

## ZUSAMMENFASSUNG

1. Die allgemeine Ansicht, dass Patienten mit schweren Rückenmarksläsionen völlig und dauernd impotent sind, ist nicht mehr haltbar.
2. Der ausgesprochen stimulisierende Effekt von Prostigmin auf die sexuellen Organe hat neue Möglichkeiten für klinische, biochemische und physiologische Untersuchungen in einem Gebiet eröffnet, wo bisher Spekulation und Deduktion an Stelle von klarem Beweis überwogen hat.
3. Verschiedene Typen und Grade sexueller Insuffizienz können durch den subarachnoidalen Prostigmintest ermittelt werden.
4. Zukünftige Untersuchungen der chemischen Zusammensetzung des Semen könnten Aufschluss über seine Morphologie und Funktion geben.
5. Der Prostigmintest kann für artifizielle Insemination verwandt werden. Eine genaue gynäkologische Untersuchung einschliesslich Bestimmung des besten Zeitpunkts für die Inseminierung ist notwendig.
6. Blutdruck und Puls muss regelmässig während des Prostigmintests gemessen werden, besonders in Läsionen oberhalb T<sub>5</sub>, um gesteigerte autonome Hyperreflexie durch geeignete Mittel (Ansolysen) auszuschalten.
7. Patienten, besonders solche mit Zervikalläsionen, sollen über mögliche unerwünschte Seiteneffekte unterrichtet werden.

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## SEXUAL FUNCTION AND DYSREFLEXIA

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In a previous paper (Rossier *et al.*, 1969), we have presented the case history of the successful delivery of a tetraplegic patient who showed symptoms of autonomic dysreflexia during labour. There were hypertension and bradycardia but no

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cardiac arrhythmia at any time during delivery. Catecholamine estimations were not carried out.

However, we felt that there was some evidence to suggest that there is a parallelism between the degree of activity of the uterus, the cardiovascular changes and the catecholamine levels. Garnier and Gertsch (1964) reported on variations of catecholamine levels in the urine of their patients during bladder dysreflexia.

With the exception of the article written by Guttmann in 1953, there is no other mentioning of a relationship between autonomic dysreflexia and sexual function. Intrathecal injections of neostigmine in spinal cord patients are known to elicit ejaculations with or without erections (Guttmann, 1953; Spira, 1956). We had the occasion to repeat a neostigmine test twice in the same tetraplegic for an artificial insemination. During a trial in January 1969 every ejaculation after the neostigmine injection was followed by severe symptoms of dysreflexia with important modifications of cardiac activity. Therefore, during another trial in August 1969, we considered it safer to look for cardiovascular changes in order to be ready to take the necessary therapeutical measures since cerebral haemorrhages are known to be a potentially dangerous complication during such hypertensive episodes (Thompson & Witham, 1948; Jung & Schmidt, 1962). We studied in detail the modifications of the blood pressure and of the heart activity by continuous intrafemoral monitoring and by electrocardiography. During the examination we measured the catecholamines in several blood samples as well as in various portions of the urine (at the beginning and at the end of the test.)

#### CASE REPORT

Following fracture-dislocation C6-C7 in a car accident on 24.11.1961, this 30-year-old patient sustained a complete tetraplegia C7-C8. He married three years after his

Sch. V. ♂ 22.5.1939

Complete tetraplegia C7-C8 bilat.

Fract. disl. C6-C7 (car accident: 24.11.1961).

Prostigmine test on 27.8.1969.

Continuous recording of blood pressure by intrafemoral catheter with simultaneous electrocardiogram.

Recording made 62 minutes after the intrathecal injection of 0,25 mg of prostigmine.



FIG. 1

Intraarterial pressure monitoring showing one out of the four short-lasting increases of blood pressure which occurred after the first intrathecal injection of neostigmine.

