1. INTRODUCTION

The concept of the viscero-vascular reflexes dates back to as early as 1899 (SHERRINGTON, 1899). SHERRINGTON described the occurance of hypertension in response to the distension of hollow viscera in spinal animals. These observations were later supplemented by clinical studies on paraplegics (HEAD and RIDDOCH, 1917; GUTTMANN and WHITTERIDGE, 1947). Along with the clinical studies a wealth of experimental evidences on this subject has also been accumulated.

1.1. Cardiovascular changes with distension of the urinary bladder

1.1.1. Changes in the arterial pressure

Over half a century ago it has been reported that patients with acute retention of the urine were exhibiting raised blood pressure, which regressed following drainage of the bladder (O'CONOR, 1920). This work was later extended on normal human subjects as well as on patients with urologic disorders. These studies showed that peripheral vasoconstriction occurs when the urinary bladder was uncomfortably filled when the intravesical pressure exceeded 50 Torr (ADAMS-RAY and NORLEN, 1951; DIGHIERO et al., 1962; TAYLOR, 1963; SZASZ and WHYTE, 1967). Interestingly enough elderly atherosclerotic patients responded with a relatively high increase of blood pressure during the filling of the bladder (GARNIER et al., 1964).

One of the first detailed experimental studies on the effects of urinary bladder distension came from TALAAT (1937) and from WATKINS (1938). Both these studies have shown an increase of the arterial pressure in response to the distension of the bladder in anaesthetized dogs and cats. Furthermore, in cats there was a positive correlation between the elevation of the

arterial pressure and the bladder pressure. Sudden emptying of the bladder resulted in a return of the blood pressure to the original level, rarely with an undershoot (WATKINS, 1938). Subsequent studies were able to confirm the elevations of the arterial pressure associated with the urinary bladder distension in anaesthetized animals (MUKHERJEE, 1957 b; TAYLOR, 1963; TULIN, 1964; SHAH et al., 1965).

On the other hand, there are some evidences showing that the distension of the bladder is not accompanied with an increase in the arterial pressure. ROBERTSON and WOLF (1950) could not observe any change in the blood pressure when the urinary bladder of normal subjects was distended to a pressure of 40 Torr. Similarly, in anaesthetized animals no increase or a negligible increase in the arterial pressure during the bladder distension was also observed by other investigators (DOWNMAN and McSWINEY, 1946; BERMAN and ROSE, 1958; MAY and BARELARE, 1958). The question arises whether or not the pressures exerted may have been too low.

TAYLOR (1965) tried to characterize the arterial pressure response resulting from bladder distension in anaesthetized cats with an intact nervous system. According to this author the amplitude of the increase in the arterial pressure was dependent upon the rate and the volume of the distension and also on the spontaneous isometric contractions of the bladder following the distension. Unless excessive bladder distension was present the elevation of the blood pressure produced was usually less than 20 Torr. The elevation of the blood pressure was caused by peripheral vasoconstriction. In contrast to rapid bladder filling, slow distension of the bladder with a flow rates of 0.3 - 1 $ml \cdot min^{-1}$, needed not necessarily be accompanied by a change in the arterial pressure. Slow distension of the bladder, however, resulted in hind limb vasoconstriction without any change in the arterial pressure and with a decrease of cardiac output and an increase of the central venous volume (TAYLOR, 1973).

SASZ and WHYTE (1967) made a detailed study on normal human subjects. They observed a significant increase in both systolic

and the diastolic pressure when the urinary bladder was distended to a maximal tolerable limit. There was a positive correlation between the increase in the arterial pressure and the bladder pressure. It is noteworthy that there was no difference in the arterial pressure taken before and after micturition.

Thus from these foregoing studies it seems that a gross distension of the bladder, and perhaps discomfort was necessary to produce an effect on arterial pressure in human beings and in anaesthetized experimental animals with an intact nervous system.

