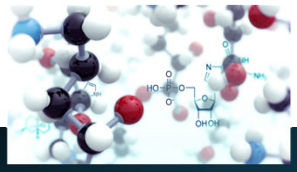
PSYKOSEMEDISINER OG HVORDAN BRUKE DEM



-Petra Thee Lybæk
Spesialist i psykiatri og klinisk farmakologi
Overlege, Psykosepoliklinikken OUS

1

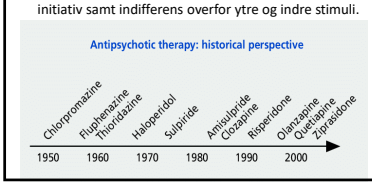
Disposisjon

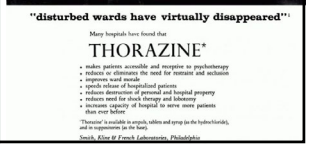
- Antipsykotika – hva er det?
- Salience og dopaminhypotesen
- Første og andre generasjon
- …men hvilken medisin skal jeg velge?
- Depot – hvorfor er det lurt?
- Injeksjonsteknikk – kan vi det?

2

Fra metylenblått mot malaria til antipsykotika

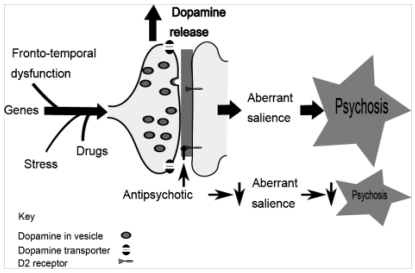
- Klorpromazin ble syntetisert i 1950 i Paris.
- Premedikasjon før kirurgi: pasientene ble indifferente overfor omgivelsene.
- 1952 utprøvning innen psykiatrien.
- Uspesifikk sedativ virkning i høyere doser, men også et helt spesielt syndrom (syndrome neuroleptique), med redusert spontan aktivitet, redusert energi og initiativ samt indifferens overfor ytre og indre stimuli.





3

Dopaminhypotesen: Dopamin styrer hva vi ilegger viktighet: **salience**

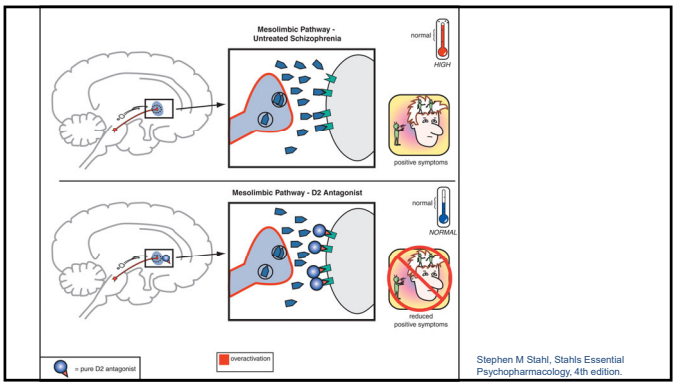


- Dopaminerg dysregulering.
- Multifaktorell utvikling
- Endrer vår vurdering av sensoriske stimuli
- Økt salience kan føre til utvikling av psykose.

Schizophr Bull. 2009 May; 35(3): 549–562. Published online 2009 Mar 26. doi: 10.1093/schbul/sbp006
The Dopamine Hypothesis of Schizophrenia: Version III—The Final Common Pathway
Oliver D. Howes[2,3] and Shitij Kapur[1,2]