Time	Remarks	Plasma samples	Urine samples	Adrenaline	Noradrenaline
09:00	BP: 105/70				
09:45	Pulse: 65				
10:10	basic value	Nr 1	Nr 1 (catheterisation: 500 cc)	$\phi$ 0.002	$\phi$ 0.011
10:37	0.25 mg neostigmine intrathecally: marked salivation				
11:16	BP: 80/50				
	pulse: 70				
11:34		Nr 2		0.124	
11:39	1st elevation of BP: 119/80. Pulse: 58				
13:50	0.25 mg neostigmine intrathecally				
13:56	BP: 130/70				
	pulse: arrhythmia between 47 and 64				
14:20		Nr 3		0.237	
14:49	BP: 220/110				
	pulse: 60				
14:53	1st ejaculation: BP: 210/120				
	many heterotopic complexes				
15:08	2nd ejaculation: BP: 210/100	Nr 4		0.734	
	pulse: 80 to 110				
	few isolated heterotopic complexes				
15:16	3rd ejaculation: BP: 220/100				
	pulse: 80				
15:25	4th ejaculation	Nr 5	Nr 2 (catheterisation: 500 cc)	0.017	0.295
15:55					0.058
17:00	BP: 160/70				
19:00	BP: 160/70				
20:00	BP: 120/65				

N.B. Urine values in gamma per mg. creatinine. Plasma values in gamma per litre plasma. Sch. V ♂ 1939. Neostigmine test on 27.8.69.

FIG. 2

Relationship between ejaculations, blood pressure, pulse and dosage of adrenaline and noradrenaline in blood and in urine.

injury. He has a balanced bladder function with sterile urine. But he has spontaneous and mechanical erections of too short a duration to permit intercourse. No ejaculation. There is a left congenital cryptorchidism. Voiding, bowel movements and erections have always been accompanied by symptoms of autonomous dysreflexia such as shivering and headaches.

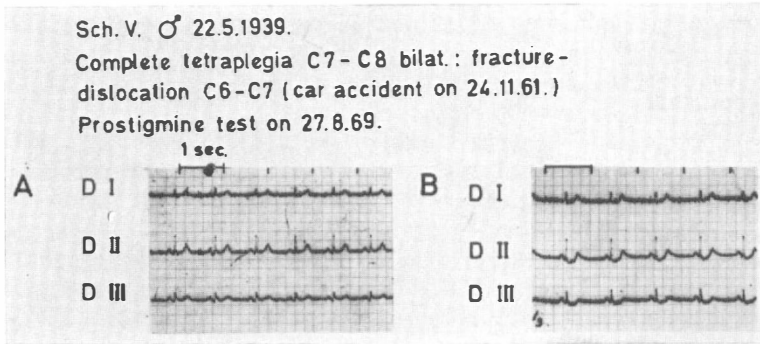


FIG. 3

A, ECG at rest. B, ECG at the end of the neostigmine test after the last ejaculation took place.

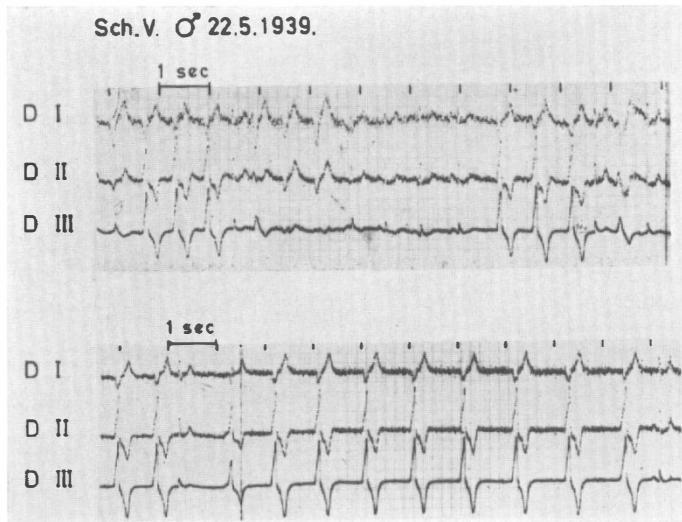


FIG. 4

Outbursts of heterotopic complexes during the first ejaculation following the second intrathecal injection of neostigmine in the same test.