In continuation of the early studies of SHERRINGTON (1899) on viscero-vascular reflexes in spinal animals, GUTTMANN and WHITTERIDGE (1947) studied the effects of vesical distension in paraplegics. They found that the rise in the blood pressure was always higher in patients having spinal cord lesions between C_8-T_5 than those with lesions between T_6-T_{10}. This difference was attributed to the effect of buffer nerves counteracting the vaso-pressor responses in patients having lesions between T_6-T_{10} more effectively than in patients having lesions between C_8-T_5. In addition, they also observed engorgement of the veins of the neck, marked dilation of the heart, feeling of tightness of the chest and shallow breathing - a situation resembling incipient cardiac failure. Later investigations on the paraplegics have shown that the blood pressure started to increase when the bladder pressure was as high as 40 to 70 Torr: bladder distension initiated vasoconstriction of the skin below the lesions associated with an increase in both the systolic and diastolic blood pressure, particularly the latter (SCHUMACHER and GUTHRIE, 1951; CUNNINGHAM et al., 1953). Similar increase in the arterial pressure was also reported by others (BORS and FRENCH, 1952; KURNICK, 1956; ARIEFF et al., 1962). Associated with the increase of the arterial pressure there was a patchy vasodilatation of the skin of the face and neck, headaches and mass involuntary peripheral muscle spasms were also noticed (HUTCH, 1955). A recent study of WURSTER and RANDALL (1975) on the problem of vesico-vascular reflexes in paraplegics is more or less in agreement with the earlier study of GUTTMANN and WHITTERIDGE (1947). These investi-

gators divided the paraplegics into two groups, one having lesions between C_4-C_5 and the other at lower levels i.e. T_4-T_5. Those patients having higher lesions responded with a gross elevation in the systolic arterial pressure and the pulse pressure during bladder distension. Whereas, a less pronounced elevation in these parameters was noticed in those having lower lesions (T_4-T_5). Moreover, there was a marked vasoconstriction in the skin areas innervated by the 'isolated' spinal cord, while passive dilatation occurred in areas supplied by the proximal cord.

Being unable to observe any increase in the arterial pressure with bladder distension in anaesthetized cats with an intact nervous system, DOWNMANN and McSWINEY (1946) studied viscero-vascular reflexes on acute spinal cats (C_8-T_1). They observed marked elevations of arterial pressure in response to visceral stimulation in these animals. Increase of systemic arterial pressure with bladder distension was consistently seen in acute spinal cats (C_8-T_1) (MUKHERJEE, 1957a) and also in spinal dogs (RUBINSTEIN and CARREA, 1961).

From these studies it is apparent that a marked elevation in the arterial pressure does occur in paraplegics and in acute spinal animals in response to vesical distension.

1.1.2. Changes in venous pressure

In addition to the arterial pressure changes, there is an evidence of venoconstriction during distension of the urinary bladder (CUNNINGHAM et al., 1953; BURCH and DE PASQUALE, 1958; TAYLOR, 1974). In one of these studies (BURCH and DE PASQUALE, 1958) it was reported that the venous pressure in the isolated superficial venous segment in the forearm increased when the bladder was filled with 50 ml of fluid. This venomotor response was inhibited after regional procaine block of the vein and was

also absent after transection of the spinal cord. Therefore this response was considered to be a segmental spinal venomotor reflex.

On the other hand, mechanical effects due to overdistension of the bladder in human subjects was also reported in the clinical literature. Overdistension of the bladder resulted in a compression of the iliac veins and if lasting long enough leading to cyanosis of the lower extremities and massive leg and scrotal edema. Some of these patients were also having high arterial pressure. All these circulatory disturbances disappeared upon emptying the bladder (CARLSON and GARSTEN, 1960; STOUTZ, 1961; SMITH et al., 1963).

1.1.3. Changes in cardiac output

CUNNINGHAM et al. (1953) did not observe any change in cardiac output in response to the bladder distension in paraplegic patients. However, in anaesthetized non-spinal dogs HOROWITZ et al. (1966) reported an increase in cardiac output during vesical distension. But slow distension of the bladder (0.3 - 1 $ml \cdot min^{-1}$) in anaesthetized cats resulted in a decrease of cardiac output, before any change in the blood pressure occured (TAYLOR, 1973). It is possible that changes in the cardiac output during the distension of the bladder depend on the species studied and also upon the rate of the distension.