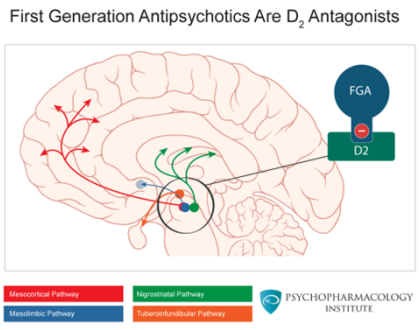
4

5



6

Virkningsmekanisme: dopaminblokkade



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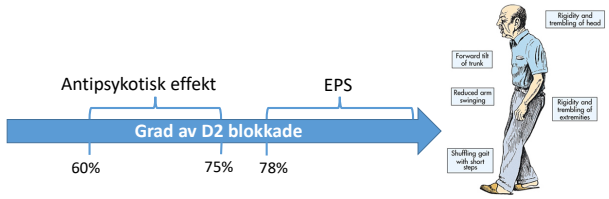
Dosekorelasjon mellom EPS og AP



Kapur S, Zipursky R, Jones C, et al. Relationship between dopamine D(2) occupancy, clinical response, and side effects: a double-blind PET study of first-episode schizophrenia. Am J Psychiatry 2000; 157:514.

8

Den antipsykotiske verktøyboks

- Førstegenerasjon : -D2-blokkere
- Andregenerasjon : -D2 og 5HT
- Partielle agonister

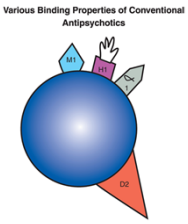
9

Førstegenerasjon / Nevroleptika / Typiske antipsykotika

- Hemmer dopamin
- Kan hemme H1, M1 og α1-reseptorer

FGA på markedet i Norge:

- haloperidol (Haldol)
- zuklopentiksol (Cisordinol)
- flupentiksol (Fluanxol)
- perfenazin (Trilafon, Peratsin)
- klorprotiksen (Truxal)
- levomepromazin (Nozinan)



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Andregenerasjon, en huskeregel

The -pines

- Klozapin (Leponex)
- Olanzapin (Zyprexa, ZypAdhera)
- Kvetiapin (Seroquel)
- Asenapin (Sycrest)

The -dones

- Risperidon (Risperdal) (?)
- Paliperidon (Xeplion, Trevicta)
- Ziprazidon (Zeldox)
- Lurasidon (Latuda)

De partielle agonistene

- Aripiprazol (Abilify)
- Brexpiprazol (Rxulti)
- Kariprazin (Reaglia)

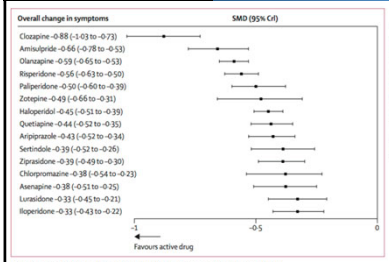
Resten

- Amisulprid (Solian)
- Sertindol (Serdolect)

11

Stefan Leucht og venner presenterer: Studien om antipsykotika du alltid har ønsket deg!

Ny versjon i 2019, med sammenlikning av 32 antipsykotika!



Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis

Figure 3: Forest plot for efficacy of antipsychotics drugs compared with placebo
Treatments are ranked according to their surface under the cumulative ranking (SUCRA) values (appendix p 98).

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Behandlingsalgoritme for schizofreni

- Antipsykotikum 1
- Antipsykotikum 2
- Klozapin

→ Norske retningslinjer

- Klozapin + aripiprazol ? → Mulig bedring av negative symptomer
- Kombinasjoner uten klozapin → Ikke evidensbasert

13

JAMA Psychiatry | Original Investigation

Association of Antipsychotic Polypharmacy vs Monotherapy With Psychiatric Rehospitalization Among Adults With Schizophrenia

Jari Tiihonen, MD, PhD; Heidi Taipale, PhD; Juha Mehtälä, PhD; Pia Vattulainen, MSc; Christoph U. Correll, MD; Antti Tanskanen, PhLic

- Registerbasert kohortstudie
- 62 000 pasienter
- **Klozapin + aripiprazol -> redusert risiko for tilbakefall / rehospitalisering sammenlignet med klozapin alene**

JAMA Psychiatry. 2019;76:499-507.

14

En lite kjent, men ganske utbredt sykdom…

- Uklar etiologi / patofysiologi
- Ingen diagnosekode
- Årsak til økt lidelsestrykk hos andre enn indekspersonene
- Rammer en svært selektert gruppe (kun psykiatere)
- Allmennleger..?

