Pre- and Para-Medications in Bronchoscopy*

The Concept of “Broncho-Softening”

R. BENDA, M.D., P. BENDA, M.D., E. ORINSTEIN, M.D., and P. DELIGNÉ, M.D.
Paris, France

It has become easy to explore the respiratory tract—the necessary instruments are greatly improved and easy to manipulate, and the use of local anesthesia is well established. Medication which, as a sedative, combines morphine and atropine, the anti-secretive effect of which is excellent, is satisfactory to bronchologists in a great majority of cases, so that few attempts have been made to modify the technique generally used.

Nevertheless, there are some difficult bronchoscopies which are not to say “impossible.” Often the difficulties are caused by the patient's fears, whether at the first trial or at a series of examinations; or they may result from buccal-mandibular malformation (for example, where the face has been mutilated). Once the glottal passage has been traversed, apart from a stricture of organic origin, one may encounter bronchial spasm, or sometimes a curve to the left more accentuated than usual.

To improve the technique and, therefore, the results of endoscopy, one would have to reinforce or perfect the means of:

1. Dissipating the patient's fears.
2. Facilitating the tracheal tube insertion.
3. Eliminating any eventual bronchial spasm and even extending the passage of the tube beyond the usual limits.

Pre-medication would be affected mostly by the first two indications, and para-medication by the third. But, indeed, several of these indications overlap and it is only for purposes of classification that we list them chronologically.

I. PRE-MEDICATION

Out of the many drugs we explored with a view to their effective use prior to intubation, only two were kept: diethazine and an anesthetic steroid (Viadril).

1. Diethazine (or 2987 R.P.)**

For the morphine-atropine pre-medication used currently we substitute a combination of diethazine with atropine.¹

Let us recall briefly the properties of 2987 R.P. This product has been used in the treatment of Parkinsonian syndromes. It is a salt of diethylamino-2'-ethyl N-dibenzopara-thiazine.

It results from the condensation of a salt derived from diethylamino-ethanol which enters into the composition of numerous medicaments (pro-

---

¹Presented at the Fourth International Congress on Diseases of the Chest, American College of Chest Physicians, Cologne, Germany, August 19-23, 1956.

**Latibon (Bayer).
caine, certain spasmolytics and sympatholitics) and of an elixir of thiodiphenyl-amine.

In the parasympathetic ganglions, 2987 R.P. causes a vagal paralysis without the effect of the acetylcholine being appreciably modified.

In the sympathetic ganglions, it produces a similar paralysis which manifests itself, for example, by its antagonism to the tension-causing effects of nicotine.

It also opposes adrenalin secretion of the adrenal medulla following the stimulation of the splanchnic nerves provoked by asphyxiation.

It also exercises a central analgesic action.

Pre-medication by diethazine aims at preventing, or diminishing, bronchospasm, an action resulting from the anti-nicotinic properties of 2987 R.P. In fact, experience has shown us further results: not only does diethazine simplify intubation, but it often permits attaining unusual depths in the bronchial tree without forcing the basal bronchi (as is shown by a cinematographic sequence showing an air cyst, distal and invisible on x-ray films, either standard or tomographical). This is the first demonstration of the "bronchial-softening" effect.

The dose of diethazine, injected intramuscularly a quarter of an hour before the local anesthetic, is the same for all patients: 250 mg, dissolved in 5 ml. of physiological saline, mixed with 1.0 mg. of atropine sulphate in the same syringe.

The product has only one drawback, and that a minor one. The day after the injection it causes a rather severe pain in situ, which may persist for two or three days. A greater dilution in physiological saline and dividing the total dose into two injections, one on the right, and the other on the left, corrects this drawback to a certain extent.

2. Anesthetic steroid (P 55 or Viadril)

Even though diethazine produces consistently satisfactory effects by a simple method, there remains, nevertheless, a certain group of patients whose emotions or tenseness risk upsetting the endoscopic exploration. For them we can use an anesthetic steroid, the succinate of 21-hydroxy-pregnandione, investigated by Laubach and his collaborators.

This product is a white crystalline powder, soluble in water, with a molecular weight of 432. In solution, its pH is 8.5 to 9.8. It has no toxic effect, and does not cause retention of sodium.