In the tests it was necessary to repeat the initial injection of 0.25 mg. neostigmine as it did not produce any ejaculation but a moderate and short-lasting increase of blood pressure with bradycardia (fig. 1). The first ejaculation started one hour after a second injection of 0.25 mg. neostigmine and it was followed by three others. An erection never occurred. During the first ejaculation the blood pressure rose to 210/120 mm. Hg and there appeared numerous heterotopic complexes. It is of interest to note that the

highest blood pressure values were found at the time of each ejaculation; however, contrary to what was to be expected, the blood pressure did not come back to normal between ejaculations and the hypertension persisted. A normal blood pressure was found, however, only about four hours after the last ejaculation took place (fig. 2).

Except for heterotopic periods there was a normal sinus rhythm. There has been, however, a progressive change of the P.Q. interval; the initial interval was 0.16 sec. and it ended with 0.12 sec. Q.R.S. remained unchanged until the end of the examination; on the other hand, a slow and progressive change of S.T. could be seen. S.T. decreased by 2 mm. in lead II (fig. 3).

The cardiac rate varied between 58 and 110; at rest it was 65. It reached 110 during the second ejaculation while the blood pressure was 210/100 mg. Hg. This tachycardia lasted about 10 seconds before it decreased and remained at 80.

There were about 20 heterotopic complexes during the first ejaculation with a widening of Q.R.S. 0.12 sec. and a T which was negative as it can be found in a branch block (fig. 4).

## DISCUSSION

There have been several papers devoted to blood pressure changes and cardiac modifications especially during bladder filling but also during uterus contractions (Guttmann & Whitteridge, 1947; Schumacher & Guthrie, 1951; Cunningham *et al.*, 1953; Kendrick *et al.*, 1953; Mertens *et al.*, 1960; Garnier *et al.*, 1963; Guttmann, 1963; Guttmann *et al.*, 1965; Roussan *et al.*, 1966; Rossier *et al.*, 1969). This work seems to be the first one to have studied cardiovascular changes by intra-arterial monitoring and by electrocardiogram during sexual activity of a cord patient where ejaculations were provoked by intrathecal injection of neostigmine which elicited severe symptoms of autonomous dysreflexia. Elevation of urinary catecholamines, which were first observed by Garnier *et al.* (1963) to play an important role in dysreflexia, were also found to be elevated not only in the urine but also in the blood of our patient. A close relationship has been established between ejaculations, hypertensive crises, changes in heart activity and level of catecholamines.

The progressive lowering of S.T. could be explained as an auricular T; it could also be the result of hypertension or express a temporary coronary insufficiency.

It is of interest to note the modification of the extreme rhythm, heterotopic complexes, which has a low frequency ranging from 65 to 55 within 9 beats. These heterotopic complexes appear when the catecholamine levels in the blood are the highest. One may imagine a compensatory regulative vagotonia which stops the stimulus at the level of the auricles in favour of a ventricular stimulus which takes over for want of something better.

As there has been an increase in noradrenaline and adrenaline production, it can be supposed that an important and temporary excitation of alpha receptors took place or at least that there was a predominant alpha stimulation. This hypothesis seems to be corroborated by the fact that alpha receptors blocking agents such as phenoxybenzamine suppress autonomic dysreflexia; this has been shown by Sizemore and Winternitz (1970) although the lack of increase in urinary catecholamines found by these authors in their patients is contrary to Garnier and Gertsch's results (1964) and to our findings. We have been able to demonstrate a urinary increase in production of adrenaline and noradrenaline. A similar increase in production of total catecholamines in blood was seen. The clinical