Klozafobi

Bilde: theinnerlynk.com
Kilde: The Art of Clozapine therapy and Clozaphobia | The BMJ

15

Depotpreparater

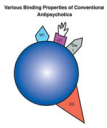
Førstegenerasjon

- Haloperidol
- Flupentiksol
- Perfenazin
- Zuklopentiksol

→ Dekanoater løst i olje

Andregenerasjon

- Risperidon – innkapslet i polymere mikrokuler
- Paliperidon - palmitat
- Olanzapin – pamoatsalt løst i vann
- Aripiprazol



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Virkestoff	Produktnavn	Doseintervall	Tmax	T1/2	Ref.omr.	Steady state
perfenazin	Trilafon dekanoat	78-156 mg hver 3-4 uke	7 dager	ca 2 uker	1-7 nmol/L	Ca 2-3 mnd
zuklopentixol	Cisordinol depot	200-400 mg hver 2-4 uke	3-7 dager	3 uker	5-50 nmol/L	3 mnd
flupentixol	Fluanxol depot	20-200 mg hver 2-4 uke	4-10 dager	3 uker	1-15 nmol/L	3 mnd
haloperidol	Haldol depot	25-150 mg hver 4. uke	3-9 dager	3 uker	2-25 nmol/L	3 mnd
olanzapin	ZypAdhera	150-300 mg hver 2. uke, 300-405 mg hver 4. uke.	2-6 dager	4 uker	30-200 nmol/L	3 mnd
risperidon	Risperdal Consta Okedi	25-50 mg hver 2. uke 75-100 mg hver 4. uke	30 dager 48 timer	3-6 d ?	20-120 nmol/L	8 uker ?
paliperidon	Xeplion / Trevicta, (Hafyera)	25-150 mg x 1 per mnd/ 175-525 mg hver 3. mnd.	13 dager/ 30-33 d	25-49 d/ 84-139 d	20-120 nmol/L	8-9 mnd / 15 mnd
aripiprazol	Abilify Maintena	300-400 mg hver 4. uke 720-960 mg hver 2. mnd.	deltoid: 4 d gluteal: 6 d	30-47 dager	200-1300 nmol/L	4-5 mnd

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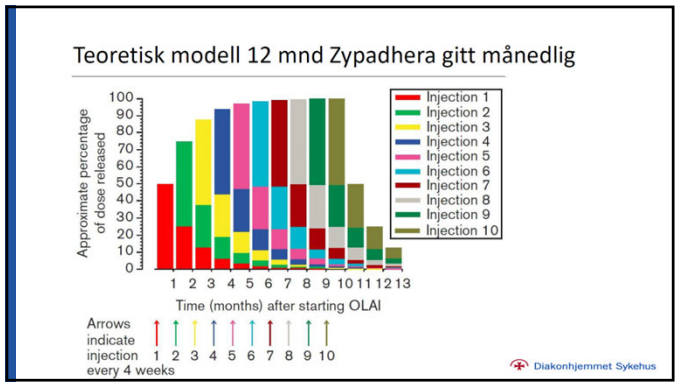

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Depotinjeksjoner

Fordeler

- Bedre etterlevelse
- Tettere oppfølging (?)
- Praktisk å slippe å huske piller hver dag.
- Lavere Cmax- mindre bivirkninger
- Høyere Cmin – mindre symptomgjennombrudd
- Jevnere konsentrasjon og mindre variasjon i eksponering over tid.
- Færre reinnleggelser, statistisk sett
- Lavere risiko for seponeringsreaksjoner

Ulemper

- Uønskede effekter og bivirkninger kan vare i månedsvis.
- Lang tid til steady state
- Lang tid å gjøre dosejusteringer og evaluere effekt
- Få preparater å velge mellom
- 3 timers observasjonstid etter ZypAdhera
- Kan vedvare i kroppen i månedsvis etter seponering og føre til utilsiktet polyfarmasi
- **Vi er sykt dårlige på I.M. injeksjonsteknikk!**