In weak doses it causes simple hypnosis. In strong doses (for example, 1.5 gm.) it produces anesthesia, which begins after five minutes and may continue for a long time.

Bronchoscopy usually requires neither deep nor prolonged anesthesia. In any particular patient, the use of P 55, as pre-medication, is justified by the state of calmness it produces and by its quasi-selective action on the striated glottal muscle, facilitating greatly the tracheal tube insertion.

It is on this account that we have been led to modify the doses injected in general anesthesia by the team from the University of California, and even the technique of injection. Two hours before the endoscopic exploration, we start an intravenous infusion into an antecubital vein (using a
<table>
<thead>
<tr>
<th>Names</th>
<th>Pre-medication I.M. injection</th>
<th>Atropine 1 mg.</th>
<th>Para-medications (Succinylcholine 2 mg. + Lignocaine 0.5 mg.)</th>
<th>Broncho- -sparing Effect</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dor...</td>
<td>I.M. injection</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Mar...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Chat...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Gol...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Tho...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>+ sleep during the procedure</td>
</tr>
<tr>
<td>Cai...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>0 organic narrowing</td>
</tr>
<tr>
<td>Azé...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>0 organic narrowing</td>
</tr>
<tr>
<td>El. H...</td>
<td>id. (+ previous Viadril)</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Dur...</td>
<td>id. (+ previous Viadril)</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Pou...</td>
<td>id. (+ previous Viadril)</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Le G...</td>
<td>id.</td>
<td>I.V. injection</td>
<td></td>
<td>++</td>
<td>visibility of the division of Nelson bronchus</td>
</tr>
<tr>
<td>Thom...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Mart...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++ left curve ++ passed over</td>
</tr>
<tr>
<td>Le F...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++ left curve + passed over</td>
</tr>
<tr>
<td>Ker...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Tid...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Der A...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>0 organic narrowing</td>
</tr>
<tr>
<td>Rol...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++ spasmodic narrowing</td>
</tr>
<tr>
<td>Aug...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Blo...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Gic...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Rem...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Yah...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Bou...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Fil...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Zac...</td>
<td>id.</td>
<td></td>
<td></td>
<td></td>
<td>++ spasmodic narrowing</td>
</tr>
<tr>
<td>Tab...</td>
<td>id. (+ previous Viadril)</td>
<td></td>
<td></td>
<td></td>
<td>+ no local anesthetics</td>
</tr>
<tr>
<td>Ves...</td>
<td>id. (+ previous Viadril)</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Luc...</td>
<td>id. (+ previous Viadril)</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Hel...</td>
<td>id. (+ previous Viadril)</td>
<td></td>
<td></td>
<td></td>
<td>++</td>
</tr>
</tbody>
</table>
20 gauge needle) of 250 ml. physiological saline to which is added 5.0 mg. of Viadril per kilogram of body weight. The speed of infusion is regulated to last for two hours.

From this, one does not obtain a true anesthetic effect, but before long a complete euphoria is established, or a total indifference to the procedure. At completion of the injection, the subject is capable of getting up unaided, and is ready for the laryngo-tracheal anesthesia. From here on the procedure becomes simple and, once the bronchoscopy is concluded, the patient quickly returns to normal activity.

This technique of preliminary intravenous infusion avoids the salivary hypersecretion, which the rapid intravenous injection of the anesthetic steroid provokes. The atropine, always concurrently used, diminishes still further the risk of sialorrhea.

As this technique is not as simple as the first, we need to use P 55 only in the following cases:

1. Anterior failure of the glottal passage.
2. Very frightened or agitated subjects.

Pre-medication, then, by diethazine alone, or by diethazine and Viadril, permits one to obtain a certain "broncho-softening" effect with the first drug, and quieting effects, accompanied often by an actual glottal gaping, with the second.

The "broncho-softening" effect is enhanced by para-medication, which we accomplish with a synthetic curare-like compound.

II. PARA-MEDICATION

The first investigations of two of the authors, with Paillas and Maroger, were concentrated on the natural alkaloid of curare (d-tubocurarine), the particular action of which, on the bronchial tonicity, has been described precisely under the name of "broncho-softening effect." We have abandoned it recently in favor of diiodide of succinylcholine, one of the most remarkable among the numerous synthetic curare-like compounds proposed in recent years, by reason of its transitory action, which makes it especially easy to handle. Bovet and his collaborators have described this product. Its brief action appears to be connected with its rapid hydrolysis by the plasma cholinesterase, whereas most of the curare-like compounds are essentially excreted by the kidneys.

