à la prescription.
- ❖ - Participation au phénomène du « Disease mongering ».
- ❖ - « Liaisons dangereuses » entre campagnes de prévention et pharma provoquant une hausse de la consommation « préventive » de médicaments.



L'absence de « Témoins fiables »

Dans le cas des maladies psychiques et des troubles du comportement, dans la grande majorité des cas, **on ne trouve pas de marqueur permettant de prouver leur étiologie biologique**. Pour contourner cette **absence de témoin fiable** la psychiatrie est partie du principe suivant: « Ne jamais essayer de transporter la pathologie, mais transporter les effets de molécules dont on a constaté, par hasard, l'efficacité chez les patients ».

Dans le cas des des troubles du comportement, « le médicament joue deux rôles: celui de thérapeutique mais aussi celui du **témoin fiable absent** ».

Pignarre Philippe (2001). Comment la dépression est devenue une épidémie. Paris. La Découverte, pp. 79 et 68.