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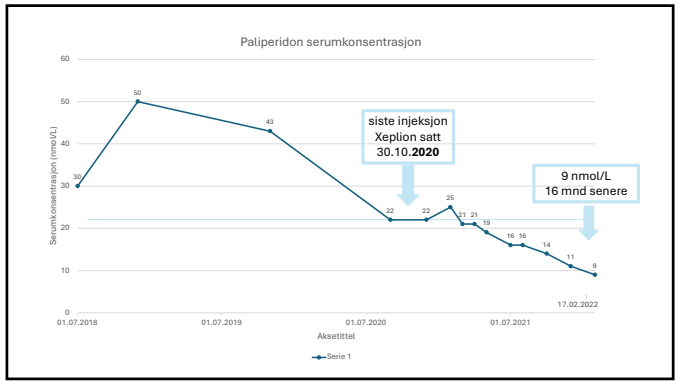

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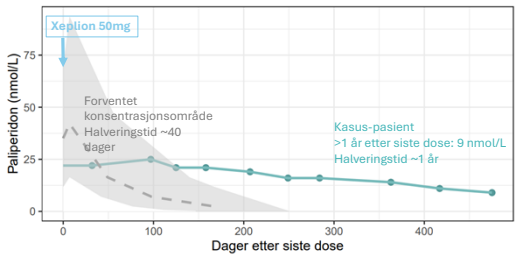
Simulert PK profil etter seponering av 50 mg Xeplion (FDA/Janssen) vs vår pasient



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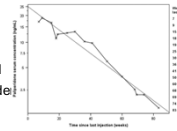
Journal of Clinical Psychopharmacology - Volume 35, Number 1, February 2015

Case report:

- 31 år mann, KMI 36
- 6 stk Xeplion injeksjoner over 4,5 mnd
- Lav S-paliperidon i behandlingsperioden (17-24 ng/mL) (ref 20-60 ng/mL)
  (40-56 nmol/L, ref 20-120 nmol/L)
- 1,3 ng/mL (ca. 3 nmol/L) 19 mnd etter siste injekson
- Normal nyrefunksjon
- Overvekt kan bidra til å forklare lavere konsentrasjon, men ikke lang halveringstid
- Ingen p-glykoproteinhemmere



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Prolonged Elimination of Paliperidone After Administration of Paliperidone Palmitate Depot Injections

To the Editors:

Paliperidone (9-hydroxy-risperidone), which is the pharmacologically active main metabolite of risperidone, has recently been

CASE REPORT

A 31-year-old obese man with schizophrenia (body weight, 125 kg; body mass index [BMI], 36.1 kg/m^2) who had been involuntarily committed to a mental health facility was given a total of 6 intramuscular injections of paliperidone palmitate (total dose in paliperidone equivalents 850 mg) in the gluteal area (alternating sides) during a 129-day (4.3-month) period.

22

The authors hypothesized that unintended injection into poorly vascularized subcutaneous fat could have led to delayed and/or erratic absorption of the drug.

Case Reports > J Pharm Pract. 2011 Dec;24(6):561-3. doi: 10.1177/0897190011426559. Epub 2011 Nov 2.

Case report: increased patient response to intramuscular haloperidol decanoate following a change in needle length

Nancy C Brahm [1], Nicole B Washington

Affiliations + expand
PMID: 22048930 DOI: 10.1177/0897190011426559

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> Eur J Radiol. 2006 Jun;58(3):480-4. doi: 10.1016/j.ejrad.2006.01.008. Epub 2006 Feb 21.

Intramuscular injections into the buttocks: are they truly intramuscular?

V O Chan [1], J Colville, T Persaud, O Buckley, S Hamilton, W C Torreggiani

Affiliations + expand
PMID: 16495027 DOI: 10.1016/j.ejrad.2006.01.008

Abstract

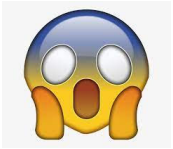
Aim: To radiologically determine if intramuscular (IM) injections into the buttocks are truly intramuscular.