With succinylcholine one finds again the broncho-softening effect of d-tubocurarine. As we stressed at the very beginning of our studies on the use of curare in bronchoscopy, "the bronchi become soft, extraordinarily flaccid; it almost seems as if they open up before the bronchoscope; they permit an easy progression of the tube, which reaches the terminal branches of the bronchial division and sometimes even goes into them. The leftward bronchial curve is easily overcome." The only cases in which observations of this extent are not possible are in the organic stenoses.

*One should carefully estimate any eventual risk in a few clinical cases, such as marked respiratory insufficiencies or severe vegetative disturbances (asthma).
In other words, this broncho-softening effect may be appreciated:
1. By the facility which one experiences, once the scope has been introduced into the respiratory tract, in moving the instrument back and forth inside the bronchial lumen.
2. By the possibility, when encountering a bronchial zone which is in spasm, of traversing it, once an injection of this product is given.

To sum up, such “broncho-softening” would not be appreciated without the presence of the tube in the bronchus; it is only noted by mediate tactile perception. One can see how this distinguishes it from bronchodilatation (Figure 1).

The interest in these facts appears to us twofold:
1. From the doctrinal point of view, they show the action of curare on smooth muscle, by the probable intermediary of the neuro-vegetative system.

Years ago Vulpian and, more recently, Langley pointed out that curare blocks the synaptic ganglionic transmission. Luco and Mesa utilized the pupillary response of the cat and the contraction of the nictating membrane, and demonstrated the blocking of cholinergic synapses. MacIntyre concedes that all the tissues where acetylcholine intervenes are susceptible to curare in varying degrees.

Clinically, Gross and Cullen point out the diminution of intestinal peristalsis; Batelli, and Switski, that of contractions of the stomach; and

![Diagram](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21309/) FIGURE 1: The “broncho-softening” would not be apparent without the presence of the tube in the bronchus. N = Normal. \( N + E \) (epsilon, ancient Greek letter meaning a very small quantity) = Moderate expansion of the bronchus from broncho-dilating agent alone. \( N + Q \) = More extensive expansion of the bronchial lumen. The bronchial wall is now more expansible when the bronchoscope is inserted and is capable of greater dilatation.
Cornet has verified for us, in the course of gastroscopies, the pyloric atony due to curare.

2. From the practical point of view—the one which interests us especially here—the same circumstances permit an extension of the field of exploration of the bronchoscope, revealing sometimes a lesion inaccessible with standard technique, and even allowing a biopsy otherwise impracticable.

In our first trials, the doses of succinylicholine, administered intravenously, varied from 5 to 30 mg. A broncho-softening effect, remarkable by its constancy and by its intensity, showed itself even in weak doses, smaller than 0.2 mg./kg. In such small doses, however, where the peripheral muscular relaxation is slight or even absent, one could still observe, in certain subjects, a short period of apnea. Although such a reaction could give no unfavorable results, it did stimulate us to seek by means of various substances (chlorpromazine, in particular), with the object of diminishing still more the dose of the active product to be injected.

At the present time, our preferences are turning to a derivative of acetanilid, lignocaine (or xylocaine), itself efficacious in small doses. Thus the mixture in the same syringe of 2 mg. of succinylicholine and 5 mg. of xylocaine (in a solution of 1 per cent) represents a uniform dosage which, introduced intravenously, obtains an undeniable broncho-softening effect, while keeping well below the apnea dose.

The curare-like compound must be ready, together with xylocaine, before starting the bronchoscopy, but held in reserve and only used when necessary. It will prove efficacious where the pre-medication has not sufficed.