1.1.4. Changes in heart frequency

With extreme distension of the bladder normal subjects responded with tachycardia and arryhtmias, usually ventricular extrasystoles (YAMAGUCHI et al., 1964; TAYLOR, 1974). In contrast, ARIEFF et al., (1962) and SAZSZ and WHYTE (1967) could not observe

any change in the pulse rate and no specific diagnostic changes in the ECG, with bladder distension up to the point of pain in normal subjects.

Bradycardia was known to occur with bladder distension in paraplegics having lesions between cervical and thoracic region of the spinal cord (HUTCH, 1955; WURSTER and RANDALL, 1975). The possibility of a positive inotropic effect was also suggested in patients having lesions below the T_5-level (WURSTER and RANDALL, 1975).

One of the early reports on the vesico-cardiac reflexes in several species of lower animals was described by CARLSON and LOCKHARDT (1921). They observed that the heart responded with a prompt brady cardia during mechanical and electrical stimulation of the urinary bladder in decerebrated frogs and salamanders. Similar bradycardia associated with strong electrical and mechanical stimulation of the bladder was also reported by other investigators (SAMONINA and UDELNOV, 1965). Increase of the heart frequency with urinary bladder distension was also reported (AKHMEDOV and PLAKHOTIN, 1966; HORWITZ et al, 1966).

This discrepancy in the observations on heart frequency seems to be settled by the work of TAYLOR (1968). According to his experimentation there was a biphasic response in the heart frequency when the bladder was distended in anaesthetized, non-spinal cats. There was a bradycardia during the early stages of bladder filling and in the later stages of filling there was a tachycardia associated with a vasoconstriction. With extreme distension cardiac arrhythmias such as ventricular or nodal extrasystoles were seen.

Thus from the foregoing review of the literature it is established that marked cardiovascular alterations accompanied the distension of the bladder. These changes are seen in normal human subjects, paraplegics and also in non-spinal and acute spinal animals. However, the magnitude of the cardiovascular

changes, especially the increase in the arterial pressure, depends on the severity of the bladder distension. In experimental studies it appears that some of these effects resulting from the bladder distension may be primary and some secondary caused by baroreceptor or other reflexes. Besides the neurogenic influences affecting the cardiovascular changes during the bladder distension, mechanical factors resulting from the overdistended bladder received little attention. It is noteworthy that in most of the experimental studies, the bladder distension was carried out for a short period of time i.e. approximately 2 min., thus leaving the question open what happens to the cardiovascular changes if the distension is maintained for a longer period; a condition simulating the clinical situation.

1.2. Respiratory changes during the bladder distension

Unlike the information available on cardiovascular changes, only few studies were reported on respiratory changes with bladder distension.

In their study on paraplegics GUTTMANN and WHITTERIDGE (1947) reported shallow breathing during vesical distension. Since they described the condition of their patients as resembling incipient cardiac failure, the breathing pattern seems to be secondary to the cardiovascular alterations rather than a direct result from the bladder distension. Also in the experimental animals respiratory changes vary to a great extent with the bladder distension. In some instances increased frequency of respiration, in others a depression of frequency of respiration was noticed (WATKINS, 1938; MUKHERJEE, 1957 b; AKHMEDOV and PLAKHOTIN, 1966; SHAH et al., 1965).

Thus from the limited literature available, it becomes apparent that little attention has been paid to respiratory changes occuring during the bladder distension.

1.3. Possible mechanisms responsible for the cardiovascular and respiratory changes during bladder distension

The possible mechanisms involved in the cardiovascular and respiratory responses to bladder distension may be subdivided into neural and humoral mechanisms.