Materials and methods: This was a prospective study conducted during a 6 month period beginning in October 2004. Fifty inpatients were recruited from a single tertiary referral hospital. Approval was obtained from the hospital research ethics committee and informed written consent was acquired from all participants. Prior to computerised tomography (CT), each patient received an IM injection of their prescribed medication along with 1 mL of air into the upper outer quadrant of the buttocks. CT images were subsequently analyzed by two radiologists to determine the position of the injected air bubble and to assess whether it was intramuscular or subcutaneous in position. Body mass index (BMI), distance to injection site, subcutaneous fat and muscle thickness were also measured.

Results: Overall, only 32% (n=16/50) of patients had intramuscular injections, with the majority of injections (68%, n=34/50) being subcutaneous. When analysed by gender, 56% (n=14/25) of males had intramuscular injections while in females, the efficacy rate was significantly lower at 8% (n=2/25).

Conclusion: The majority of assumed intramuscular injections are actually subcutaneous.

- Bare 32% av antatte IM injeksjoner treffer i muskel!
- Bare 8% hos kvinner!!!



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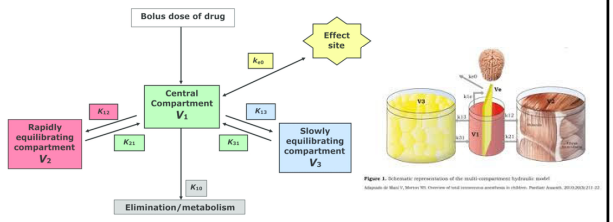
3rd space, tredje kompartment



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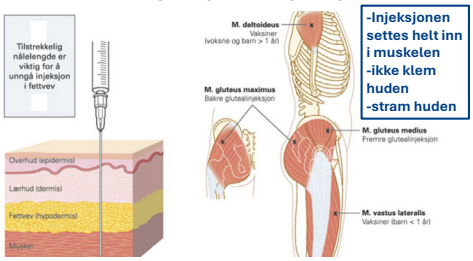
Intramuskulær injeksjon - injeksjonsteknikk



-Injeksjonen settes helt inn i muskelen
-ikke klem huden
-stram huden

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J Clin Nurs. 2021 Nov 17. doi: 10.1111/jocn.16126. Online ahead of print.

Dorsogluteal intramuscular injection depth needed to reach muscle tissue according to body mass index and gender: A systematic review

Pamela Strohfus [1], Sara Palma [1], Chelsea Tindell Wallace [1]
Affiliations + expand
PMID: 34791732 DOI: 10.1111/jocn.16126

Results: A significant number of dorsogluteal intramuscular injections are administered into subcutaneous tissue rather than muscle because needles are too short for populations with body mass indexes over 25, especially women. Poor landmarking often results in improperly placed injections.

Conclusions: To prevent administering a dorsogluteal intramuscular injection into subcutaneous tissue, women with a BMI of 25 and over require needles longer than 38 mm (1.5 inches).

If administering a **Deltoid** injection		If administering a **Gluteal** injection	
If patient weighs:		If patient weighs:	
Less than 90 kg blue hub	23G×1″	**Less than 90 kg** gray hub	22G×1½″
90 kg or more gray hub	22G×1½″	**90 kg or more** gray hub	22G×1½″

Nållengde Xeplion: 1 inch (25.4 mm) og 1.5 inches (38.1 mm)

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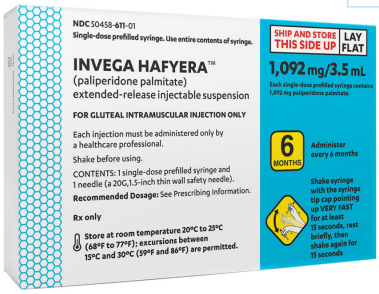
T1/2= ca. 150 dager.



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Takk for oppmerksomheten!
-Spørsmål?

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