	pH	Count (million/cc)	Total count (per ejacul.)	Mobility (in %)	Degree	Type of progression	Abnormal form (in %)
1st trial (27.9.67) without insemination	7	24	108	40	2+(3+)	?	?
	7	30	96	40	3+(2)	?	?
	7	26	44.2	40	3+(2+)	?	?
2nd trial (10.1.69) with insemination	6.7	43	2.967	10	2-	Jerky to erratic	—
	6.9	45	990	10	2-	Jerky to erratic	—
	6.9	16	256	10	2-	Jerky to erratic	—
Treatment with HMG (pergonal)							
3rd trial (27.8.69) with insemination	7	8	36	10	2	Erratic	30
	7.2	7	14.7	< 10	2	Erratic	64
	7.2	7	5.6	—	2-	Erratic	70

Sch. V, ♂ 1939. Results of neostigmine tests.

FIG. 5

Spermiograms showing the evolution of the quality and quantity of the spermatozoa in three different neostigmine tests.

features shown by our patient (arrhythmia, hypertension, bradycardia, headaches, sweating) correlate well with these biochemical results.

One might suppose that changes in blood pressure are produced by changes in the heart output. Cunningham *et al.* (1953) have shown that this is not the case and that changes in peripheral vascular resistance are responsible for it. Likewise Schumacher and Guthrie (1951) have shown that headaches are caused by a secondary passive distension of cranial arteries due to the elevation of the systemic arterial pressure which follows the vasoconstriction of the limbs and visceral bed.

Initial bradycardia could be explained either by an overproduction of norepinephrine (Allwood *et al.*, 1963) or by a central regulative mechanism via receptors from the aortic arch and carotid sinus and the tenth cranial nerves, or by both. The switch from bradycardia to tachycardia could be explained by a maximal liberation of catecholamines, a condition leading to hypertension and arrhythmia.

There is a marked difference between the hypertensive crises which are provoked by bladder or uterine contractions and those which are elicited by ejaculations. In fact, there is a fast decrease in blood pressure between bladder and uterine contractions, but in our patient hypertensive values around 160/170 and 190/100 mm. Hg were recorded between ejaculations. The blood pressure came back to its normal value only more than four hours after his last ejaculation took place. This apparent discrepancy could be due to the intrathecal pharmacological effect of the neostigmine, which acts upon the medullary elements.

It may be of interest to note that in one of our tests the first ejaculation took place 63 minutes after the second injection of neostigmine, and 75 minutes later in the other one. Guttmann (1953) and Spira (1956) reported similar figures.

Unfortunately none of our tests resulted in a pregnancy. Looking at the results of the spermograms on three different occasions (fig. 5), a decrease in the quality of the spermatozoa can be observed. It has to be mentioned that our patient received a treatment with human menopausal gonadotrophins between the last two tests.

## CONCLUSION

It can be said that there exists a close relationship between sexual activity, symptoms of autonomous dysreflexia and catecholamine levels in blood and urine of patients with high spinal cord lesions. In view of the known potential danger of intracranial haemorrhage during hypertensive episodes in dysreflexia one should encourage a better control of cardiovascular changes by monitoring of blood pressure and by electrocardiogram during neostigmine tests which have been shown to provoke a marked elevation of the blood pressure and an important arrhythmia. Such a test is not without danger and ought to be carried out under careful observation. In view of the value which a successful pregnancy after a neostigmine test would represent and in order to increase our knowledge regarding fertility of spinal cord patients it is hoped that this paper will stimulate wider interest in this field.

## SUMMARY

The authors have discussed the case history of a tetraplegic patient with complete cord transection at C7-C8 who ejaculated after intrathecal injections of

neostigmine. The ejaculations were accompanied by severe symptoms of autonomous dysreflexia consisting of hypertension and cardiac arrhythmia recorded by continuous intraarterial pressure monitoring and electrocardiography. Catecholamines were measured in blood and urine during the examination. A close relationship was found between ejaculations, blood pressure, cardiac rate, cardiac rhythm as well as calibration on one hand, and catecholamine levels on the other hand. A predominant excitation of alpha receptors is suggested.

