CHANGES IN THE DUODENAL CONTENT FOLLOWING CARBACHOL

BY

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Our knowledge of the effects of choline and its derivatives on the human pancreatic secretion is of comparatively recent date. This is partly because studies in the human subject require a special technique for the recovery of the content of the duodenum and partly because of the uncertain composition and unstable nature of the earlier preparations of the chemical mediator. Ågren and Lagerlöf (1936) overcame the first difficulty by resorting to a combined gastro-duodenal tube, which allowed the stomach and the duodenum to be drained simultaneously. Methacholine chloride *B.P.* (acetyl- β -methylcholine chloride, "methylol") was among the first of the synthetic analogues of acetylcholine to be investigated. It was shown by Comfort and Osterberg (1940) to affect the pancreas in a manner almost indistinguishable from that resulting from vagal stimulation. As is now well known, methacholine promotes an increase in the flow of secretion which, though less in quantity than that following humoral stimulation, is much richer in the three ferments; and the effect on the hydrogen-ion concentration is negligible. "Urecholine," the urethane of methylcholine chloride, is similar in its action (Kyle *et al.*, 1950).

It appears that these choline derivatives also exert an influence on the bile flow, as evidenced by an increase in the concentration of bilirubin and its total value per unit of time. This effect is usually detected with the naked eye. Comfort and Osterberg were inclined to ascribe these changes to contraction of the gall-bladder, but, as Kyle *et al.* pointed out, it may occur in those who have had their gall-bladder removed. There are grounds, therefore, for assuming that the cholines stimulate the flow of hepatic bile. Needless to say, much has been written about the nervous control of the bile flow.

The purpose of this investigation was to study the effects of carbachol (carbaminoylecholine chloride) on the duodenal contents, with particular reference to the changes in (1) volume and colour, (2) lipase concentration, and (3) the total lipase per unit of time.

Methods

Contamination of the duodenal juice was reduced to a minimum by the use of a modification of the gastro-duodenal tube, which was not procurable at the time this work was undertaken. Two Ryle's duodenal tubes were stuck together throughout their length by rubber solution. The bulbous extremity of the one intended for the stomach was then cut off and the cut end slit for a short distance to allow this part to be wrapped round the duodenal one about 10 cm. from the latter's extremity. Perforations were made in the gastric tube at a site which would ensure simultaneous emptying of the stomach and duodenum. The paired tubes were passed at 8 a.m., after a fast lasting approximately 10 hours. Ten healthy young adult male volunteers were studied. The technical procedure adopted for the withdrawal of the duodenal content followed that described by Diamond *et al.* (1939). After a basic flow had been established the duodenal fluid was decanted for testing every 10 minutes, the gastric fluid being discarded. Each subject

received 0.25 mg. of carbachol intramuscularly. Four 10-minute fractions were taken off before and four after its administration. The lipase estimations were carried out by the method described by Cherry and Crandall (1932), and it was found convenient to dilute each sample to a strength of 1:10 with distilled water.

The Resting Duodenal Fluid

This is a clear yellow-to-amber-coloured fluid with an approximate pH of 8. The presence of turbidity or a fall in the pH values was taken to indicate contamination with gastric chyme. Suspected samples were discarded.

The volume recovered in the 10-minute periods varied from 0.5 to 15.2 ml., the average for all of the control samples withdrawn from the 10 subjects being 3.5 ml. This may seem a wide variation, but to the best of one's knowledge the fractions were composed of pancreatic juice, bile, and such secretions as came from the duodenal mucosa with the barest minimum of gastric juice.

The concentration of lipase expressed in terms of millilitres of N/20 sodium hydroxide per ml. of duodenal fluid ranged from 46 to 136, the average being 91.7 ml.

The total value for lipase expressed in terms of millilitres of N/20 sodium hydroxide per total sample varied from 35 to 1,155.2, with an average of 303 ml.

The Effects of Carbachol

The volume of the duodenal content was increased in 7 of the 10 experiments. The change was most noticeable after 30 minutes.

In all except the first, a pronounced deepening of the normal bile-staining was observed within 10 minutes of the administration of the drug. The affected samples also became appreciably more viscous.

Composite graph showing average findings for volume of duodenal content and lipase concentration per 10-minute sample and lipase per total sample before and after carbachol.

The concentration of lipase was raised in all but two of the subjects. In three instances the values were modified within 10 minutes, but the response was not maximal until the third or fourth fractions.

The total values for lipase appeared to be raised in all except one, and again it was observed that the highest values were usually obtained 30 minutes after carbachol.

The averages for all the above findings are presented in the form of a composite graph.

Summary

"Pure" duodenal juice was obtained by applying continuous suction to two Ryle's tubes, one of which lay in the stomach, the other in the duodenum.

An intramuscular injection of 0.25 mg. of carbachol was given to 10 fasting young adult males. An increase in the volume of the duodenal content resulted in 7, an increase in the lipase concentration in 8, and an increase in the total value for lipase per unit of time in 9 of the subjects. On the whole these effects were most pronounced about 30 minutes after the giving of carbachol.