We are reporting, in Table I, 30 unselected cases of endoscopic examinations done recently, which illustrate the possibilities and the limits of the means employed. One can see, as we stated at the beginning of this paper, that pre- and para-medications have overlapping indications. Thus, diethazine has broncho-softening effects; likewise it is a central sedative, but the broncho-softening effects are more marked with succinylicholine. On the other hand, the anesthetic steroid, even though it has no broncho-softening effect, acts on the striated glottal muscle and facilitates tube insertion. In this respect, its action completes, on the laryngeal level, the broncho-softening effects of curare-like compounds and of diethazine at the level of the smooth bronchial muscle. It is, besides, a powerful sedative, with hypnotic effect.

Finally, we propose the following schema for pre- and para-medication in bronchoscopy:

a) In non-nervous subjects
   1. The injection of diethazine-atropine preceding by a quarter of an hour the beginning of:
   2. Local anesthesia.
   3. When necessary (for example, a difficult leftward curve, spasm, etc.) succinylicholine, in very small, non-apnea producing doses, combined with xylocaine, injected intravenously.
b) In nervous subjects

During the two hours which precede the bronchoscopy, an intravenous infusion of P 55 should be administered, designed solely to facilitate the tube insertion.

Following this infusion of P 55, one returns to the above schema (a): that is, the preparation by diethazine-atropine; and subsequently, when necessary, intravenous injection of a combination of succinylcholine and xylocaine in very small doses.

SUMMARY

With a view to improving the technique and, consequently, the results of bronchial endoscopy, the authors have systematically employed, as premedication, diethazine combined with atropine; and in some cases, an anesthetic steroid (P 55). A certain “broncho-softening effect” is obtained with the first drug; a tranquilizing effect, accompanied by a veritable glottal gaping, with the second.

But the broncho-softening effect is, first and foremost, linked with paramedication, which consists of a small dose of a synthetic curare-like compound, díodide of succinylcholine, the action of which is potentiated by the addition of an equally small dose of lignocaine.

The concept of “broncho-softening” under the influence of succinylcholine, in particular, permits an extension of the field of exploration of the bronchoscope, revealing sometimes a lesion which would be inaccessible with standard technique, and even allowing an otherwise impracticable biopsy.

Addendum

Recently, we employed Chlorpromazine as a premedication: 25 mg., dissolved in 5 ml. of physiological saline, injected intramuscularly 20 minutes before the local anesthesia.

This drug had favorable effects: we noted its strong tranquilizing properties. Also its anti-secretive power was evident on endoscopic examination of the tracheobronchial tree, although no atropine had been given.

RESUMEN

Con la mira de mejorar la técnica y consecuentemente los resultados de endoscopía bronquial, los autores han empleado sistemáticamente la premedicación por la Diethazine combinada con atropina; y en algunos casos un esteroides anestésico (P-55).

Cierta “efecto de ablandamiento bronquial” se obtiene con la primera droga; un efecto tranquilizante, acompañado de una verdadera relajación glótica con la segunda.

Pero el efecto de ablandamiento bronquial es primero y principalmente ligado a la paramedicación que consiste en una pequeña dosis de un compuesto sintético análogo al curare, díoduro de succinilcolina, cuya acción es potencializada por el agregado de una dosis igualmente pequeña de lignocaina.

El concepto de “ablandamiento bronquial” bajo la influencia de la succinilcolina en particular, permite una extensión en el campo de la exploración de la broncoscopia revelando a veces una lesión que sería inaccesible
con la técnica común y permitiendo aún una biopsia de otra manera impracticable.

RESUME

En vue d’améliorer la technique et, partant, les résultats de l’endoscopie bronchique, les auteurs ont utilisé, à titre de prémédication, systématiquement : la diéthazine associée à l’atropine ; éventuellement : un stéroïde anesthésique (le P 55). Un certain effet “broncho-émollissant” est obtenu avec la première drogue ; un effet apaisant, s’accompagnant d’une véritable béanée glottique, avec la seconde.

Mais l’effet broncho-émollissant est surtout lié à la para-médication qu’ils font avec de très faibles doses d’un curarisant de synthèse, le diiodure de succinylcholine (dont l’action est potentialisée par l’adjonction de doses également très faibles de lignocaine).

La notion de “broncho-émollients” sous l’influence de la succinylcholine, en particulier, permet d’étendre le champ d’exploration du bronchoscope, de décéler parfois une lésion inaccessible avec la technique standard et même d’exécuter une biopsie autrement impraticable.

ZUSAMMENFASSUNG


REFERENCES