1.3.1. Neural mechanisms

1.3.1.1. Afferent pathways

The term 'vesico-vascular reflex' has been liberally used in the literature cited in the foregoing résumé. So at this point it is desirable to review the pertinent literature dealing with the afferent pathways. The hypogastric, the pelvic and the pudic nerves contain afferent fibers originating from the bladder and the urethra. TALAAT (1937) recorded the sensory impulses from all the three afferent nerves of the bladder.According to him the activity of the hypogastric nerve increases with high bladder pressures and the sensory receptors belonging to this nerve are of the slowly adapting type. Whereas, the pelvic nerve activity increases even when the bladder was filled with small volumes and also with low intravesical pressures. Most of the nerve endings belong to the rapidly adapting and some of them to the slowly adapting type. The sensory receptor fibers in the pudic nerve are exclusively of the rapidly adapting type. After establishing the nature of the bladder sensory receptors, he distended the urinary bladder and observed an increase in the arterial pressure. After bilateral denervation of the hypogastric nerves the increase in the arterial pressure was either abolished or reduced, whereas cutting the pelvic nerves had no effect. From these observations he suggested that the hypogastric nerve is the principle afferent nerve for the hypertensive responses during bladder distension. In contrast are the findings of WATKINS (WATKINS, 1938), who states that the arterial pressure changes resulting from the bladder distension would be completely abo-

lished after bilateral denervation of the pelvic and hypogastric nerves and lays much emphasis on the pelvic nerves as the main afferent pathway. He also suggests that the bladder pressure is the effective stimulus responsible for the increase of the arterial pressure.

Later TAYLOR (1968) from his studies concluded that vesicovascular reflexes are initiated mainly by tension changes in the region of the trigone and bladder neck rather than by the pressure, volume or ischemia of the bladder. These regions of the urinary bladder correspond with the maximum sensory innervation as demonstrated by histology (GARRY and GARVIN, 1957; UEMURA et al., 1975). Electrophysiological investigations have shown that the receptors of the pelvic nerve afferents are concentrated in the bladder neck region and belong to the tension type of sensory receptors (IGGO, 1957; 1966). TAYLOR (1968) reported that the cardiovascular responses were reduced after section of the sacral posterior roots but were abolished only when the posterior roots as high as T_{10} were cut. He suggested that the major afferent pathway could be either the pelvic nerve or hypogastric nerve.

From these studies it seems that an uncertainty exists whether the pelvic or the hypogastric nerves constitute the afferent pathway. This means that the question of their relative contributions to the increase of the arterial pressure observed during bladder distension still remains open.

1.3.2. Efferent mechanisms

1.3.2.1. Neurogenic mechanisms

Bladder distension has been found to affect all parts of the sympathetic nervous system. Reported reflex responses in human subjects include peripheral vasoconstriction (ADAMS-RAY and NORLEN, 1951; TAYLOR, 1963; GARNIER et al., 1964), and peripheral

venoconstriction (BURCH and DE PASQUALE, 1958).

In anaesthetized cats renal vasoconstriction was known to occur in response to the bladder distension. Bilateral splanchnicotomy not only abolished the renal vasoconstriction but also the hypertensive response induced by vesical distension. Therefore it was suggested that splanchnic nerves are the major efferent pathway in the vesico-vascular reflex (MUKHERJEE, 1957 b).

Bradycardia which was observed during the initial stages of the bladder distension is mediated through the efferent vagus nerve. During mild stimulation of the urinary bladder there is a decrease in the neural activity of the efferent vagus nerve, while with strong stimulation an increase of the activity in the vagal fibers associated with the inhibition of the cardiac contraction was noticed (SAMONINA and UDELNOV, 1965).

Any information regarding the possible mechanisms of the respiratory changes is lacking in the literature.

1.3.2.2. Humoral mechanisms

Besides the neurogenic mechanisms, the participation of vasopressor hormones was also suggested (HORWITZ et al., 1966). There was an increase of the norepinephrine excretion in the urine with vesical distension in paraplegics (GARNIER et al., 1963). Recently GILMORE and VANE (1971) reported an increase of the blood catecholamine concentration and also of prostaglandin like material during the vesical distension in anaesthetized dogs.

Thus it seems that some of the cardiovascular changes could be due to the release of adrenergic substances. However, the possibility of the release of other pressor substances during the bladder distension still remains a promising working hypothesis.