Evidence is presented that this drug also stimulates an increased flow of bile.

The findings indicate that carbachol excites the external pancreatic secretion in humans.

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Medical Memoranda

A Cauda Equina Lesion due to Spondylolisthesis

The following interesting case is rare enough to be placed on record.

CASE REPORT

A man aged 52 had complained of partial incontinence of urine since October, 1945. In the previous January a road accident was the cause of a transient haematuria. Investigation at the former date revealed a distended bladder and a well-developed inferureteric bar, which was divided through a cystotomy incision. This failed to improve the incontinence.

He was seen again in September, 1949, and in addition to his urinary difficulties his left foot felt useless and often caused him to fall. He had normal control over his bowels except when he had an enema or when he had diarrhoea and his bowel tended to prolapse.

On examination he was found to be a thin pale man dribbling urine and passing flatus without regard to social conventions. He had bilateral inguinal herniae and an incisional hernia below the umbilicus. No neurological abnormalities were found in the cranial nerves or arms. The optic disks were normal and the abdominal reflexes brisk. His left foot was seen to be plantar-flexed and inverted, and there was obvious wasting of the left calf and both buttocks. The knee-jerks were present, but the ankle-jerks were very weak even with reinforcement. Tone was normal and there was no clonus. Stimulation of the outer border of the soles brought no response. There were gross sensory changes. The areas supplied by L 1, 2, 3, 4, and 5 dermatomes had normal sensibility, but he had well-defined saddle anaesthesia over his lower buttocks and round the front of his anus and the posterior aspects of both thighs corresponding

to S 1, 2, and 3. The anus was patulous. There was also alteration of the sensation on the lateral side of both soles, accounting for the absent plantar reflex. His joint and vibration sense was normal.

Detailed examination of his muscles revealed the following state of affairs (muscles found to have normal power are omitted from the Table):

Muscle	Main Segmental Innervation	Power (M.R.C. Classification)	
		Right	Left
Gluteus maximus	L 5 S 1	4	4
" medius	L 4 and 5 S 1	4	5
Peroneus	L 5 S 1	3	3
Tibialis posterior	L 4	5	4
Gastrocnemius	S 2	5	3
Ext. hallucis longus	L 5	3	1
" digitorum	L 5	3	4
" " brevis	S 1	0	0
Flex. " longus	S 2	5	2
" " hallucis "	S 2	5	2

Investigations.—His Wassermann reaction was negative. Radiological examination showed a gross localized osteoarthritis involving the third and fourth lumbar vertebrae and a second-degree spondylolisthesis (Prip Buus, 1943) at the lumbo-sacral articulation, with considerable osteoarthritic changes. These changes were present in the film taken in 1945, thus absolving the accident from blame. Cystoscopy: The bladder capacity was 1 pint (570 ml.), and the patient had the normal sensation of distension. There was fine trabeculation of the vesical wall, and the posterior urethra presented a funnel-shaped deformity, allowing extensive visualization of the prostatic urethra. No "bite" was felt when a large steel bougie was passed.

The patient was readmitted in October, 1949, with a transverse fracture of his left patella and again in March, 1951, with a similar fracture of his right patella, from a fall on each occasion. Both were sutured and united satisfactorily.

COMMENT

Organic nervous changes in spondylolisthesis are rare in spite of the extreme degree of subluxation which can occur. Burns (1931-2, 1934-5) and other authors deny that it ever happens. Heinrich and Krupp (1938) suggest that such changes are seen only in pure traumatic lesions such as fracture or total dislocation of the vertebra. They emphasize that riding-breeches anaesthesia and sphincter disturbances are but rarely seen. Lane (1893) reported a case in which he operated, but this was probably due to a prolapsed intervertebral disk. Friberg (1939) found sensory changes in 8 out of 302 cases, and Meyerding (1931, 1938) in less than 2% of his 583 patients. Of the 27 patients reported by Prip Buus, three had sensory changes and only one a cauda equina lesion.

The mechanism of the lesion is not as obvious as it first appears. By extradural myelography Prip Buus has shown that the posterior longitudinal ligament becomes detached from the posterior surface of the slipping vertebral body (usually the fifth lumbar), and that there is no narrowing of the spinal canal. If anything, the antero-posterior diameter is increased. Even in Stage IV, when the fifth lumbar vertebra is in front of the first sacral and its lower border sunk below the level of the upper border of S 1 (spondylolisthesis), he considers that the size of the canal is still adequate to accommodate the cauda equina. Furthermore, the intervertebral foramen is situated close to the vertebral body and accompanies its related body during the forward shift. Thus the nerve is not impressed directly and, if anything, becomes more relaxed. This I have confirmed by direct measurement on the skeleton.

A coincidental prolapsed intervertebral disk has been incriminated for the neurological disturbance, but in Prip Buus's case of cauda equina lesion no such disk was demonstrated on myelography. Prip Buus concludes that the nervous dysfunction is attributable to a chronic irritative arachnoiditis or to a chronic inflammation of the extradural tissue.