### RÉSUMÉ

Les auteurs discutent le cas d'un patient atteint d'une tétraplégie traumatique complète C7-C8 qui présenta des éjaculations après des injections sous-arachnoïdiennes de néostigmine. De sévères symptômes de dysréflexie autonome accompagnèrent ces éjaculations sous forme d'hypertension et d'arythmie enregistrées par moniteur de pression intra-artérielle et par électrocardiogramme. On procéda à des dosages des catécholamines dans le sang et dans l'urine et on put démontrer qu'il y avait un rapport étroit entre les éjaculations, la pression artérielle, la fréquence, le rythme et la calibration cardiaques d'une part et le taux des catécholamines de l'autre. Les auteurs suggèrent une prédominance d'excitation des récepteurs alpha.

### ZUSAMMENFASSUNG

Die Autoren diskutieren den Fall eines traumatischen Tetraplegiker, der Ejakulationen nach subarachnoidaler Injektion von Neostigmin hatte. Schwere autonome Dysreflexie begleitete die Ejakulationen in Form von Hypertension und Arrhythmien, gemessen bei intraarteriellen Druck und Elektrokardiogramm. Katecholamine im Blut und Urine wurden bestimmt zwischen den Ejakulationen mit arteriellen Druck und Rhythmusfrequenz. Die Autoren nehmen eine Prädominanz von Stimulation der Alpha-rezeptoren an.

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### Discussion

Dr. R. SPIRA (*Israel*). I will speak about a successful case of artificial insemination, of which I am bound to say that it is the only success, and in view of the other failures about which you heard there might possibly be some doubt about the paternity in this case. I should mention that it wasn't all that smooth sailing, as we had three previous prostigmine tests in this case which weren't successful, and between the second and third we had done very intensive hormone treatment, which improved considerably the sperm count. On the fourth attempt, which was the last one, it was successful. The pregnancy and delivery were normal and the geneticians and cytologists found it difficult to understand what all the fuss was about, the case was authentic because of the blood group which was suitably matched, and which almost conclusively proved the paternity of the father. There was a second child born in the same family two or three years later. Since a prostigmine test was done in a different centre I cannot claim the authenticity of the second child. All other cases we have done prior to that one were unsuccessful. The last one was done at our hospital on a tetraplegic C6 complete, and we then injected what seems now to be too large a dose, which was 0.4, and there was a very large rise of blood pressure and the injection at that test did not result in obtaining a pregnancy.

Dr. A. JOUSSE (*Canada*). I wonder if you can inform me as to how many of these patients were clinically complete and how many were incomplete. I have one incidence, a man and a woman I knew very well so I assumed there was no collaboration on the side in this case, that I always suspected having listened to Dr. Munro's residents many years ago, who were very sceptical about the results that he hoped had occurred. This man, when he enquired from me as to the possibility of procreation, followed my sage advice, I told him never to give up, and indeed his wife did bear a child. So, for some reason or another it can happen without chemical stimulation, other than that which is inborn. I wonder, too, why prostigmine is not effective if given orally in adequate doses; why must it be given intrathecally?

With regard to what Mr. Talbot said, I have some experience about sex problems with paraplegic patients, I have interviewed many patients on this point. One of the things they told me is that in several cases there was a sort of erogenic area above the highest segment of anaesthesia, to compare with what we see with reflexes. So, they could have satisfaction by rubbing of that area and by touching or letting it be touched. I think it is worth while to know this. I have some questions, apart from this prostigmine injection: Is there experience with conserving of hyperfertile sperma with the use of it for artificial insemination later on? Because, some of my patients ask me the following question: Is it possible for young, male paraplegics, fresh cases, to obtain their sperm and to conserve it for artificial insemination when they are later married? And the last question: I have been told that Dr Schwarzmann in Brussels sometimes makes spermatocele with the help of the vena saphena. In that case, you can get sperms by puncture